




# Nutritional status of old people with Parkinson's disease and its associated factors: an integrative review

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## Abstract

**Objective:** Identify the factors associated with the Nutritional Status of old people with Parkinson's disease (PD) through an integrative literature review. **Method:** The databases LILACS, MEDLINE, BDNF, Scielo and Pubmed were used with no filters for year of publication nor study design. We included the studies with old population (age  $\geq 60$  years) in Portuguese, English or Spanish. Studies not addressing the subject, publications not available in full, and those that did not answer the guiding question were excluded. In addition to the associated factors, information regarding the objectives, study design, investigated sample, instruments for nutritional assessment, and main results were extracted. The methodological quality of the studies was assessed by the instruments *Critical Appraisal Skill Program* and *Agency for Health care and Research and Quality*. To summarize the associated factors, the percentage of studies whose intergroup analysis, association or correlation was significant for the expected outcome was considered. **Results:** The final analysis resulted in 8 papers. The factors associated with the Nutritional Status among the PD-related clinical variables were duration and severity of the disease, motor symptoms, and cognitive function. Regarding the clinical-nutritional variables, they were associated with body fat, biochemical parameters, physical, domestic and mobility activities, energy intake, and eating habits. **Conclusion:** Weight loss in PD is a complex and multifactorial consequence, and the early diagnose of nutritional changes in these patients is essential. Further studies in this population are necessary in order to better understand this process of weight loss in old patients with PD.

**Keywords:** Health of the Elderly. Nutritional Status. Nutritional Assessment. Parkinson's Disease.

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## INTRODUCTION

Neurodegenerative diseases such as Parkinson's disease (PD) - the second most common one among people aged 60 and over - become frequent with the aging process, and the number of cases tend to double by 2050<sup>1</sup>.

PD has an incidence of 0.5% to 1% for people aged 65 to 69 years, and 1 to 3% for those aged 80 and over<sup>2-4</sup>. It is caused by the reduction of the neurotransmitter dopamine, of slow progression, in the central nervous system (CNS), characterized by four basic components: bradykinesia, rest tremor, stiffness, and postural instability resulting from the impairment of the nigrostriatal pathway<sup>5,6</sup>. Motor symptoms can progressively lead to severe disability, and together with non-motor complications can contribute considerably to alterations in the nutritional status during the course of the disease<sup>7-9</sup>.

About 3% to 60% of PD patients are at risk of malnutrition<sup>10</sup>. Weight loss in these patients is related to increased energy expenditure due to high muscle activity characterized by tremors, stiffness, and dyskinesias induced by levodopa, in addition to low food intake due to the presence of anorexia, depression, cognitive impairment, and gastrointestinal symptoms (dysphagia, nausea, reflux, constipation, and delayed gastric emptying), resulting in increased satiety and reduced nutrient absorption. The person also becomes more dependent on others due to the impairment for the activities of daily living,<sup>11-13</sup> which may lead to the progression of malnutrition<sup>10</sup>.

Malnutrition in PD patients impairs the quality of life, as well as increases the rate of morbidity and mortality<sup>14</sup>. The factors associated with the nutritional status are well defined in the old population<sup>15</sup>. However, in the old population with PD there is a lack of evidence on the impact of malnutrition, and a reduced number of studies. Therefore, due to the importance of malnutrition in old people with PD, the growth of the old population, and the impact on the Nutritional Status, the present study aims to identify the factors associated with the Nutritional Status of old people with PD through an integrative literature review.

## METHOD

This is an Integrative Literature Review. In order to do so, six steps were followed: 1 - identification of the subject and development of the guiding question for the research; 2 - establishment of criteria for inclusion and exclusion of studies; 3 - definition of the information to be extracted from the selected studies and their further categorization; 4 - evaluation of studies included in the review; 5 - interpretation of the results; 6 - presentation of the review and synthesis of knowledge<sup>16</sup>. For the first step, the following guiding question was created: What is the published scientific evidence on factors associated with the Nutritional Status in old people with PD?

Then, we established the eligibility criteria for the search and selection of articles between November 2019 and January 2020 on the Virtual Health Library (VHL) portal. In this portal we could search the relevant publications simultaneously in the three main scientific databases in the national and international fields: LILACS (Latin American and Caribbean Literature in Health Sciences), MEDLINE (International Literature in Health Sciences) and BDENF (Nursing Database). We also searched in Scielo (electronic library *Scientific Electronic Library Online*) and PubMed (*National Library of Medicine and National Institutes of Health*).

The articles included should address factors associated with Nutritional Status in old people with PD. No filters were used for the year of publication and study design. We included the studies with old population (age criterion  $\geq 60$  years) in Portuguese, English or Spanish. References to the papers selected were considered for inclusion ("reverse search" strategy). Two independent reviewers extracted data and checked the agreement of the selection of the studies, and validated the final list made by a third reviewer.

Studies with the presence of other parkinsonian syndromes, other neurological diseases, absence of definition of age of the subjects in the study, publications not available electronically free of charge, studies of the types dissertation, thesis, book/book chapter, editorial, newspaper article, integrative or systematic literature review, letter to

the editor, reflective study, experience report, and congress summary were excluded. The papers were searched using the keywords indexed to the Health Sciences Descriptors (DeCS) - "diet", "diet regime", "nutritional status", "nutrition status", "nutritional assessment", and "Parkinson's disease" - and to the *Medical Subject Headings* (MESH) - "factors", "nutritional assessment", "nutritional status", "nutritional", "diet", "Food Regime", "Parkinson", "Parkinson disease", "parkinsonism". The Boolean operator of choice was "AND" and "OR".

For the methodological critical analysis of the papers included, two instruments were used to allow the evaluation of different study designs: 1- *Critical Appraisal Skill Programme* (CASP)<sup>17</sup> (adapted), and 2- *Agency for Health care and Research and Quality* (AHRQ)<sup>18</sup>.

The original CASP<sup>19</sup> considered eight specific tools for the evaluation of different delineations of study such as reviews, cohorts, clinical trials, and cross-sectional studies, among others. In the present review, an instrument adapted from CASP was used, which included 10 items to be scored, including: 1) objective; 2) adequacy of the method; 3) presentation of theoretical and methodological procedures; 4) sample selection criteria; 5) details of the sample; 6) relationship between researchers and subjects (randomization/blinding); 7) respect for ethical aspects; 8) rigor in data analysis; 9) property to discuss the results, and 10) contributions and limitations of the research. In the end, the studies were classified as level A (score between 6 and 10 points), being considered of good methodological quality and reduced bias, or level B (up to 5 points), meaning satisfactory methodological quality, but with considerable risk of bias<sup>17</sup>.

The AHRQ divides the studies into six levels according to the level of evidence: (1) systematic review or meta-analysis; (2) randomized clinical trials; (3) clinical trials without randomization; (4) cohort and case-control studies; (5) systematic review of descriptive and qualitative studies, and (6) single descriptive or qualitative study<sup>18</sup>.

To summarize the associated factors, the percentage of studies whose intergroup analysis, association or correlation was significant for the expected outcome was considered. The percentages presented refer to the number of studies whose results were significant divided by the total number of studies<sup>20</sup>. When the number of significant studies is greater than the total number of studies, which indicates an association factor with nutritional status, it receives a positive code "+". In the case of a tie or analysis of only one significant study, there is no consensus on the association between the factor and the nutritional status. These studies received a "?" code. And the cases with no study with a significant result or a minority of studies with a significant result, the factor receives a negative code "-"<sup>20,21</sup>.

## RESULTS

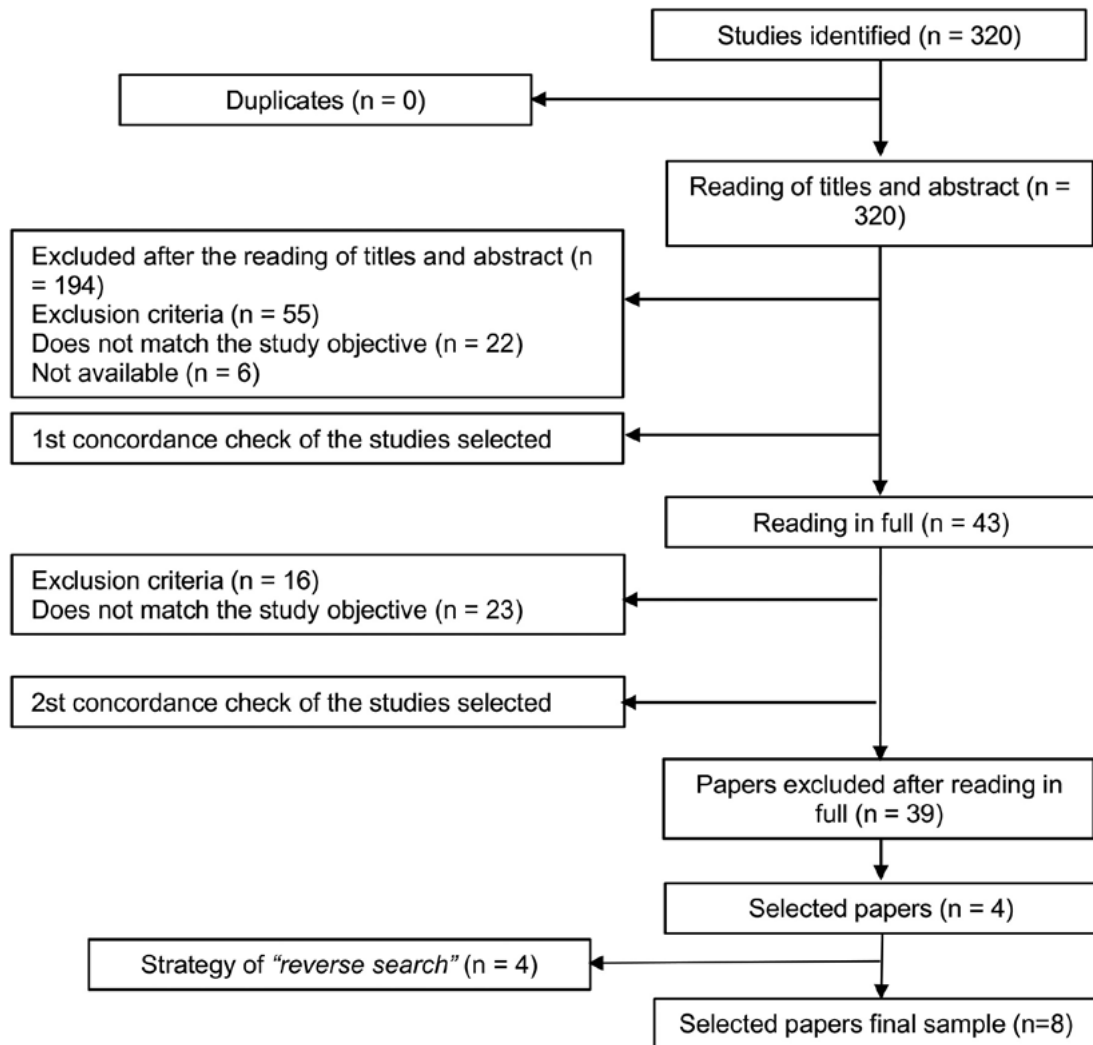
Five databases were analyzed using a combination of keywords related to the topic. The search results are summarized in Table 1.

We found 320 papers. However, 316 were not eligible, resulting in eight papers for final analysis, with four papers selected through reverse search (Figure 1). Regarding the exclusion criteria for the Medline database, six papers were excluded after the reading of the title and abstract (75%) because they were not related to the subject, and two because they were not studies with the old people (25%). During the first check for the agreement of the studies selected in Pubmed, 53 papers met the exclusion criterion, of which 188 were excluded after the reading of the title and abstract (62.17%) because they were not related to the subject, with three systematic reviews (5.66%), 13 integrative reviews (24.52%), 19 (35.84%) which were not studies with old people, and 18 (33.96%) were studies in animal models. In the second concordance check, 16 studies were not carried out with old people.

**Table 1.** Databases analyzed and number of papers comprising the study sample. Recife, PE, 2020.

Database	Combination of keywords	Papers found	Papers meeting the inclusion criteria	Papers meeting the exclusion criteria	Sample
LILACS	("diet" or "diet regime") and ("nutritional status" or "nutrition status") and ("nutritional assessment") and ("Parkinson's disease")	0	0	0	0
MEDLINE		8	0	8	0
BDENF		0	0	0	0
SCIELO		0	0	0	0
PUBMED	("factors") AND ("nutrition assessment" or "nutritional status" or "nutritional" or "diet" or "Food Regime") AND ("parkinson" OR "parkinson disease" OR "parkinsonism")	312	4	308	4
TOTAL	-	320	4	316	4

Source: Prepared by the authors.



Source: Prepared by the authors.

**Figure 1.** Flowchart of the study selection process. Recife, PE, 2020.

All papers in the final sample were published in English and in foreign journals. As for the years of publication, half of the papers were published between 2004 and 2008, and the other half between 2009 and 2017. The study sites comprised five European countries (87.5%), and 1 (12.5%) in the United States of America.

All studies were classified as level A in methodological quality using an instrument adapted from CASP<sup>17</sup>. An evaluation using the AHRQ<sup>18</sup> showed

that four papers were Case-Control studies - level four of evidence<sup>22-25</sup>, one was a prospective cohort - level four of evidence,<sup>26</sup> and three were cross-sectional observational studies - level six of evidence<sup>27-29</sup>. None of the studies employed a qualitative approach. The main information from the papers included in the present review is shown in Table 2.

The factors associated with the Nutritional Status of old people with PD extracted from the studies in the present review are shown in Table 3.

**Table 2.** Compiled description of each study included in the integrative review. Recife, PE, 2020.

Author, place and year	Study design, objective, and instruments used to determine the Nutritional Status	Sample	Main results related to the Nutritional Status of old people with PD
Lorefält et al. <sup>22</sup> , Sweden, 2004	Case-control study. Objective: to find the factors underlying weight loss in patients with PD using the following instruments: DXA, indirect calorimetry, and respiratory quotient.	n = 28 patients with PD (18 women / 10 men) 28 healthy controls matched by gender and age ( $\pm$ 5 years) n = 26 PD patients treated with l-dopa for a minimum of 2 years. Evaluated twice / one year interval.	During the 1-year interval, there was a reduction in both body weight (from 0.5-8.0 kg/year), and in BMI $24.2 \pm 2.8$ to $23.2 \pm 3.5$ , and in fat mass. But 10% of patients who lost weight had a BMI $<22\text{kg/m}^2$ .
Lorefält et al. <sup>23</sup> , Sweden, 2005	Case-control study. Objective: to investigate eating habits and nutrient intake in old patients with or without PD, in addition to checking if there was weight loss, using the following instruments: Food Record for three consecutive days and Calculation of energy and nutrient intake.	n = 26 patients with PD (17 women / 9 men) 26 healthy controls matched by gender and age ( $\pm$ 5 years) Evaluated twice / one year interval.	There was no significant difference between the number of food events per day by the groups in relation to weight loss In the 1-year interval, the number of complete meals prepared decreased to all patients, as well as the activities of daily living in need of help with food Regarding energy requirement in the group with weight loss which had increased needs, the consumption of calories was insufficient. But in the group without weight loss, the caloric requirement reduced The weight loss group had a higher consumption of fat and protein.

to be continued

Continuation of Chart 2

Author, place and year	Study design, objective, and instruments used to determine the Nutritional Status	Sample	Main results related to the Nutritional Status of old people with PD
Lorefält et al. <sup>24</sup> , Sweden, 2009	Case-control study. Objective: to evaluate leptin levels in PD patients and its possible role in weight loss using the following instruments: DXA and Assessment of body fat mass.	n = 26 patients with PD (17 women / 9 men) 26 healthy controls matched by gender and age ( $\pm$ 5 years)	Serum leptin correlated with body weight, both in the first year and in the second year in all female PD patients; however, it did not occur in male patients. In women with PD with and without weight loss, serum leptin levels decreased significantly between one and two years. Serum leptin levels were correlated with body mass in all female and male participants. The body fat mass in PD patients decreased by 1.4 kg between the 1st and 2nd years. Both in the 1st year and in the 2nd year, body fat mass was lower in patients with weight loss Leptin levels were low in both PD patients and controls.
Cheshire and Wszolek <sup>25</sup> , USA, 2005	Case-control Study. Objective: to compare the weight loss of PD patients with controls and patients with ET or without neurological disease, and observe whether this difference preceded the symptomatic onset of PD using BMI.	n = 100 patients with PD; n = 24 patients of a subgroup of PD with pre-morbid data (pre-PD); n = 50 patients with ET; n = 50 cases of CS.	BMI was on average 9% lower in PD than in the comparison groups with ET or control with CS. A similar reduction in BMI occurred prior to diagnosis in 24 cases of PD.
Barichella et al. <sup>26</sup> , Italia, 2008	3-year cohort study. Objective: to monitor the Nutritional Status of PD patients using MNA.	n = 61 patients with PD (37 men / 24 women) There were 2 losses after 3 years	Body weight and BMI decreased significantly between 2004 and 2007. There was an increase from 22.9% (8 patients) in 2004 to 34.3% (12 patients) in 2007 with Nutritional Risk (score $\leq$ 23), according to MNA.
Jaafar et al. <sup>27</sup> , England, 2010	Cross-sectional study. Objective: to evaluate the prevalence of malnutrition in people in the community with PD and the associated factors using the following instruments: BMI, MUST, MUAC, TSF and HGS.	N = 161, n = 123 patients with PD, 82 with nutritional data collected (34 men / 48 women).	15% of patients had malnutrition (BMI <20 Kg/m <sup>2</sup> ) 23.5% of patients had a medium or high risk of malnutrition, according to MUST. In women, low weight (BMI <20 kg/m <sup>2</sup> ) was associated with greater unintentional weight loss, lower values of MUAC, TSF and HGS. Said associations were not found in men.
Van Steijn et al. <sup>28</sup> , Netherlands, 2013	Cross-sectional study. Objective: to assess the prevalence of (risk of) malnutrition in Dutch PD patients, as well as their risk factors using the following instruments: MNA, BMI, CNAQ and Oral Nutritional Supplement.	N = 140 patients with PD, n = 102 (54 men / 49 women) Divided into 2 groups: Normal (79) and at risk of malnutrition (23).	MNA 2% of patients had malnutrition (score <17); 20.5% of patients had risk of malnutrition (17 $\leq$ score $\leq$ 23.5). BMI 2% of the patients had malnutrition (BMI <20 kg/m <sup>2</sup> ). The risk group had less appetite (CNAQ), used more oral nutritional supplements, and was more dependent on care compared to the normal group (KAT'Z).

to be continued

Continuation of Chart 2

Author, place and year	Study design, objective, and instruments used to determine the Nutritional Status	Sample	Main results related to the Nutritional Status of old people with PD
Tomic et al. <sup>29</sup> , Croatia, 2017	Cross-sectional study. Objective: to determine the prevalence of malnutrition and factors influencing patients with PD using MNA.	n = 107 patients with PD; n = 96 patients with PD (57 men / 39 women) Age in three groups (40-60 years, 60-80 years, and >80 years); n = 74 (60 - 80 years); n = 10 (>80 years).	MNA 60 - 80 years old: 83.3% with Risk of Malnutrition; 75% with Malnutrition >80 years old: 3.7% with Risk of Malnutrition; 0 Malnutrition.

PD: Parkinson's disease; DXA: Dual X-ray absorptiometry; BMI: Body mass index; ET: essential tremor; CS: cervical spondylosis; MNA: Mini Nutritional Assessment; MUST: Malnutrition Universal Screening Tool, MUAC: Mid-upper arm circumference; TSF: Tricipital Skinfold; HGS: hand grip strength; CNAQ: Nutrition Board Questionnaire on Appetite; KATZ: Index of Independence in Activities of Daily Living. Source: Prepared by the authors.

**Table 3.** Compiled description of the factors associated with the Nutritional Status of old people with Parkinson's disease. Recife, PE, 2020.

Category	Associated factors	Papers related to the associated factors	% of studies reporting it factor association	Codes
Personal variables	Age	25, 26, 27 * $p < 0.01$ , 29 * $p = 0.041$	2/4 (50%)	?
	Gender	22 * $p < 0.0001$ , 24 * $p < 0.05$ , 26, 27	2/4 (50%)	?
PD-related clinical variables	Disease stage	27, 28, 29 * $p = 0.017$	1/3 (33,33%)	-
	Medication	22 * $p < 0.01$ , 24 * $p = 0.05$ , 28, 29	2/4 (50%)	?
	Disease duration and severity	24 * $p < 0.001$ , 25, 26 * $p = 0.0096$ , 27 * $p = 0.006$ , 28, 29 * $p = 0.017$	4/6 (66,66%)	+
	Motor symptoms	22 * $p < 0.01$ , 23 * $p < 0.01$ , 25, 27, 29 * $p < 0.001$	3/5 (60%)	+
	Non-motor symptoms	23 * $p < 0.01$ , 25, 27, 29	1/4 (25%)	-
	Cognitive function	22 * $p < 0.01$ , 23 * $p < 0.05$ , 27, 29 * $p = 0.004$	3/4 (75%)	+
Clinical-nutritional variables	Body fat	22 * $p < 0.01$ , 23 * $p < 0.01$ , 27 * $p < 0.05$	3/3 (100%)	+
	Biochemical parameters	24 * $p < 0.001$ , 29 * $p = 0.018$	2/2 (100%)	+
	Physical, domestic and mobility activities	22 * $p < 0.01$ , 23 * $p < 0.05$ , 28 * $p < 0.001$	3/3 (100%)	+
	Energy Intake	22 * $p < 0.05$ , 23 * $p < 0.05$	2/2 (100%)	+
	Resting energy expenditure (REE)	22 * $p < 0.01$	1/1 (100%)	?
	Respiratory quotient	22 * $p < 0.01$	1/1 (100%)	?
	Eating Habits	23 * $p < 0.05$ , 25, 26 * $p = 0.0009$ , 28 * $p = 0.008$ , 29	3/5 (60%)	+
	Use of alcohol and tobacco	27	0/1 (0%)	-
	Gastrointestinal symptoms	25, 28	0/2 (0%)	-

+: Factor associated with nutritional status; - or ?: Lack of consensus on the association of the factor; \*Study with significant association or whose parameter evaluated was significant. Source: Prepared by the authors.

## DISCUSSION

Malnutrition is a disorder affecting a large part of the old population<sup>30</sup>, also presenting a high prevalence in patients with PD. It was observed that 62.5% of the old population with PD had malnutrition or risk of malnutrition, according to the MNA<sup>31</sup>. In view of this high frequency, the importance of an earlier and more careful look at the nutritional condition of these patients is demonstrated. In addition, factors associated with the Nutritional Status were found among the clinical variables related to Parkinson's disease and among the clinical-nutritional variables.

Among the personal variables, age and gender, there were no associations. However, it is worth mentioning that although few studies measure these associations, there seems to be a relation between increased age and worsening of the Nutritional Status, a fact that can be explained by the physiological changes inherent to aging associated with a neurodegenerative disease, which can lead to the worsening of the Nutritional Status. Regarding females, there may be a connection with more nutritional disadvantages due to hormonal factors influencing the metabolic regulation<sup>22</sup>.

According to the clinical conditions related to Parkinson's disease, disease duration and severity, motor symptoms, and cognitive function stood out. Regarding time, it was observed that an average of six to nine years was associated with a decrease in the BMI value (BMI <20kg/m<sup>2</sup>)<sup>27</sup> and with a reduction in the score of MNA<sup>26</sup>. Although this result has been found, time is related to the severity of the disease because the years added from the diagnosis culminate in the progression of the disease, since it has no cure.

Corroborating these findings, a study<sup>32</sup> compared the two groups based on the median BMI of PD patients, verifying that the lower the BMI (<22kg/m<sup>2</sup>), the greater the duration of the disease, the greater the severity of motor aspects of daily life and motor complications, and the greater the equivalent dose of levodopa (LED). It is suggested that weight loss is related to the increase in energy expenditure as the disease progresses<sup>26,32</sup>, as generated by dyskinesias, not being compensated by adequate intake, both in quantitative and qualitative terms<sup>28</sup>.

Regarding inadequate food intake, it is important to consider possible alterations in swallowing. Oropharyngeal and esophageal dysphagia are very common in PD and affect more than 80% of individuals<sup>33</sup>, reflecting the underlying motor deficiencies and the extent of the disease progression<sup>34</sup>. It is also associated with reduced quality of life, social isolation, dehydration, malnutrition, and aspiration pneumonia<sup>35</sup>. The latter is one of the leading causes of death in PD<sup>36</sup>. Changes related to dysphagia have a direct influence on the nutritional status, since changes in food consistency and the difficulty of ingestion itself can hinder dietary adjustments<sup>36</sup>.

As PD progresses, there is a worsening of the motor symptoms such as tremor, stiffness, and dyskinesias, which can contribute to increased energy expenditure. One possible explanation is that increased energy expenditure can play a role in the early stage, and increased caloric intake is a compensation for weight loss. In the early stages of PD, increased energy expenditure would be the main cause, while in the advanced stages the main determinant of weight loss would probably be a decrease in energy consumption<sup>37</sup>.

Motor disorders can impel the old person to social isolation, loss of will for daily activities, dependence on others for activities of daily living, loss of autonomy, and consequently reduced quality of life<sup>38</sup>. Increased disability in daily tasks such as shopping, cooking, and eating may exacerbate the symptom effect of nutritional impact and life situation on food intake<sup>39</sup>.

Intellectual decline and cognitive disorders may also be present in PD, usually intensifying with the progression of the disease, especially in the old people<sup>40</sup>. Thus, these old people may lose their sense of self-control, self-efficacy, and often present symptoms of depression<sup>41</sup>, favoring changes in eating behavior with low food intake and higher occurrence of malnutrition<sup>42</sup>.

Regarding the clinical-nutritional variables, we emphasize body fat, biochemical parameters, physical, domestic and mobility activities, energy intake, and eating habits.



A study<sup>43</sup> found that the higher the stage of the disease, the lower the amount of total fat (body, visceral, and subcutaneous), as well as lower levels of leptin, a hormone produced mainly by adipocytes or fatty cells directly related to fat production. In addition, a reduction in body weight associated with the time of diagnosis of the disease also suggests that in addition to the alteration in fat distribution in PD patients, there is a reduction in subcutaneous adipose tissue and an increase in the ratio of visceral fat. This altered redistribution may be associated with weight loss,<sup>43</sup> and may also be influenced by the aging process that entails changes in body composition<sup>44</sup>.

Another study observed that PD patients had a progressive reduction in body weight, BMI, and increased protein and calorie intake, with reduction in REE, level of physical activity, and calculation of total energy expenditure. The increase in calorie intake is assumed to be secondary, but it is not enough to compensate for the increase in energy requirements associated with stiffness and dyskinesias<sup>45</sup>.

Gastrointestinal dysfunctions in PD are well-recognized problems because they are an initial symptom in the pathological process that eventually results in PD. Gastrointestinal symptoms may result from central or enteric nervous system involvement, or these symptoms may be side effects of antiparkinsonian medications. Sialorrhoea, dysphagia, nausea/gastroparesis, constipation, and defecation dysfunction may occur,<sup>46</sup> and when associated with depression and/or dementia may contribute to weight loss in PD patients<sup>47</sup>.

Among the limitations observed in this review, we can emphasize the small number of studies addressing PD in old people, as well as the insufficiency of papers in the Brazilian population and longitudinal studies.

One difficulty found was the lack of longitudinal studies following the patient since before diagnosis, which is a finding, so we encourage future research with longitudinal studies given its importance, since some studies show that weight loss is continuous and may present before the onset of the disease.

## CONCLUSION

The variables that were associated with the Nutritional Status of old people with PD were the clinical conditions related to PD represented by the disease duration and severity, motor symptoms and cognitive function, and among the clinical-nutritional variables were body fat, biochemical parameters, physical activity, domestic activity and mobility. The personal characteristics of age and gender were not associated with the Nutritional Status. However, there seems to be a relation with increased age and the disadvantages of female aging.

In view of the above, it is suggested that weight loss in PD is a complex and multifactorial consequence. It is not a beneficial phenomenon, and has several clinical and prognostic consequences with increased morbidity and mortality. Thus, the early diagnosis nutritional changes in PD patients with specific nutritional tools such as MNA is of paramount importance in the routine of healthcare services in order to prevent malnutrition and improve their quality of life.

Further studies in this population are also necessary, as well as studies in the Brazilian population, in order to better understand this process of weight loss in old patients with PD.

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