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Correlation between Quality of Life and severity of Parkinson's Disease by assessing an optimal cut-off point on the Parkinson's Disease questionnaire (PDQ-39) as related to the Hoehn & Yahr (H&Y) scale

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Abstract

Purpose. **S**trong evidence shows that symptoms in individuals with Parkinson's Disease (PD) restrict both their independence and social participation, leading to a low Quality of Life (QoL). Conversely, a reduced QoL has a negative impact on symptoms. The aim is to evaluate the correlation between QoL and severity of PD by assessing the presence of an optimal cut-off point on the Parkinson's disease questionnaire (PDQ-39) as related to the Hoehn &Yahr (H&Y) scale in a cohort of Italian adults with PD.

Methods. A multicenter, cross-sectional study was performed. This study was conducted on a cohort of consecutive individuals. All participants were evaluated with the PDQ-39, and the severity of PD was recorded according to the H&Y scale by a neurologist. Receiver operating characteristic (ROC) curves and coordinates, visually inspected, were used to find cut-off points with optimal sensitivity and specificity. These were in turn used to determine the optimal PDQ-39 cut-off score for identifying disease severity according to H&Y stages.

Results. 513 individuals were included in the study. The ROC curve analysis showed that QoL worsened with an increase in disease severity and age. Moreover, QoL was worse in females.

Conclusions. The results of this study allowed for the correlation of QoL and disease severity in a cohort of individuals with PD. With this cut-off point, it is now possible to make a determination of QoL of an individual with PD at a certain stage of the disease, in a specific age range, and of a particular gender. ***Clin Ter 2022; 173 (3):243-248 doi: 10.7417/CT.2022.2427***

Key words: *age, gender, Parkinson, quality of life, severity*

Introduction

The severity of illness and disability in Parkinson's disease (PD) is due to the presence of both motor and non-motor symptoms. Around 80% of patients with PD have limb tremors (1–3), while one-quarter to 60% of patients experience movement freezing, usually several years after the onset of symptoms. Speech disturbances, such as very quiet and hurried speech, occur in more than one-half of patients, while swallowing problems have been reported in 40–80% of patients. Moreover, individuals with PD may have a variety of non-motor symptoms. One recent study showed that symptoms such as a lack of emotional involvement and interest (apathy), sleep disorders, and constipation, may occur in up to 60–70% of patients prior to diagnosis. (1) With advancing disease, the non-motor symptoms generally become more troublesome for patients than the motor symptoms.(1,4)

Quality of life (QoL) has been a focal point of PD research in the last few decades. There is strong evidence that motor and non-motor symptoms in individuals with PD restrict their independence and social participation, leading to a low QoL for both patients and their caregivers. Symptoms often impede activities essential to daily living and social functioning. Impairment in these areas can alter social roles by interfering with employment status, household management, friendships, and other relationships. Conversely, a reduced QoL may have a negative impact on both motor and non-motor symptoms. Information about the QoL of those with PD as well as studies on the relationship between QoL and severity of disease are necessary for both research and clinical practice, to make informed health care and rehabilitation decisions.

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Thus, this study aimed to evaluate this relationship by assessing the presence of an optimal cutoff point on the Parkinson's Disease Questionnaire (PDQ-39), one of the most widely used QoL assessment tools for individuals with PD, as related to the H&Y scale, a commonly used system for describing how the symptoms of PD progress, in a cohort of Italian adults with PD. Youden Index, was used to define the point that maximizes Sensitivity and Specificity. The secondary aim of the study was to evaluate the internal consistency of PDQ-39 and its concurrent validity and correlation with the H&Y scale. To the authors' knowledge, this study presents the first association between severity of PD and QoL. This study's results add to existing evidence on the PDQ-39 cutoff points and thus add great value to current clinical practice and research. Moreover, thanks to these results it is possible, when considering individuals' age, gender, and H&Y stage, to determine their QoL, and make a prevision of QoL progression with more precision than previously thought. This will help in clinical practice to plan interventions in order to prevent worsening QoL. Finally, the results of this study extend our understanding of the PDQ-39's reliability and validity.

Methods

The present study was conducted at Sapienza University in Rome by R.O.M.A Association. A multicenter, cross-sectional study was performed in central and northern Italy. The study was conducted by a neurologist, a physiotherapist, and an occupational therapist. Moreover, the occupational therapist and the physical therapist were responsible for the clinical data and were present when participants completed the questionnaires in case of any difficulties.

For reporting the study Strengthening the reporting of observational studies in epidemiology (STROBE) guidelines have been used.

Study design and participants. In literature, sample size for cross-sectional study recommendations range from 2 to 20 subjects per item, in the articles analyzed in a recent (2014) systematic review about sample size used to validate a scale, the mean subject to item ratio was 28, with a minimum of 1 and a maximum of 527.5 This study was conducted on a cohort of consecutive individuals with Parkinson's disease (PD) at neurologic outpatient clinics at Policlinico Umberto I in Rome, the movement disorders clinic of Istituto di Ricovero e Cura a Carattere Scientifico (IRCC) San Martino Hospital in Genova, and the "Ospedale Riuniti" University Hospital in Trieste, Italy, from February 2018 to March 2019. Inclusion criteria included diagnosis of idiopathic PD (according to the United Kingdom Parkinson's Disease Society Brain Bank criteria),(4) age >50 but< 90 years, Hoehn & Yahr (H&Y) stages I, II, III, and IV, a mini-mental state examination > 22 points, and a minimum level of five years of education. Individuals with history of neurologic disorders (except PD) were excluded from the study were excluded from the study. After the participants were selected according to the eligibility criteria, they were informed of the finality and modalities of the study and were asked to sign an informed consent form (5). Those who declined to sign the informed consent form were excluded from the study.

Procedures. For each participant, the following demographic information was recorded: age, gender, years of education, employment status, and disease duration (in years). The participants' demographic data collection sheet and the assessment tool were self-administered. The participants could receive help from the reference caregiver if needed. Parkinson's severity was recorded according to the H&Y scale by the neurologist.

Outcomes. The Parkinson's Disease Questionnaire (PDQ-39) was used to evaluate Quality of Life (QoL) as the primary outcome. The PDQ-39, developed in 1995 by Petoet al.,(6) is one of the most thoroughly tested and applied tools for assessing QoL in PD individuals. The questionnaire consists of 39 items, divided into eight sub-tests: mobility (10 items), activities of daily living (6 items), emotional well-being (6 items), stigma (4 items), social support (3 items), cognition (4 items), communication (3 items), and bodily discomfort (3 items). For each item, there are five possible answers: never, occasionally, sometimes, often, and always. The PDQ-39 is a self-administered instrument, one which shows optimal psychometric properties and reflects the entire spectrum of QoL in PD individuals. Research has shown the instrument to be feasible, reliable, valid, comprehensive, and sensitive to change. Additionally, the instrument has been tested before in the Italian context, on 104 individuals (7).

The H&Y(8) is a scale compiled by neurologists based on the signs and symptoms that the patient reports. The scale classifies individuals into five stages of illness based on the severity of the signs present. The first stage corresponds to a patient who is still autonomous in activities of daily living (ADL) and has a tremor or/and bradykinesia or/and rigidity on only one side of the body. Stage 5, on the other hand, corresponds to a dependent patient in all ADL and who is in bed or in a wheelchair.

Statistical analysis. Receiver operating characteristic (ROC) curves and coordinates of the curve were visually inspected to find cut-off points with optimal sensitivity and specificity, presented in percentages (%).(9) The aim of this analysis was to determine the optimal PDQ-39 cut-off score for identifying disease severity according to H&Y stages. The PDQ-39 values that have a higher sensitivity and specificity score were chosen as the cut-off, such that both false positive and false negative errors were minimized. Area under the curve (AUC) with confidence intervals were also presented. When defining cut-off points, indices calculated from an ROC curve provide an empirical basis for determining the most appropriate threshold value or cut-off point. AUC values of ≥ 0•90 are considered excellent; values between 0•80– 0•89 are deemed good; values between 0•70–0•79are considered fair; values< 0•70 are considered poor(5). Youden Index, was used to define the point that maximizes Sensitivity and Specificity. Finally, the Cronbach's alpha value of PDQ-39 was evaluated to measure the internal consistency of the scale and to confirm previous values on a larger sample;7 moreover, a Pearson's correlation coefficient between PDQ-39 and H&Y stages was assessed in order to measure the correlation between the two instruments. The significance level was set for a p-value less than or equal to 0•05. All statistical analyses were performed using IBM-SPSS version 23•00.

Results

The full study protocol was published on October 2019 on ClinicalTrials.gov available at https://clinicaltrials.gov/ct2/show/NCT04110106?term=quality+of+life&cond=Parkinson+Disease&rank=2 (ClinicalTrials.gov Identifier: NCT04110106).

According to the inclusion criteria, 513 individuals with PD were recruited, all of whom agreed to participate and were thus included in the study. Demographic characteristics of the sample are reported in Table 1. From the general analysis, it can be observed that participants between the age of 50 and 69 were mainly stage I or II, while participants aged 70 to 89 had a greater severity of PD. Most women were in H&Y stage II and III, while most men were mainly in stage II. A common result for all analyses was the presence of a very low number of participants with stage IV. A t-student test was performed on participants stratified by age and gender in order to detect any statistical differences in these sub-groups. T-student values showed that the sample was homogenous only for gender, with p> 0•05. All participants were evaluated with the self-reported PDQ-39 and the H&Y scales.

The ROC curve analysis showed that QoL worsened with the increase in disease severity and age. In Table 2, the cut-off points of PDQ-39 for H&Y stage I, II, III, and IV are reported as well as sensitivity/specificity values calculated through Youden Index. Moreover, in Tables 3, the cut-off points in the two age groups and for gender are reported, respectively. From the tables, it can be observed that the QoL worsened with increased age and was worse in females. The internal consistency of the PDQ-39 confirmed previous results showing high values of Cronbach's alpha for all sub-scales, representing good interrelations between them, as shown in Table 4. The Pearson's correlation coefficient showed a statistically significant correlation between all items of the PDQ-39 and H&Y stages, as shown in Table 5.

Table 1. Demographic characteristics of all participants; participants stratified by age; and participants stratified by gender.

	All participants	**Participantsstratified by age**			**Participantsstratified by gender**		
		50-69	70-89	p value	Females	Males	p value
Sample	513	250	263		201	312	
Age mean±SD	69.8±8.3	62.8±5.2	76.5±4.3	NA	70.9±7.7	69.1±8.6	0.04
Gender number (%)							
Females	201(39.2)	88 (35.2)	113 (43)	0.72*	-	-	-
Males	312 (60.8)	162 (64.8)	150 (57)		-	-	-
H&Y number (%)							
1	114(22.2)	89 (35.6)	25 (9.5)	0.001	32 (15.9)	82 (26.3)	0.037
2	186(36.3)	91 (64.4)	95 (36.1)		74 (36.8)	112 (35.9)	
3	147(28.7)	58 (23.2)	89 (33.8)		63 (31.3)	84 (26.9)	
4	66(12.9)	12 (4.8)	54 (20.5)		32 (15.9)	34 (10.9)	

*not statistically significant difference; NA not applicable

Table 2. Cut-off points of Parkinson's Disease Questionnaire-39 (PDQ-39) for the total sample

							ConfidenceInterval 95%	
H&Y	**PDQ-39 Score**	**Sensibility**	**Specificity**	**Area**	**Standard Error**	**Sign.**	**Lower Limit**	**Upper Limit**
I	<32.5	83%	81%	0.90	0.02	0.001	0.87	0.93
II	>32.5	83%	81%	0.90	0.02	0.001	0.87	0.93
III	>51.5	81%	75%	0.86	0.02	0.001	0.83	0.89
IV	>72.5	85%	80%	0.90	0.02	0.001	0.87	0.93

Table 3. Cut-off points of Parkinson's Disease Questionnaire-39 (PDQ-39) for the sample stratified by age and gender

	50-69 years old			70-89 years old			Females			Males		
H&Y	PDQ-39 Score	Se	Sp	PDQ-39 Score	Se	Sp	PDQ-39 Score	Se	Sp	PDQ-39 Score	Se	Sp
I	<29.50	83%	80%	<38.50	80%	74%	<39.5	81%	75%	<30.5	81%	75%
II	>29.50	83%	80%	>38.50	80%	74%	>39.5	81%	75%	>30.5	81%	75%
III	>49.5	80%	80%	>54.5	80%	70%	>59.5	80%	76%	>46.5	80%	73%
IV	>72.5	83%	85%	>79.5	82%	83%	>79.5	81%	80%	>67.5	82%	80%

Se= sensibility; Sp=specificity

Table 4. Cronbach's alpha of PDQ-39 for 513 participants

	Cronbach's Alpha if item deleted
ITEM 1	0.952
ITEM 2	0.952
ITEM 3	0.952
ITEM 4	0.952
ITEM 5	0.953
ITEM 6	0.953
ITEM 7	0.952
ITEM 8	0.952
ITEM 9	0.953
ITEM 10	0.952
ITEM 11	0.952
ITEM 12	0.953
ITEM 13	0.953
ITEM 14	0.953
ITEM 15	0.952
ITEM 16	0.953
ITEM 17	0.953
ITEM 18	0.954
ITEM 19	0.954
ITEM 20	0.954
ITEM 21	0.954
ITEM 22	0.954
ITEM 23	0.954
ITEM 24	0.953
ITEM 25	0.953
ITEM 26	0.953
ITEM 27	0.954
ITEM 28	0.954
ITEM 29	0.954
ITEM 30	0.953
ITEM 31	0.953
ITEM 32	0.953
ITEM 33	0.954
ITEM 34	0.953
ITEM 35	0.953
ITEM 36	0.954
ITEM 37	0.954
ITEM 38	0.954
ITEM 39	0.954
Total PDQ-39	0.954

Table 5. Pearson's correlation coefficient between PDQ-39 and H&Y scale

	H&Y
PDQ-39 - MOBILITY	0.73**
PDQ-39 – ADL	0.64**
PDQ-39- EMOTIONAL WELL-BEING	0.51**
PDQ-39 – STIGMA	0.40**
PDQ-39 - SOCIAL SUPPORT	0.34**
PDQ-39 – COGNITION	0.48**
PDQ-39 – COMMUNICATION	0.50**
PDQ-39 – PAIN	0.40**
PDQ-39 – TOTAL	0.73**

**. p<0.01

Discussion

Literature review showed that in the last few decades, QoL has been a focal point of research on PD.(10–12) There is strong evidence on the impact of classic symptoms of PD on QoL, mounting evidence has shown that both motor and non-motor symptoms significantly and independently contribute to worse QoL. In fact, symptoms often impede activities essential to daily living and social functioning. Impairment in these areas can alter social roles by interfering with employment status, household management, friendships, and other relationships (13). Conversely, a reduced QoL has a negative impact on both motor and non-motor symptoms (14,15).

The aim of the study was to evaluate the correlation between QoL and disease severity by assessing the presence of an optimal cut-off point on thePDQ-39 questionnaire as related to H&Y stages in a cohort of Italian adults with PD.

The secondary aim of the study was to evaluate the internal consistency of PDQ-39 and its concurrent validity and correlation with the H&Y scale.

A sample of 513 individuals with PD was included in the study and was assessed with both the PDQ-39 and H&Y scales.(8) A t-student test performed on the sub-sample stratified by age showed that the groups were homogenous in terms of gender but not regarding H&Y stages: the group of individuals younger than 69 were at an earlier stage of the disease. The same test performed on the sub-sample stratified by gender showed that both groups differed in terms of age: the women were older and, for H&Y stages, were at a later stage of the disease. However, this is understandable, because most women develop PD after menopause due to estrogen withdrawal, which has a role in disease pathogenesis (16–17).

The results of this study allow both researchers and clinicians to assess PDQ-39 cut-off points, which suggest that, in a certain H&Y stage of the disease; we can expect to see a certain level of QoL, according to the scale. Specifically, a patient in stage III of PD, according to H&Y, is expected to have a score between 51•5 and 71•5 on the PDQ-39. The results also showed that QoL decreased with the increase of both disease severity and age. From the results, women in the same stage of PD, according to H&Y, have a worse QoL than men. Particularly, a female patient in stage III of PD is expected to have a score between 59•5 and 79•5 on the PDQ-39, while a male patient in the same stage would have a score between 46•5 and 67•5. The literature suggests that estrogen is a likely contributor to the gender differences in PD.(18-19) Indeed, abundant evidence demonstrates that PD in women starts with a more benign phenotype, likely due to the effect of estrogen. However, as the disease progresses, women are at higher risk of developing highly disabling treatment-related complications, such as motor and non-motor fluctuations as well as dyskinesia, compared with men.(20) Moreover, in the literature, gender-related differences in the frequency and severity of non-motor symptoms of PD have been reported. Although few non-motor symptoms have been consistently reported to have a higher prevalence in a particular gender, the results of the majority of studies have been non-uniform. This is perhaps secondary to the non-uniformity in the type of rating scales used to document the frequency and severity of non-motor symptoms. Of the nine domains in the validated Non-Motor Symptoms Scale (NMSS), (21) sexual dysfunction and mood changes have been commonly observed to have associations with a specific gender. While sexual dysfunction has been commonly reported to affect a significantly higher proportion of men, (22–26) mood symptoms, which encompass loss of interest in surroundings, lack of motivation, feeling nervous, flat affect, and difficulty experiencing pleasure, have been more frequently reported among women with PD compared to men (27–29). Finally, the results of the current study confirm those reported by Balash et al., (30) who found that the comparison of PDQ-39 domains in both genders in early PD stages (H&Y I-II) revealed significant differences in QoL between men and women in terms of emotional condition and pain perception, with women being more prone to depression and more sensitive to pain. In advanced PD stages (H&Y III–V), males more often complain of memory decline, and their QoL is significantly worsened in the cognitive domain. Male PD patients regard their QoL better than do female patients in both early and advanced disease stages. This is largely due to the contribution of mobility items as well as emotional items and pain, all of which have a greater effect on women. These differences persist in both the early and more advanced stages of the disease. As PD progresses from H&Y stages I-II to III–V, the QoL worsens in both male and female patients, primarily related to the mobility domain (30).

Finally, according to the secondary aim of this study, the results confirmed that the PDQ-39 has good internal consistency and shows positive and statistically significant correlations with the H&Y scale.

Limits of the study. This study has certain limitations, the first of which is that the sample was not homogenous for gender and age, mainly because of differences in the distribution of the population in terms of the progression of PD. For instance, the older the population, the higher the disease stage. Second, a homogenous sample was chosen, including only individuals between 50 and 90 years of age and in H&Y stages I to IV, which means that stage V individuals were excluded. Therefore, further studies should also consider this segment of the population. Moreover, H&Y often drops out in regression models of QOL when more fine-grained (e.g. motor UPDRS) or non-motor instruments are used, this limit should be considered in future studies (31). Further studies should also use models to control for age and gender and examine other clinical variables examined.

Conclusion

QoL in PD has been the focus of much interest in the recent scientific literature. The results of this study allowed for the creation of a correlation between QoL and disease severity by assessing the presence of an optimal cut-off point on the PDQ-39 as related to H&Y stages in a cohort of individuals with PD. With this cut-off point, it is now possible to make a determination of QoL of an individual with PD at a certain stage of the disease, in a specific age range, and of a particular gender.

Ethics Approval: Authors certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed. All procedures were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration as revised in 2008. Informed consent was obtained from all participants for being included in the study. Institutional Review Board approval was not required. The research involved the analysis of data collected such that individual subjects cannot be identified in any way.

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