Original Research Article

The Validity of Health-Related Quality of Life Instruments in Patients With Late-Stage Parkinson's Disease

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Abstract

Objective: To examine the validity of health-related quality of life (Hr-QoL) measures in patients with late-stage Parkinson's disease (PD). **Methods:** We analysed data from patients with late-stage PD and their carers who were assessed with a range of clinical measures and the EQ-5D-3 L. The DEMQOL-Proxy was completed for 157 patients with a diagnosis of dementia and the PDQ-8 by 401 patients without dementia. Convergent validity was assessed using correlations with measures of Parkinson's severity, independence and cognitive function, and construct validity using correlations with patients' own EQ-5D-3 L scores. In addition, we assessed divergent validity using correlations with carers' own EQ-5D index, EQ-VAS and Zarit caregiver burden scores. **Results:** In patients without dementia, both the PDQ-8 and EQ-5D-3 L correlated with measures of disease severity, dependence and carer burden scores, and PDQ-8 scores moderately with EQ-5D-3 L and EQ-5D-3 L VAS scores. In patients with dementia, EQ-5D-3 L scores correlated with disease severity, cognition and dependence scores, but DEMQOL-Proxy scores were moderately associated only with patients' dependence and carers' own EQ-5D-3 L scores but not patients' disease severity, EQ-5D-3 L or cognitive scores. **Conclusions:** The PDQ-8 and EQ-5D-3 L have adequate validity in late stage PD without dementia, but in those with PD and dementia the EQ-5D-3 L may be preferable to the DEMQOL-Proxy.

Keywords

parkinson's disease, brain, neurodegeneration, dementia, scale, demqol

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease, affecting approximately 8.5 million people worldwide.[1] Advancing disease is associated with rising dependence and increasing prevalence and severity of motor and non-motor features.[2] Dementia is a common complication of PD, with up to 78% of the evaluated patients having dementia after 15 years.[3]

As treatment of PD aims to alleviate symptoms, the assessment of health-related quality of life (Hr-QoL), reflecting the individual's own perception of disease impact on everyday life is of particular importance.[4] Measurement of Hr-QoL in PD is typically done using self-completed questionnaires, such as the disease-specific Parkinson's disease Questionnaire-8 (PDQ8)[5] and the generic EQ-5D-3 L (Index and Visual Analogue Scale (VAS)), which have been shown to be valid, reliable, and responsive in PD.

Only few studies have assessed Hr-QoL in late-stage parkinsonism and little is known about the validity of Hr-QoL measures in patients in the late stages of PD, when symptoms are most severe, and patients rarely participate in research studies. In particular, significant challenges arise in assessing those with dementia. As stated by Fan et al, 2020, "partial data coming from questionnaires based on patient self-administered might be relatively less reliable for PDD patients".[6] An alternate method to patient-completed questionnaires is utilising proxy reports from caregivers or health-care professionals to provide information. However, previous studies which have evaluated the extent of patient–proxy agreement regarding Hr-QoL

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in PD patients, have reported lower levels of agreement in patients with PD at advanced stages of the disease (Hoehn and Yahr ≥3 and with motor fluctuations) than those in less advanced stages (Martínez-Martín et al 2004). The carer completed DEMQOL-Proxy was developed to assess Hr-QoL in patients with dementia.[7] However, no studies have evaluated the DEMQOL-Proxy scale for its validity in patients with PD. We here analysed the validity of the PDQ-8 in patients with PD without dementia and the DEMQOL-Proxy scale in patients with PD and dementia to inform their use in this population.

Methods

Patient Population

This study used baseline data from the Care of Late Stage Parkinsonism (CLaSP) study, a cohort study of patients with late-stage parkinsonism recruited from general practitioners, hospitals, nursing homes, patient advocate groups and self-help groups in six European countries.[8] Inclusion criteria were diagnosis of PD for at least 7 years classified as Hoehn and Yahr stage (Hoehn and Yahr) IV or V in the "On"-state or have significant independence (Schwab and England stage ≤50%) in the "On"-state.

Outcome Measures

Hr-QoL was assessed using the PDQ8 in patients with PD without a diagnosis of dementia and the DEMQOL-Proxy in those with a clinical diagnosis of dementia. On the self-administered, disease-specific PDQ8 patients are asked to evaluate the impact of Parkinson's in eight domains on a Likert scale from 0 to 4: Activities of Daily Living, Attention and Working Memory, Communication, Depression, Quality of Life, and Social Relationships. Higher scores on the PDQ8 summary score indicate a worse quality of life. The DEMQOL-Proxy is a 31-item instrument to assess Hr-QoL in patients with dementia and is designed for completion by a family member or carer. It has a two-factor structure of 'emotion' and 'functioning' arranged over sections that ask about feelings, memory and everyday life. In the first section the instruction is to evaluate the relative's feelings in the last week; in the second section proxies are asked to evaluate how worried they would say their relative has been about aspects of cognition; in the third section proxies are asked how worried they would say their relative has been about aspects of self-care, activities of daily living and social activities, finances and physical health. Items are scored on a Likert scale from one to four. Higher overall scores indicate better Hr-QoL.

The following instruments were used to collect further information on health and well-being in patients and their caregivers: The patient-completed EQ-5D-3 L is a generic measure of self-reported health status. It consists of five questions with three levels of answers on the dimensions Mobility, Self-Care, Usual Activities, Pain/Discomfort, and Anxiety/Depression, and a visual analogue scale (EQ-VAS) on general health. Disease severity was assessed using the Hoehn and Yahr staging and UPDRS part 1-4 scores, independence with the Schwab and England scale, cognitive function using the Mini mental state examination (MMSE). Caregiver burden was rated using the Zarit caregiver burden interview (as no PD-specific scale was available at the time of planning) and caregivers' own health status with the Carer EQ-5D (Table 1).

Analysis

Construct validity was examined by comparing correlations of PDQ-8 and DEMQOL-Proxy scores with patients' own EQ-5D-3 L index and EQ-VAS scores. Convergent validity of the PDQ-8 and EQ-5D-3 L in patients without dementia and of the DEMQOL-Proxy and EQ-5D-3 L in patients with dementia was assessed by correlation with measures of Parkinson's severity (UPDRS part 1-4 scores and Hoehn and Yahr), independence (Schwab and England score) and cognitive function (MMSE). In addition, we assessed divergent validity of these scales using correlations with carers' own EQ-5D index, EQ-VAS and Zarit caregiver burden scores. Spearman's rank-order correlations were performed, and strength of correlation classified (<.1 considered no correlation, .1-.2 considered weak, .2 to .5 moderate, >.5 strong). The PDQ-8 was hypothesised to correlate with other measures of Hr-QoL and of PD severity in patients without dementia; in patients with dementia, the DEMQOL-Proxy was hypothesised to correlate with other measures of Hr-QoL (patient completed) and cognitive function (clinician completed), as it was developed to be a measure of quality of the patient's health in dementia.[7] Both measures were expected to have weaker correlations with both carer burden and Carer EQ-5D scores, as they are completed by the carer on their own health state. The threshold for statistical significance was set at .05. All statistical analyses were performed with SPSS 11.5 for MacOS.

Results

The sample included 558 patients who participated in the study and completed all assessments used in this analysis (Table 2). Out of these, 401 patients without a diagnosis of dementia completed the PDQ-8 and in 157 patients who had a diagnosis of dementia their carers completed the DEMQOL-Proxy. All patients who completed the PDQ-8 also completed the EQ-5D, but only 116 of the 157 patients with DEMQOL-Proxy data completed the EQ-5D. Patients with self-completed EQ-5D or PDQ-8 data had

Table 1. Description of questionnaires used in the study.

Description of Questionnaires			Description of Variable Used in This Analysis
Assessment description		Conversion of questionnaire data to numerical score	Range of possible values
Patient-completed			
EQ-5D-3 L	Five dimensions: mobility, selfcare, usual activities, pain/discomfort, and anxiety/depression	Index utility score generated using a general population valuation of the health states	-.2-1
EQ-VAS	Visual analogue scale	Range between 100 (best imaginable health) and 0 (worst imaginable health)	0-100
PDQ-8	Eight domains: Activities of daily living, Attention and Working memory, communication, depression, quality of life, and social relationships	Each question is scored from 0-4. The PDQ-8 summary index (PDQ-8-SI) is summed over the eight domains and standardized from 0 to 100	0-100
Carer-completed			
DEMQOL-proxy *	31 items on appearance, memory, positive emotions, and negative emotions	DEMQOL is converted to an index utility score (DEMQOL-proxy) using a general population valuation of the health states	.36-.94
Zarit caregiver burden interview	22-Items on a 5-point scale on carer burden	Answer options range from 0 (never) to 4 (nearly always) with the sum of scores ranging between 0-88. Higher scores indicate greater burden	0-88
Carer EQ-5D index	Five dimensions: mobility, selfcare, usual activities, pain/discomfort, and anxiety/depression	Index utility score generated using a general population valuation of the health states, completed by the carer on their own health state	-.2-1
Assessments clinician-completed			
UPDRS	Four parts: Mentation, Behaviour and Mood, activities of daily living, motor examination, and complications of Therapy	A score of 199 on the UPDRS scale represents the worst disease severity	UPDRS1 (0-15) UPDRS2 (7-47) UPDRS3 (10-92) UPDRS4 (0-17)
Hoehn and Yahr scale	Staging system for PD severity	Range from 1 to 5. Higher stages indicate higher the disease severity	Categories 1-5
Schwab & England scale	Assesses the patient's ability to perform activities of daily living	0 indicates complete dependence/bedridden and 100% complete independence	0-100%
Cognitive assessment and neuropsychiatric and other non-motor symptoms scales			
Mini-mental state examination (MMSE)	General cognitive impairment, with higher overall total scores (range 0-30) specifying better performance	A score of 20 to 24 suggests mild dementia, 13 to 20 suggests moderate dementia, and less than 12 indicates severe dementia	0-30

* Information on the patient completed by the carer.

significantly higher MMSE scores than those who did not (both P<.001). The mean MMSE scores of the individuals who completed the EQ-5D (23.84 (SD 5.5)) was significantly higher (P < .001) than that of those who did not complete the EQ-5D (9.57 (SD 4.7)), and that of those who completed the PDQ-8 (25.67 (SD 3.4)) than that of those who did not (15.11 (SD 6.7; P < .001)).

In those without a diagnosis of dementia, the PDQ-8 correlated moderately with both the EQ-5D-3 L and EQ-VAS scores (see Table 3 and figure 1). It also correlated moderately with measures of Parkinson's disease severity as assessed on the UPDRS part 1, 2 and 3, and the Schwab and England independence score and as well as with the MMSE score and Zarit caregiver burden scores, and weakly with the Hoehn and Yahr and UPDRS part 4 scores. Similarly, the patient-completed EQ-5D-3 L score correlated moderately with measures of disease severity (UPDRS part 1-3 and Hoehn and Yahr), MMSE scores and Schwab and England scores, whereas EQ-VAS scores correlated only weakly with UPDRS part 1, 2 and 4 and Schwab and England, and with Zarit caregiver burden scores and Carer EQ-VAS scores.

In those with a diagnosis of dementia, the DEMQOL-Proxy scores were not significantly associated with either

Table 2. Baseline characteristics. MMSE: Mini-Mental State Examination.

	Patients without Dementia N = 401		Patients with Dementia N = 157	
Measure	PDQ-8	EQ-5D	DEMQOL-proxy	EQ-5D
Sex (%)				
Male, n	217 (54.11%)	217 (54.11%)	93 (59.24%)	67 (57.76%)
Female, n	184 (45.89%)	184 (45.89%)	64 (40.76%)	49 (42.24%)
Age (years)				
Median	76	76	78	78
Range	42-94	42-94	24-96	56-96
Age of onset (years)				
Median	60	60	63	63
Range	17-85	17-85	15-85	34-85
Years of Education				
Mean (SD)	10.29 (3.79)	10 (3.77)	9 (4.45)	8.7 (4.19)
MMSE				
Mean (SD)	25.67 (3.4)	25.67 (3.4)	15.1 (6.7)	16.9 (6.4)

the EQ-5D-3 L or the EQ-VAS scores. The DEMQOL-Proxy scores were also not associated with UPDRS part 2 and 3 scores, and only weakly with UPDRS 1 and 4, MMSE, Hoehn and Yahr and Carer EQ-5D. However, the DEMQOL-Proxy moderately correlated with the carer EQ-VAS and the Schwab and England independence score. In contrast, the patient's EQ-5D-3 L score correlated moderately with UPDRS 1, Carer EQ-5D index and MMSE and strongly with Hoehn and Yahr and UPDRS part 2, 3 and Schwab and England independence score. There were only weak correlations with Zarit caregiver burden scores. The EQ-VAS also correlated moderately with UPDRS part 1, 2 and 3 and Hoehn and Yahr, MMSE, Schwab and England independence scores and the carers' EQ-VAS scores.

Discussion

In this study we found the PDQ-8 has good construct and convergent validity in patients with late-stage PD without dementia, as demonstrated by the significant moderate correlations with the examined measures of disease severity, independence and health-related quality of life, as well as carer burden. These results were similar for the generic EQ-5D-3 L in patients without dementia, confirming previous reports in PD patients without dementia in earlier stages previously.[2]

In patients with PD and dementia, the patient-reported EQ-5D-3 L correlated moderately or strongly with measures of disease severity, including the UPDRS part 1, 2, and 3, Hoehn and Yahr and Schwab and England independence scores and cognition assessed on the MMSE. These findings support the validity of the EQ-5D in PD also in this population, and are similar to those reported previously in patients with mild moderate dementia in other populations.[9,10] Although dementia makes it difficult for patients to complete an assessment and rate of completion of Hr-QoL scales reduces with advancing dementia in this and other studies,[11] it has previously been reported[12] that patients who are mild to moderate cognitively impaired living with dementia are able to rate their own Hr-QoL using the EQ-5D-3 L albeit with often higher scores than informal carers.[10] It has also been demonstrated in other recent studies[13-15] that in PD the PDQ-39 can be used to measure QoL in cognitively impaired PD patients. These results indicate that the responses to the PDQ-39 are reliable for PD patients with low MOCA scores in most PDQ-39 subdomains.

On the other hand, DEMQOL-Proxy scores did not correlate with measures of patient-reported health-related quality of life as assessed on EQ-5D-3 L score and EQ-VAS, or with key measures of PD severity (UPDRS part 2 and 3), and only correlated weakly with measures of cognition (MMSE), some measures of PD severity (Hoehn and Yahr, UPDRS1 and UPDRS4) and Carer EQ-5D. Furthermore, we found that the DEMQOL-Proxy correlated moderately with the carers' own EQ-VAS and Schwab and England independence scores. These findings suggest that DEMQOL-Proxy scores do not adequately capture the patients' own Hr-QoL in patients with PD and dementia, but primarily reflect carers' own wellbeing and health status. Whilst the DEMQOL proxy has not been previously validated in patients with PD, our results suggest lower validity of the DEMQOL-Proxy in PD patients with dementia than previous work has reported in patients with dementia. In previous studies[16,17] the DEMQOL-(Relative) Proxy was reported to have moderate correlations to the self reported EQ-5D-3 L. It is likely that the failure of the DEMQOL-

Table 3. Associations between DEMQoL-Proxy and PDQ-8 and other patient- and carer-completed health measures.

DEMQOL-proxy		P value	EQ5D from DEMQOL patients	P value	EQ-VAS	P value	PDQ-8	P value	EQ5D from PDQ-8 patients	P value	EQ-VAS	P Value
Patient-completed												
EQ-5D-3 L *	.03 (116)	.76	-	-	-	-	-.43**(400)	<.001	-	-	-	-
EQ-VAS	-.03 (99)	.77	-	-	-	-	-.32**(392)	<.001	-	-	-	-
Clinician-completed												
Hoehn and Yahr	.12 (157)	.13	-.66** (116)	<.001	-31**(99)	.002	.15**(401)	.003	-.36**(400)	<.001	-.03 (392)	.56
UPDRS-1	-10 (156)	.21	-.42**(115)	<.001	-.36**(98)	<.001	.46**(401)	<.001	-.28**(400)	<.001	-.16**(392)	.002
UPDRS-2	-.08 (157)	.35	-.60** (116)	<.001	-26*(99)	.01	.41**(401)	<.001	-.48**(400)	<.001	-16**(392)	.002
UPDRS-3	-.01 (157)	.90	-.60** (116)	<.001	-.26*(99)	.01	.33**(401)	<.001	-.42**(400)	<.001	-.08 (392)	.10
UPDRS-4	-.19*(157)	.02	-.003 (116)	.97	.05 (99)	.60	.17**(401)	<.001	-.01*(400)	.838	-.11*(392)	.04
Schwab and England	-.23** (157)	.004	.51** (116)	<.001	.33**(99)	<.001	-.30**(401)	<.001	.45**(400)	<.001	.13**(392)	.01
Carer-completed												
Zarit caregiver burden interview	-.07 (146)	.41	.13 (108)	.18	-.09 (93)	.37	.29**(294)	<.001	-.09 (293)	.12	-.15*(285)	.01
Carer EQ-5D	-.11 (135)	.22	.21*(96)	.04	.18 (82)	.10	-.02 (276)	.74	-.01 (276)	.93	.03 (271)	.64
Carer EQ-VAS	.23**(135)	.01	.06 (96)	.55	.24*(82)	.03	-.03 (279)	.66	-.01 (279)	.92	.11 (272)	.06
Cognitive assessment												
MMSE	-.13 (131)	.14	.27**(101)	.01	.22*(90)	.04	-.25**(392)	<.001	.23**(392)	<.001	.04 (386)	.41

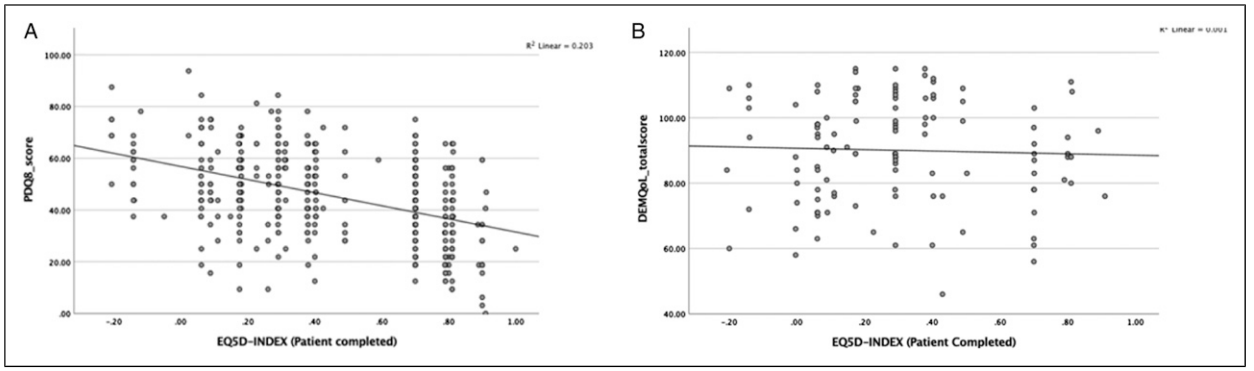

Figure 1. (A) Scatterplot of PDQ-8 and EQ-5D-3 L R^2 =.203 and (B) DEMQOL-Proxy and EQ-5D-3 L R^2 =.001.

Proxy to capture quality of life of patients with PD and dementia may at least partly be contributed to by the complexity of symptoms of PD and of the wording of the DEMQOL-Proxy, as this requires the carer to make a judgment about the patient's experience with regard to their concern about their physical health and impact on daily activities.[11] At least in this population, carers may perceive patients' experiences as different, as they may expect them to feel worse given their physical difficulties. The significant physical problems in late stage PD and their impact may perhaps also not be recognised by patients (with a degree of anosognosia) in those with dementia, and carers may also not be aware of cognitive features such as apathy/abulia which may be mistaken as lack of concern or disinterest.

Differences in the patients and carers views could also be due to deterioration of the relationship between carers and patients, as features of advanced PD such as neuropsychiatric disorders, depression and sleep disorders are related to higher caregiver burden[18-20] and decreased relationship satisfaction.[21] Furthermore, deterioration of motor functioning and speech difficulties can affect communication and impact on caregiver burden.[22] These changes may cause a decrease in meaningful conversations between patients and caregivers, resulting in a feeling of emotional distance and reduced intimacy and could lead to differences in the patients and carers views. This high caregiver burden of late stage PD, particularly through the impact of neuropsychiatric features and communication difficulties, may therefore affect caregivers' evaluation of patients quality of life.

The carer completed DEMQOL-proxy was developed to assess Hr-QoL in patients with dementia[7] and has reasonable validity in this population where evaluation of Hr-QoL is difficult.[16,17] Nevertheless, our findings suggest that in PD, the DEMQOL-Proxy primarily reflected the carers views of the resident's health status independence and their own health status. Given the limited agreement between patient and proxy responses in patients with dementia, use of patient-reported EQ-5D-3 L or other measures is preferable when still possible particularly at advanced stages of PD. The EQ-5D-3 L may be a more appropriate measure to capture Hr-QoL of PD patients with dementia than the DEMQOL-Proxy.

Conclusion

Our findings demonstrate that whilst the PDQ-8 and EQ-5D-3 L have adequate validity in late stage PD without dementia, the DEMQOL-Proxy in its current form does not, with the EQ-5D-3 L and EQ-VAS being more appropriate measures. There is a need for proxy-rated measures that take into account the complexities of combine physical and cognitive aspects of PD.

Appendix

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