

Malnutrition in Patients with Parkinson's Disease: Associated Clinical Factors

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Abstract

Objective: Parkinson's disease (PD) is a chronic, progressive disease commonly affecting the elderly. Among patients with PD (pwPD), those above 60 years old are considered to be at high risk of malnutrition. Weight loss is a common complaint in pwPD. Thus, we defined the risk factors for malnutrition in geriatric pwPD.

Materials and Methods: We enrolled 66 pwPD above the age of 60 years. Socio-demographic features were recorded and comprehensive geriatric assessments were evaluated. Malnutrition was assessed using a mini-nutritional assessment questionnaire. Anthropometric measurements including body mass index, mid-upper arm circumference, and calf circumference (CC) were recorded.

Results: Seven (10.6%) pwPD had malnutrition, 22 (33.3%) pwPD were at risk of malnutrition. Univariate logistic regression analysis results revealed that low CC, presence of dyskinesia, advanced Hoehn & Yahr stage, levodopa doses of ≥ 400 mg/day, and difficulty in swallowing ($p=0.035$, $p=0.041$, $p=0.048$, $p=0.027$ and $p=0.007$, respectively) were strongly related to malnutrition among the pwPD. Difficulty in swallowing was independently related to malnutrition in pwPD [odds ratio: 7.81 (confidence interval: 2.17-28.10), $p=0.002$].

Conclusion: PD is the second most common neurodegenerative disease in the geriatric population and is likely to cause malnutrition because of several disabling symptoms in the progressive course of the disease, such as dysphagia. To avoid or delay poorer outcomes, clinicians should be careful to identify malnutrition with appropriate screening tools during follow-up of pwPD.

Keywords: Parkinson disease, geriatric population, malnutrition, risk factors, mini-nutritional assessment

Introduction

Parkinson's disease (PD), the second most common neurodegenerative disease among the population above 65 years of age worldwide, is characterized by cardinal motor symptoms, including bradykinesia, rigidity, rest tremor, postural instability, and non-motor symptoms (1). Due to its progressive course, not only the disabling symptoms and complications, which are more likely to be seen as the disease advances, but bradykinesia itself affecting the gastrointestinal tract as well as other motor systems, autonomic involvement

also acts an important role in the occurrence of malnutrition (2). In patients with PD (pwPD), there are many factors affecting malnutrition. It is stated that non-motor and motor symptoms, diagnosis in older age, higher levodopa equivalent daily dose/body weight, depression, dementia, and hallucinations are related to malnutrition among pwPD (3). Moreover, dysphagia, delayed gastric emptying, constipation, malabsorption-like disturbances in the gastrointestinal system, and weak hand-mouth coordination may affect the dietary status (4).

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Malnutrition can be described as an imbalance between nutritional intake and requirements that eventually causes changes in body weight, body composition, and physical function (3). As a well-known entity, the prevalence of malnutrition in the geriatric population increases with aging, comorbid diseases, and the level of care (4). In accordance with aging, the reported risk of malnutrition is 3–60%, and the prevalence of malnutrition was found to be 0–24% in pwPD who are mostly geriatric (2,5). Detecting possible malnutrition early and related lifestyle characteristics is crucial. Being prone to infection, decubital ulcer, and behavioral and autonomic disorders, pwPD that do not feed well have deficits in their quality of life (6). An improved nutritional status will also improve the quality of life in pwPD.

With regard to these aspects, we investigated the possible factors affecting the risk of malnutrition in older pwPD patients who are an important part of the geriatric population.

Materials and Methods

This study was cross-sectionally designed. Sixty-six pwPD above the age of 60 were enrolled in the present study. Written approval was obtained from all patients and the relatives of patients with dementia before enrollment. Ethical approval was obtained from the Erciyes University Clinical Researches Ethics Committee (decision no: 2016/595, date 18.11.2016). The exclusion criteria were active malignancy, active infectious disease, history of cerebrovascular disease, hepatic failure, and renal failure. The socio-demographic features of the participants were recorded.

The nutritional status of the pwPD was evaluated using a mini-nutritional assessment (MNA) questionnaire, which had 18 questions with a total score of 30 (7). The normal nutrition scores were 23.5 to 30 points. Scores 17 to 23 points were considered as "risk of malnutrition", and scores below 17 points were considered "malnutrition". Study population was categorized into two groups according to MNA scores for analysis. Patients with an MNA score ≤ 23.5 points were defined as the group with malnutrition (including both patients with malnutrition and at risk of malnutrition), and the second group with an MNA score ≥ 24 points was defined as the normal nutritional status.

Anthropometric assessments of the groups were performed by height in centimeter (cm), weight measurements in kilogram (kg), body mass index [BMI (kg/m^2)], mid-upper arm circumference (MUAC) in cm, calf circumference (CC) in cm, and triceps skinfold thickness in cm. Because the participants had pwPD, the severity of PD was assessed using the Hoehn & Yahr score (8). Disease characteristic features, therapy regimens, and daily levodopa equivalent doses were recorded. Associated complaints of pwPD, including dyspepsia, constipation, and weight loss in 1 year, were also investigated by self-reported

questions regarding the related symptomatology. Swallowing function was evaluated subjectively by the question "do you have difficulty swallowing solid food?".

The cognitive status of pwPD was assessed using a mini-mental status exam (MMSE). This assessment included eleven questions with a total score of 30/30 points. Since the cut-off score for cognitive impairment is 24 points, patients with an MMSE score of 24 to 30 points were considered to be normal, while mild scores between 18 and 23 points were considered "mild dementia" and those ≤ 17 points "severe dementia" (9).

Mood assessments for depression were performed using the geriatric depression scale which has 30 items. The scores ≥ 14 points were considered depression (10).

Statistics

The Shapiro-Wilks test, histogram, and q-q plots were examined to evaluate data normality. The independent samples t-test and Mann-Whitney U test were applied for continuous variables. Pearson's chi-square test or Fisher's exact test was applied for categorical variables. Univariate and multivariate binary logistic regression models were applied to examine the risk effect of variables on malnutrition. The odds ratios (ORs) were estimated using 95% confidence intervals (CIs). Significant variables with potential risk factors of malnutrition on univariate analysis with $p < 0.1$ were taken into multivariate analysis including marital status, H&Y scale, levodopa dose, deep brain stimulation (DBS), difficulty in swallowing, and depression. Backward stepwise selection was applied using the likelihood ratio statistic at $p < 0.10$ stringency level. Goodness of fit was assessed by the Hosmer-Lemeshow test ($p = 0.840$).

Statistical Package for Social Sciences (SPSS) version 22.0 (SPSS for Windows) database was used to organize data. P values < 0.05 were accepted to indicate statistical significance.

Results

Sixty-six pwPD (37 men, 29 women) above the age of 60 years participated in the study. The mean age of pwPD was 67.50 years (minimum-maximum = 60–86 years). The mean BMI of pwPD was $30.13 \pm 5.04 \text{ kg}/\text{m}^2$ (minimum-maximum = 22.9–42.0). In the study group, 37 (56.1%) pwPD had normal nutrition status, 22 (33.3%) had malnutrition risk, and 7 (10.6%) had malnutrition. Although malnutrition was more common among widowed patients, there were no statistically significant differences in terms of socio-demographic features between the patients regarding nutrition status ($p > 0.05$). A comparison of the socio-demographic and clinical characteristics of pwPD according to their nutrition status is given in Table 1.

As shown in Table 1, pwPD with malnutrition had lower CC ($p = 0.041$) and MUAC ($p = 0.080$) than pwPD with normal nutrition. In addition, in the group of pwPD with malnutrition,

the stage of PD was more advanced ($p=0.048$) and levodopa daily doses were higher ($p=0.027$) than in the group with normal nutritional status. Dyskinesia was also more frequent in patients with malnutrition ($p=0.048$). Moreover, most of the pwPD in malnutrition group were under the treatment of DBS ($p=0.018$), had difficulty in swallowing ($p=0.008$) and had weight loss ($p=0.020$) (Table 1).

Univariate logistic regression analysis of the data revealed a strong relationship between marital status, CC, dyskinesia, stage of PD, levodopa doses, DBS procedure, difficulty in swallowing, weight loss, and malnutrition. Multiple regression analysis demonstrated an independent relationship between difficulty in swallowing and malnutrition (OR: 7.81, CI: 2.17-28.10, $p=0.002$). The results of the univariate and multivariate logistic regression analyzes determining the risk factors for malnutrition are shown in Table 2.

Discussion

PD is an important disabling neurodegenerative disease that interferes with patients' quality of life and is more prone to affect the geriatric population (11,12). Not only motor problems, including rigidity, tremor, postural instability, and bradykinesia, leading to dysphagia, constipation, and other problems in daily activities, but also health-related problems, such as mood changes, cognitive decline, and fatigue, may lead to malnutrition in pwPD (4). In this study, we observed that the presence of dyskinesia, advanced stages of PD, higher levodopa doses, DBS procedure, difficulty in swallowing, and depression were strongly related to malnutrition in pwPD. Among these variables, difficulty in swallowing was independently related to malnutrition in pwPD.

Malnutrition is common in pwPD but is often under-reported by both patients and clinicians. The main reasons why pwPD are at high risk of malnutrition are, first, disease characteristic features, defined as the motor findings of the disease; second, the negative effects of the disease on nutrition in older individuals, such as depression and cognitive damage, which are highly prevalent in pwPD as non-motor symptoms; and third, the drugs used for the treatment of PD (3). In addition, studies have shown that pwPD have a lower BMI than age-matched healthy controls (13). Because there is an increased risk of malnutrition reported in the literature for pwPD, it is crucial to screen nutrition in pwPD (14,15). Similar to our study, the common methods used to assess nutritional status are anthropometric measurements, including weight and BMI, and the MNA questionnaire, which is the most frequently used tool for nutritional status assessment (14).

In the literature, the prevalence of malnutrition and malnutrition risk has been stated to be up to 24% for malnutrition and 60% for malnutrition risk in PD (3-11). Similar to the literature, our results revealed a malnutrition rate of 43.9%, which

approximately corresponds to half of our study population. Tomic et al. (3) examined 96 patients, and from among 96 patients, 55.2% were at risk of malnutrition, whereas 8.3% had already been malnourished. Several determinants of malnutrition have been implicated in PD patients. It has been reported that age, severity of motor symptoms, duration of the disease, and intensity of stage, especially "off" states, rigidity dominant type with "off" periods, mostly affect the nutritional status (3-16). Moreover, Fávoro-Moreira et al. (17) analyzed the risk factors of malnutrition among older adults above 65 years of age and reported that age and PD were independent risk factors for malnutrition. In the above-mentioned study, the presence of PD in older individuals was found to be independently associated with malnutrition, reflecting that PD poses a very high risk for malnutrition.

Interestingly, pwPD are shown to be overweight in the beginning stages of the disease, but as the disease progresses and the patients end up in the advanced conversely, lower BMI and weight loss are reported to be extremely common and the latter was shown to be associated with nigrostriatal depletion, cognitive impairment, deteriorated motor functions, and a poorer quality of life (18). In this study, BMI, which is one of the anthropometric determinants of malnutrition and is frequently used in clinics, was not associated with malnutrition in PD, whereas decreased MUAC and CC were closely associated with malnutrition. In this case, although it has been stated that BMI in PD patients is lower than that in normal healthy controls, especially in advanced stages, we observed that BMI alone may not be sufficient in PD patients in the evaluation of malnutrition. It may be more effective to use a valid and safe screening tool, such as MNA, in the evaluation of malnutrition in these patients. Because one of the main manifestations of malnutrition is weight loss, the possible risk factors of weight loss in pwPD may include dysphagia, which may lead to low dietary uptake, slowed gastric motility and emptying because of bradykinesia, and increased energy consumption due to levodopa-induced dyskinesia in some patients (19). Similar to the literature, our results disclosed that the risk of malnutrition was significantly higher in patients experiencing the advanced stage, in need of increased daily doses of levodopa, who had difficulty swallowing, levodopa-induced dyskinesia, and weight loss. However, the possible reasons for malnutrition in pwPD, apart from weight loss, and considered "not related" to weight loss are hyposmia, reduced appetite, changed reward mechanism due to degeneration in the mesocorticolimbic network, and decreased levels of orexin (20,21).

In this study, difficulty in swallowing was the only clinical determinant that was independently related with malnutrition in PD, and 33% of the patients had difficulty in swallowing. It has been reported that approximately 80% of pwPD develop dysphagia as the disease progresses. Swallowing disorder

Table 1. The comparison of the socio-demographic and clinical characteristics of the people with Parkinson's disease according to their nutrition status

Variables	Nutritional status			p
	All n=66 (100)	Malnutrition (MNA score \leq 23.5) n=29 (43.9)	Normal (MNA score \geq 24) n=37 (56.1)	
Age	67.5 (63.0-72.0)	66.0 (63.0-73.0)	68.0 (63.0-71.0)	0.990
Gender				
Men	29 (43.9)	16 (55.2)	13 (35.1)	0.136
Women	37 (56.1)	13 (44.8)	24 (64.9)	
BMI, kg/m²	30.1 \pm 5.1	29.3 \pm 4.8	30.9 \pm 5.2	0.231
Education				
Illiterate	17 (25.8)	9 (31.0)	8 (21.9)	0.609
5 years	29 (43.9)	11 (37.9)	18 (48.6)	
Over 5 years	20 (30.3)	9 (31.0)	11 (29.7)	
Marital status				
Married	51 (77.3)	19 (65.5)	32 (86.5)	0.074
Widow	15 (22.7)	10 (34.5)	5 (13.5)	
Income				
Low	49 (74.2)	20 (69.0)	29 (78.4)	0.410
Middle/high	17 (25.8)	9 (31.0)	8 (21.6)	
MUAC, cm	29.4 \pm 3.6	28.5 \pm 4.1	30.2 \pm 3.0	0.075
CC, cm	36.1 \pm 4.4	35.6 \pm 4.4	37.9 \pm 4.1	0.035
TSF, mm	17.2 \pm 7.3	15.8 \pm 7.1	18.4 \pm 7.4	0.158
Dyskinesia				
Yes	17 (26.2)	11 (39.3)	6 (16.2)	0.048
No	48 (73.8)	17 (60.7)	31 (83.8)	
H&Y scale				
Early stages	30 (45.5)	9 (31.0)	21 (56.8)	0.048
Advanced stages	36 (54.5)	10 (69.0)	16 (43.2)	
Levodopa dose				
\geq 400 mg	35 (53.0)	20 (69.0)	15 (40.5)	0.027
<400 mg	31 (47.0)	9 (31.0)	22 (59.5)	
DBS				
Yes	8 (12.1)	7 (24.1)	1 (2.7)	0.018
No	58 (87.9)	22 (75.9)	36 (97.3)	
Dyspepsia				
Yes	18 (29.0)	10 (35.7)	8 (23.5)	0.400
No	44 (71.0)	18 (64.3)	26 (76.5)	
Constipation				
Yes	41 (62.1)	19 (65.5)	22 (59.5)	0.799
No	25 (37.9)	10 (34.5)	15 (40.5)	
Difficulty in swallowing				
Yes	22 (33.3)	15 (51.7)	7 (18.9)	0.008
No	44 (66.7)	14 (48.3)	30 (81.1)	
Weight loss				
Yes	25 (37.9)	16 (55.2)	9 (24.3)	0.020
No	41 (62.1)	13 (44.8)	28 (75.7)	
Depression score [(GDS) \geq14]				
Yes	28 (42.4)	16 (55.2)	12 (32.4)	0.082
No	38 (57.6)	13 (44.8)	25 (67.6)	
Cognitive impairment (MMSE score <24)				
Yes	10 (15.2)	6 (20.7)	4 (10.8)	0.315
No	56 (84.8)	23 (79.3)	33 (89.2)	

Values are stated as n (%), mean \pm standard deviation or median (1st-3rd quartiles). MNA: Mini-nutritional assessment BMI: Body mass index, CC: Calf circumference, DBS: Deep brain stimulation, H&Y: Hoehn and Yahr, MUAC: Mid-upper arm circumference, TSF: Triceps skin fold thickness, GDS: Geriatric depression scale, MMSE: Mini-mental status exam

Table 2. The univariate and multivariate logistic regression analysis results, determining the risk factors of malnutrition				
Variables	Univariate		Multivariate	
	OR (95% CI)	p	OR (95% CI)	p
Age	0.99 (0.91-1.08)	0.807	Not selected	
Gender				
Men	1	0.106	Not selected	
Women	2.27 (0.84-6.15)			
BMI (kg/m²)	0.940 (0.85-1.04)	0.230	Not selected	
Education				
Illiterate	1		Not selected	
5 years	0.543 (0.16-1.83)	0.324		
Over 5 years	0.727 (0.19-2.67)	0.630		
Marital status				
Married	1	0.050		
Widow	3.37 (1.001-11.345)			
Income				
Low	1		Not selected	
Middle/high	0.61 (0.20-1.86)	0.387		
MUAC (cm)	0.88 (0.77-1.16)	0.080	Not selected	
CC (cm)	0.88 (0.78-0.99)	0.041	Not selected	
TSF (mm)	0.95 (0.89-1.02)	0.159	Not selected	
Dyskinesia				
No	1		Not selected	
Yes	3.34 (1.05-10.64)	0.041		
H&Y scale				
Early stages	1			
Advanced stages	2.92 (1.05-8.09)	0.040		
Levodopa dose				
<400 mg	1			
>400 mg	3.26 (1.17-9.08)	0.024		
DBS				
No	1			
Yes	11.46 (1.32-99.46)	0.027		
Dyspepsia				
Yes	1		Not selected	
No	1.81 (0.60-5.46)	0.296		
Constipation				
No	1		Not selected	
Yes	1.30 (0.47-3.55)	0.615		
Difficulty in swallowing				
No	1		1	0.002
Yes	4.59 (1.53-13.78)	0.007	7.81 (2.17-28.10)	
Weight loss				
No	1		Not selected	
Yes	3.83 (1.34-10.93)	0.012		
Depression				
No	1			
Yes	2.56 (0.94-7.00)	0.066		
Cognitive impairment				
No	1		Not selected	
Yes	2.15 (0.55-8.49)	0.274		

OR: Odds ratio, CI: Confidence interval, p<0.005, BMI: Body mass index, CC: Calf circumference, DBS: Deep brain stimulation, H&Y: Hoehn and Yahr, MUAC: Mid-upper arm circumference, TSF: Triceps skin fold thickness

complicates drug intake in pwPD, leads to malnutrition and aspiration pneumonia, and thus reduces quality of life and increases mortality in pwPD. Although the fundamental pathophysiology is not fully understood, dopaminergic and non-dopaminergic mechanisms play a role in the development of dysphagia in PD. Clinical assessment of dysphagia in pwPD is difficult and often yields discordant results (22). However, in this study, it was observed that pwPD who were evaluated only with a single question and described difficulty in swallowing were highly associated with the risk of malnutrition.

Study Limitations

There are some limitations to this study. The most important limitation of the study is that swallowing function was not evaluated with an objective method such as functional swallowing tests, an instrumental method such as videofluoroscopic evaluation, or a PD-specific swallowing questionnaire. However, studies in the literature have shown that a single screening question for dysphagia as difficulty in swallowing is closely related to the results of evaluations made by dysphagia diagnostic tools, both in cancer patients and older people living in the community (23,24). In addition, the relationship between a one-question dysphagia screening test and difficulty in swallowing pills was investigated in Parkinson's patients, and the sensitivity of the single question in estimating dysphagia was found to be moderate, whereas the specificity was found to be high (25). In addition, this was a cross-sectional study with a relatively small sample size. It is important to emphasize that further investigation through large-scale longitudinal studies is mandatory to detect early malnutrition risk in geriatric pwPD. Because aging and neurodegenerative diseases such as PD have a strong impact on patients' nutritional status, leading to weight loss and malnutrition via direct and indirect mechanisms, it is important to be aware of the risk of malnutrition, especially in geriatric pwPD. To prevent the damaging effects of weight loss on motor function in pwPD, especially in the geriatric population, clinicians should be aware of the risks of malnutrition, such as advanced stages of the disease, increased doses of daily levodopa, dysphagia, and dyskinesia. When swallowing dysfunction is detected, treatment approaches should be applied with pharmacological interventions and therapy by speech and language therapists. Regular screening of malnutrition in pwPD with a validated tool such as MNA alongside anthropometric measures such as body weight and BMI in follow-ups is another clue for early recognition of malnutrition and application of essential interventions for malnutrition to maintain a better quality of life in pwPD.

Conclusion

In conclusion, pwPD are at risk of malnutrition. PwPD should be regularly followed up for malnutrition by clinicians,

particularly those with high risk factors associated with disease characteristics such as dysphagia. In addition, the common treatment plan for PD should include a nutritional consultation with a dietary regime.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Erciyes University Clinical Researches Ethics Committee (decision no: 2016/595, date 18.11.2016).

Informed Consent: Written approval was obtained from all patients and the relatives of patients with dementia before enrollment.

Authorship Contributions

Surgical and Medical Practices: M.G., F.F.Ö., S.A., A.Ö., Y.D., Concept: M.G., F.F.Ö., S.A., A.Ö., Y.D., Design: M.G., F.F.Ö., S.A., A.Ö., Y.D., Data Collection or Processing: M.G., F.F.Ö., S.A., Analysis or Interpretation: M.G., F.F.Ö., S.A., A.Ö., Y.D., Literature Search: M.G., F.F.Ö., Writing: M.G., F.F.Ö.

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