Duration of disease does not equally influence all aspects of quality of life in Parkinson's disease

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Abstract

Health related quality of life (HRQoL) is negatively impacted in patients suffering from Parkinson's disease (PD). For the specific components that comprise HRQoL, the relationship between clinical variables such as disease duration is not fully characterized. In this cross-sectional study (n=302), self-reported HRQoL on the Parkinson's disease questionnaire (PDQ-39) was evaluated as a global construct as well as individual subscale scores. HRQoL was compared in three groups: those within 5 years of diagnosis, those within 6-10 years of diagnosis, and those greater than 11 years since diagnosis. Non-parametric analyses revealed lower HRQoL with increasing disease duration when assessed as a global construct. However, when subscales were evaluated, difficulties with bodily discomfort and cognitive complaints were comparable in individuals in the 1-5 years and 5-10 year duration groups. Exploratory regression analyses suggested disease duration does explain unique variance in some subscales, even after controlling for H&Y stage and neuropsychiatric features. Our findings show that HRQoL domains in PD patients are affected differentially across the duration of the disease. Clinicians and researchers may need to tailor interventions intended to improve HRQoL at different domains as the disease progresses.

Introduction

Health related quality of life (HRQoL) in Parkinson's disease (PD) is a multifaceted construct, encompassing the emotional, physical, and social impacts of the condition ¹. In recent years, HRQoL has emerged as an increasingly important outcome measure for evaluating the efficacy of interventions in PD². Studies of HRQoL in PD have revealed strong associations with several features beyond the core motor symptoms, including depression³, fatigue,⁴ and other non-motor symptoms⁵. Given that PD is progressive with increasing motor and non-motor symptoms over time⁶, it stands to reason that disease duration might be strongly correlated with HRQoL. However, some studies have found little relationship between disease duration and HRQoL⁷ or found that the relationship attenuates after accounting for other demographic or clinical factors⁸. According to a recent systematic review³, of 20 studies examining factors influencing HRQoL, disease duration was retained as a significant predictor in only six.

One potential explanation for these discrepant findings is that the association between disease duration and HRQoL might be more complex than a simple direct linear relationship. For example Soh⁹ proposed that disease duration contributes to HRQoL via its impact on motor, non-motor, mental, and self-care limitations. However, the fit indices of their structural equation models were not fully desirable. In a similar vein, Visser and colleagues¹⁰ found that depression and psychological functioning continue to influence HRQoL throughout the course of the disease, while pain and impaired activities of daily living (ADL) are only predictors of HRQoL in the early, but not in the later stages of PD.

In addition to a more complex relationship between disease duration and HRQoL, it is also important to point out that the above studies often treated HRQoL as a unitary construct, by using a summary score in their analysis. Because multiple domains of daily life define HRQoL, summary scores alone may miss more focused impacts of the disease on a particular facet of daily existence. This assertion is supported by previous factor analytic studies that suggest multiple components of HRQoL exist which overlap, but also explain a unique portion of the variance in the global construct¹¹. These individual facets of HRQoL may be differentially impacted by disease duration. As an example, a 12-month study

of patients with PD found that the Parkinson's Disease Questionnaire (PDQ-39) subscales of stigma, communication and body pain alone changed over the study course, while other subscale scores remained unchanged¹². In another study, when comparing subscales of treated vs. untreated early stage PD patients over 18 months¹³, 6 of the 8 subscales of the PDQ-39 improved with treatment over the course of 18 months, while all domains declined in the non-treated early PD group. Interestingly, in the treatment group it was mobility and ADL scores that did not change, and the magnitude of decline in the control group was not uniform between domains.

In light of these findings, the current study seeks to evaluate differences in HRQoL at the subscale level in a cross sectional study of PD clinical outpatients. Specifically, we sought to evaluate any difference in PDQ-39 subscales across patient groups in the early (0-5 years), middle (6-10 years) and later (11+ years) periods of disease duration. Preliminary analyses to establish any independent relationship with disease duration and domains of HRQoL are also undertaken.

Methods

Participants and Data Acquisition

All patients with a diagnosis of idiopathic PD in the Plummer Movement Disorders Center of Baylor Scott & White Hospital were asked to complete yearly surveys that include the PDQ-39 as well as various demographic and clinical factors. Pertinent to this survey, individuals were also asked to select their disease duration from several different options: 0-5 years, 6-10 years, 11-15 years, and 15+ years. Given small sample sizes in some of the advanced groups, these were combined into 0-5, 6-10, and 11+ years duration for this study.

The current study retrospectively evaluated the data collected in 2012 with the approval of Baylor Scott & White Hospital's Institutional Review Board. Of the 337 surveys collected in 2012, 35 were incomplete and eliminated from the statistical analysis. For the remaining 302 patients, demographics, disease duration and HRQoL data (measured by PDQ-39) were extracted. On the demographic questionnaire, items such as age were asked in terms of ranges rather than ratio level data. In addition, Hoehn & Yahr (H&Y¹⁴) ratings or the information necessary to obtain the H&Y score was abstracted

from neurology notes and coded by a trained research coordinator. Demographic and clinical variables are found in table 1.

Instruments

The PDQ-39¹¹ is a 39-item questionnaire in which the frequency of PD-related interference on a number of activities, situations, and symptoms is rated using a 0 (never) to 4 (always) scale. The items are grouped in 8 domains: mobility, activities of daily living (ADL), emotional well-being, stigma, social support, cognition, communication, and bodily discomfort. Each subscale's scores are transformed into a 0–100 scale by summing the items' raw scores, divided by the maximum possible raw score, and then multiplying by 100 (higher scores mean poorer HRQoL). A Summary Index (SI) is also calculated from the mean of the eight domain scores.

In addition to the PDQ-39, patient's provided relevant clinical and demographic data in a multiple choice format in an accompanying questionnaire. Pertinent to the current study, patients were asked to endorse whether they were experiencing depression, anxiety, or thinking problems. This information was also utilized in the analyses below and is summarized in Table 1.

Data analysis

All statistical analyses were completed in Stata 13¹⁵. Demographic and clinical variables were compared between groups with chi-square tests. Initial analysis of the PDQ-39 variables revealed significantly non-normal distributions. As such, Kruskal Wallis tests (a non-parametric variant of the analysis of variance) were used to compare the groups on the subscales and summary index of the PDQ-39. Given the multiple comparisons, Bonferonni correction on the omnibus tests was used, with a significance level for each analysis set to $p \leq 0.006$ for all analyses. For significant findings, Dunn's test was employed as post-hoc analyses between the three duration groups¹⁶. To help determine the potential impact of disease stage and neuropsychiatric covariates on these analyses, exploratory multiple regressions were conducted to evaluate the impact of these variables on HRQOL domains.

Results

As would be expected, there was an increasing proportion of higher HY score with increasing disease duration ($\chi^2 = 44.46$, $p < .0001$) though age difference was not significant ($\chi^2 = 7.21$, $p > .8$). However, the duration groups did not differ significantly in terms of frequency of endorsed depression ($\chi^2 = 3.64$, $p > .15$), anxiety ($\chi^2 = .40$, $p > .8$) or cognitive problems ($\chi^2 = .09$, $p > .95$).

Kruskal Wallis test revealed a significant group effect (duration of PD) on each of the aspects of HRQoL as well as the summary score, with the exception of Social Support ($H = 5.95$, $df(2)$, $p = .05$). According to the post-hoc analysis, the PDQ-39 Summary Index increased with increasing disease duration ($H = 29.43$, $df(2)$, $p < .001$). The domains mobility ($H = 22.07$, $df(2)$, $p < .001$), activities of daily living ($H = 30.02$, $df(2)$, $p < .001$), emotional well-being ($H = 16.53$, $df(2)$, $p < .001$), stigma ($H = 28.50$, $df(2)$, $p < .001$), and communication ($H = 23.93$, $df(2)$, $p < .001$) showed a pattern where individuals in the 6-10 and the 11+ years disease duration groups did not differ significantly, while patients in the 0-5 years disease duration range had significantly lower scores than both of them. On the other hand, with regards to cognition ($H = 12.79$, $df(2)$, $p = .002$), and bodily discomfort ($H = 10.38$, $df(2)$, $p = .005$), individuals in the 0-5 and 6-10 years of disease duration showed similar quality of life scores, which were significantly lower than those reported by individuals with longer (11+ years) disease duration. This can be seen graphically in Figure 1. Table 2 displays the means and standard deviations of all PDQ-39 domains for all three disease duration groups and the results of the post-hoc analyses.

Given the multicollinearity between disease duration and severity as well as the non-normal distributions of the variables, the results of multiple regression analyses must be considered only cautiously given the increased likelihood for increased standard error for beta weights, reduction in the size of the multiple correlation measures, and reduced confidence in understanding of the relative importance of predictors¹⁷. With these caveats in mind, Table 3 demonstrates statistically significant variance explained by disease duration in several domains, even after accounting for H&Y stage or self-reported depression, anxiety, or cognitive difficulties. The strongest relationships were observed for activities of daily living (ADL), stigma, and communication domains. Smaller but still statistically

significant additions to the explained variance were seen in mobility, emotional well being, and cognition. PD duration did not contribute significantly to predicting bodily discomfort and social support.

Discussion

Decline in HRQoL is a major concern in those with neurodegenerative disorders. In Parkinson's disease, clinicians aim to improve the HRQoL in their patients via symptomatic therapies as well as psychosocial and other interventions. However, just as interventions to improve HRQoL are multifaceted, so too is the construct itself. While HRQoL measures are frequently condensed to a single summary score, the construct encompasses several domains that in turn may be differentially impacted by various disease-related, personal, or environmental factors. The current research clearly demonstrates this complexity. As measured by the PDQ-39, HRQoL as a whole was lower in individuals of longer disease duration in a predictable fashion. However, this decline was not uniform across subscales, as cognitive complaints and bodily discomfort were elevated and similar to one another in the 0-5 and 6-10 year groups. This does not mean that cognitive difficulties and bodily discomfort would be insignificant problems for individuals early on in the disease. On the contrary, these domains had some of the highest mean scores from all domains at 0-5 years of disease duration, indicating that the negative effects of cognitive and bodily discomfort symptoms on everyday life are seen in individuals of short disease duration.

In concurrence with the results of Chapuis, Ouchchane, Metz, Gerbaud and Durif¹⁸, we found significant difference in quality of life with increasing disease duration in mobility, activities of daily living, stigma and communication; however contrary to their results we did not find a significant difference between duration groups in the domain of social support, and the difference between disease duration groups was significant for the cognition and bodily discomfort domains in our study. The discrepancy in the results might be in part due to the smaller sample size in the study of Chapuis and colleagues or the fact that they treated disease duration as a continuous variable. The overall disease duration in their sample was also greater.

The question remains as to whether disease duration contributes any unique variance to understanding HRQoL after controlling for other predictors such as neuropsychiatric variables and overall disease. Our retrospective dataset cannot answer this question definitively, and psychometric limitations of the data (significant non-normality) and assessment methods (i.e. single item self-reported measures for depression, anxiety, and cognitive impairment) make interpretation of our regression results tentative. However, our results would suggest that duration does make small and unique contributions to the variance in HRQoL, particularly for activities of daily living, stigma, and communication over and above disease duration.

Given these findings, researchers utilizing HRQoL as an endpoint should consider features such as disease duration and individual subscale scores when interpreting results. Studies could focus on evaluating specific aspects of HRQoL at different disease stages. In addition, controlling for the impact of disease duration when gauging the effectiveness of an intervention on HRQoL will be important to avoid confounding results.

For multi-disciplinary clinics following individuals over time, these results may help to provide more tailored care across the disease course. For example our findings suggest that targeting cognitive and bodily discomfort early in the disease course may be particularly relevant to patients, especially while they still may be engaged in activities such as work and caregiving/family responsibilities. Indeed, recent work has revealed that in early PD, the non-motor features of the disease seem to be more strongly related to HRQoL than motor dysfunction¹⁹. Later on in disease, interventions can be extended to incorporate other aspects of quality of life as well, for example including communication and adaptive strategies for improving ADL performance. Furthermore, identifying correlates of positive HRQoL and psychosocial outcomes in PD could help identify those factors, such as coping strategies, that might improve the day to day experience of living with PD²⁰.

Limitations of this study includes the cross sectional nature of our data. Another limitation is the low sample sizes in the later stages of the disease (especially in the 11+ years disease duration group). While the non-parametric techniques utilized in this study are robust to deviations in sample size and

normality, the conservative nature of the techniques employed and smaller sample sizes at more advanced disease durations should be considered when interpreting results. Given limitations within the available data, clinical variables such as more precise disease severity could not be explored or controlled for. Disease duration was also retrospectively rated by patients, and this may introduce bias in the rating. Disease duration data was collected categorically rather than in free response, precluding more advanced statistical analysis.

In summary, our results indicate that disease duration has a differential effect on the various domains of health related quality of life. Some of these domains, like cognition and bodily comfort are impacted earlier in disease progression and appear similar when comparing groups in the first decade of the disease, while other areas are lower about 6-10 years in the disease relative to those early in the disease course. Future studies assessing quality of life predictors may want to consider domain-specific effect of disease duration. Further assessment of progression related quality of life changes may lead to more effective targeting of interventions.

Disclosures

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Tables [Tables 1 and 2 are uploaded as separate files]

Figures [Figure 1 is uploaded as a separate file]

Table 1

Table 1: Demographic and Clinical Variables for the Sample

Variable	0-5 Years		6-10 Years		11+ Years		Total Sample	
	%	N	%	N	%	N	%	
Male Gender	50.21	122	63.41	26	55.56	10	52.32	
Age								
<50	3.29	8	0.00	0	0.00	0	2.65	
51-60	10.29	25	19.51	8	5.56	1	11.26	
61-70	32.51	79	36.59	15	38.39	7	33.44	
71-80	34.57	84	24.39	10	38.89	7	33.44	
81+	19.35	47	19.51	8	16.67	3	19.21	
H&Y								
1	25.00	58	21.95	9	0.00	0	23.10	
2	71.98	167	63.41	26	64.71	11	70.34	
3	3.02	7	4.88	2	17.65	3	4.14	
4	0.00	0	7.32	3	11.76	2	1.72	
5	0.00	0	2.44	1	5.88	1	0.69	
Self-Reported:								
Depression	29.10	71	34.15	14	50.0	9	31.02	
Anxiety	34.02	83	39.02	16	33.33	6	34.65	
Cognitive Difficulties	46.31	113	46.34	19	46.34	9	50.00	

Note: H&Y - Hoehn & Yahr ratings

Table 2

Table 2: PDQ-39 Subscales across 3 levels of disease duration

Subscale	(A) 0-5 Years		(B) 6-10 Years		(C) 11+ Years		Post-Hoc
	Mean	SD	Mean	SD	Mean	SD	
Total	23.47	14.95	33.08	17.70	46.02	19.75	A<B<C
Mobility	32.18	28.19	45.85	26.72	64.17	33.31	A< (B=C)
Activities of Daily Living	22.81	22.09	38.92	27.76	56.48	32.78	A<(B=C)
Emotional Well Being	25.40	20.58	34.25	23.19	45.60	22.84	A<(B=C)
Stigma	13.32	17.94	27.74	22.62	37.15	27.16	A<(B=C)
Social Support	8.54	14.30	14.43	21.97	21.30	22.73	ns
Cognition	28.66	19.45	32.47	23.06	47.22	18.96	(A=B)<C
Communication	19.43	17.62	31.30	21.23	40.74	24.07	A<(B=C)
Bodily Discomfort	37.36	21.55	39.63	26.40	55.55	20.61	(A=B)<C

Note: Dunn’s test for significant omnibus tests were employed as a post-hoc analysis; ns = not significant

Table 3

Table 3: Hierarchical Multiple Regression Analyses Predicting PDQ Subscales from PD Severity, Self-Reported Neuropsychiatric Variables, and Disease Duration

Predictor	PDQ-39 Domain															
	Mobility		Activities of Daily Living		Emotional Well-Being		Stigma		Social Support		Cognition		Communication		Bodily Discomfort	
	ΔR ²	B	ΔR ²	B	ΔR ²	B	ΔR ²	B	ΔR ²	B	ΔR ²	B	ΔR ²	B	ΔR ²	B
Step 1: H&Y, Depression, Anxiety, Cognitive Problems	.14*		.17*		.40*		.13*		.11*		.29*		.23*		.09*	
Step 2: PD Duration	.04*	.23	.08*	.31	.03*	.18	.07*	.28	.02	.14	.03*	.17	.06*	.27	.02	.15
Total R ²	.18*		.25*		.43*		.21*		.14*		.31*		.29*		.11*	

Notes: * p<.006;

Figure 1: Select PDQ-39 Subscale Scores by PD Duration Groups