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Non-motor symptoms in Parkinson's disease

Verbaan, D.

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A comprehensive model of health-related quality of life in Parkinson's disease

Martine Visser¹, Stephanie M. van Rooden¹, Dagmar Verbaan¹, Johan Marinus¹,
Anne M. Stiggelbout^{2*}, Jacobus J. van Hilten^{1*}

* both authors contributed equally to this work

Department of Neurology¹, Leiden University Medical Center, Leiden,
The Netherlands

Department of Medical Decision Making², Leiden University Medical Center, Leiden,
The Netherlands

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Abstract

Background: Insight in how impairments and disabilities related to Parkinson's disease (PD) influence health-related quality of life (HRQoL) is required to review adequacy of current management strategies.

Methods: The Scales for Outcomes in Parkinson's disease (SCOPA) evaluation was used to assess impairments and disabilities. HRQoL was assessed with the EuroQoL-5D Visual Analogue Scale. 378 patients with PD who participated in the SCOPA/PROPARK cohort were assessed while on their usual treatment. Multiple linear regression analysis and structural equation modelling were used to construct a model of factors that influence HRQoL.

Results: A model with good fit was constructed that identified various impairments and disabilities as important contributors to HRQoL in PD. Of the disabilities, psychosocial well-being had a larger impact on HRQoL than physical functioning. Of the impairments, depression had the largest contribution to HRQoL, followed by axial motor symptoms, gastrointestinal symptoms, and urinary symptoms. In addition, pain, psychiatric and motor complications, and daytime sleepiness had small but significant influences on HRQoL.

Conclusions: Multiple factors, including disabilities, non-motor symptoms and axial motor symptoms, affect HRQoL in patients with PD. In patients who are on symptomatic treatment aiming to alleviate mainly motor symptoms, there is a large impact on HRQoL of non-motor and non-dopaminergic symptoms. Research is warranted to develop and evaluate management strategies for the aspects that currently impact on HRQoL as psychosocial well-being, depressive symptoms, axial motor symptoms, gastrointestinal symptoms, and urinary symptoms. These findings call for a multidisciplinary approach in the care of these features.

Introduction

Parkinson's disease (PD) is generally known as a movement disorder in which dopamine replacement therapy may alleviate some of the motor symptoms early in the disease but eventually fails with the progression of the disease. However, there is now an increasing awareness that the clinical spectrum is much broader, encompassing also many non-motor features including depression, autonomic dysfunction, cognitive dysfunction, night-time sleep problems and daytime sleepiness.¹ In addition, dopaminergic treatment may induce both motor and psychiatric complications. Together, the debilitating effects of PD and its therapy have a considerable impact on health, physical and psychosocial well-being and are associated with a decrease in health-related quality of life (HRQoL). HRQoL is defined as those aspects of self-perceived well-being that are related to or affected by the presence of disease or its treatment.² Numerous factors impact on HRQoL in PD, including disease severity, disease duration, postural instability and falls, motor complications, depression, anxiety, pain, sleep, cognitive impairment, hallucinations and problems with activities of daily life (ADL).³⁻⁵ However, for some of these factors, like motor complications, studies have yielded inconsistent findings.^{6,7} Furthermore, many studies have explored relations between one or two domains and HRQoL without taking into account the broadness of the clinical spectrum of PD or the complex interplay of domains that make up the pathway that links impairments to disability to HRQoL. The Scales for Outcomes in Parkinson's disease (SCOPA) model is a comprehensive evaluation of PD that is based on the disablement process: a pathway linking impairments, disability and global outcomes of health.⁸ Using the SCOPA evaluation, we aimed to identify which impairments and disabilities contribute to HRQoL and to construct a model based on these disease-specific determinants in PD.

Methods

Study design

The study is part of the "PROfiling PARKinson's disease" (PROPARK) study, a longitudinal cohort study of patients with PD, who are profiled on phenotype,

genotype, disability, and global outcomes of health. Valid and reliable measurement instruments for the different domains of PD were derived from the SCOPA project (www.scopa-propark.eu). Data obtained from the first annual evaluation of 420 patients who were included in the period from May 2003 to March 2006 was used for analysis.

Participants

All patients fulfilled the United Kingdom Parkinson's Disease Society Brain Bank criteria for idiopathic PD.⁹ Age at onset and disease duration are important determinants of disease course in PD and are related to various manifestations of the disease.^{10,11} To obtain an adequate distribution of these characteristics across the cohort, we constructed four strata, based on age at onset (onset of the first symptoms as perceived by the patient (\leq / $>$ 50 years)) and disease duration (\leq / $>$ 10 years). Recruitment stopped if approximately 100 patients per stratum were included. The principal centre (Leiden University Medical Centre (LUMC)) recruited 186 patients (44%), other university hospitals recruited 54 patients (13%) and regional hospitals recruited 180 patients (43%). No other selection criteria were applied. The study was approved by the medical ethical committee of the LUMC and all participants gave informed consent.

Outcome measures

Information was obtained on clinical and sociodemographic variables and included age at onset, disease duration, disease severity measured with the Hoehn and Yahr scale (H&Y)¹², medication, falls in the last year, age, marital stage, educational level, and employment status. Levodopa equivalent (LDE) units were calculated according to the formula described by Esselink.¹³ The following domains were assessed:

Impairments

Motor symptoms and motor complications (SPES/SCOPA, sections motor symptoms (MS) and motor complications (MC))¹⁴, cognitive dysfunction (SCOPA-COG)¹⁵ and Mini Mental State Examination (MMSE)¹⁶, psychiatric complications (modified

version of the Parkinson Psychosis Rating Scale (PPRS): the SCOPA-PC)¹⁷, depressive symptoms (Beck Depression Inventory (BDI))¹⁸, night-time sleep problems (NS) and daytime sleepiness (DS) (SCOPA-SLEEP sections NS and DS)¹⁹, autonomic dysfunction (SCOPA-AUT)²⁰, and pain (Visual Analogue Scale (VAS) for pain). Patients were asked to rate their average pain in the last month on a line ranging from 0 (no pain) to 100 (worst imaginable pain).

Disability

Activities of Daily Living (SPES/SCOPA-ADL)¹⁴ and psychosocial wellbeing (SCOPA-PS).²¹

Quality of Life

HRQoL was measured using the VAS from the EuroQoL (EQ-5D), a generic HRQoL instrument.²² Patients were asked to rate their current health status on a line ranging from 0 (death) to 100 (best imaginable health state).

Except for the SCOPA-COG and the EQ-VAS, higher scores reflect more problems. Data were collected by means of self-report questionnaires (SCOPA-SLEEP NS and DS, SCOPA-AUT, BDI, SCOPA-PS, EQ-VAS, VAS-PAIN), which patients completed at home two weeks before their assessment. Furthermore, a trained researcher assessed the SPES/SCOPA sections MS, MC, and ADL, SCOPA-COG, and the SCOPA-PC. A partner, relative, or caregiver was requested to be present during the examination. The majority of the patients were assessed at the LUMC. To avoid bias towards recruiting less severely affected patients, patients who were unable to come to the hospital were assessed at home.

Statistical analysis

If patients had 25% or more missing data on one of the impairment or disability domains, they were excluded from the analysis. If patients had less than 25% missing data on a scale, the missing data were imputed. For most of the scales, the missing

values were imputed by the mean values of the non-missing items of that patient. Missing values on items addressing sexual problems in the SCOPA-AUT (2 items) and SCOPA-PC (1 item) were imputed by the median value of patients from the same gender and in the same disease duration and age onset group. If only one of the two items addressing sexual problems in the SCOPA-AUT was missing in a particular patient, the non-missing item value was imputed in the missing item. Means and standard deviations for all impairment and disability domains and HRQoL were calculated. Pearson correlations were calculated between all impairment and disability domains and HRQoL. Path analysis was used to test the linkages among model variables.²³

Estimating path coefficients

Using SPSS 14.0, path coefficients were estimated using multiple linear regressions for the following dependent variable in the model: the (1) SPES/SCOPA-ADL and (2) SCOPA-PS as dependent variable and all impairment domains as independent, and (3) the EQ-VAS as dependent variable and all impairment and disability domains as independent variables. Non-significant path coefficients ($p > 0.05$) were excluded from the model.

Multiple linear regressions were also performed using subdomain scores instead of the total score for domains that significantly contributed to the model, in order to get more insight in their contribution. The SPES/SCOPA-MS was divided into the subdomains "bradykinesia-rigidity" (items 3a,b + 4a,b), "tremor" (items 1a,b + 2a,b), and "axial symptoms" (items 5-10). The SPES/SCOPA-MC was divided into "dyskinesias" (items 18 + 19) and "motor fluctuations" (items 20 + 21). The SCOPA-AUT consists of the subdomains "Gastrointestinal" (GI), "Urinary" (UR), "Thermoregulatory" (TR), "Cardiovascular" (CV), "Pupillomotor" (PM), and "Sexual Dysfunction" (SX).

Model fitting

The overall fit of the final model was assessed using the structural equation modelling program EQS 6.1 for Windows.²⁴ Multiple indices can be calculated that show how well the data fit the model. The χ^2 test for goodness-of-fit should be non-significant (indicating that the model does not differ from the data) but is sensitive to sample size. Five other goodness-of-fit indices were evaluated. The Bentler-Bonnet normed fit index (NFI), the non-normed fit index (NNFI), and the comparative fit index (CFI) range between 0 and 1, whereby 0.90 is the minimally acceptable value, with 0.95 being the minimum if the χ^2 test is significant. The root means square error of approximation (RMSEA) estimates the lack of fit in a model compared to a perfect model; above 0.1 indicates a poor fit, under 0.08 indicates a reasonable fit, and under 0.05 indicates a good fit.²⁵ The standardized root mean square residual (SRMR) indicates good fit if the value is less than 0.08.²⁶ To evaluate the influence of disease duration and age at onset in the model, the path analysis was performed in two subgroups based on disease duration (disease duration shorter or longer than 10 years) and two subgroups based on age at onset (age at onset under or above 50 years). Although it would be interesting to perform the analysis in the four strata based on disease duration and age at onset, the sample size is too small to perform a path analysis.²⁷

Results

Patients

Forty-two patients (10%) had more than 25% missing data in one of the scales and were excluded from the analysis. Complete data was obtained from 378 PD patients (66% men). The mean (SD) age was 60.0 (11.2) years and the mean (SD) disease duration was 10.2 (6.4) years (Table 1). Patients who were excluded from the analysis because of missing data were significantly older, were more often female, had longer disease duration, a higher H&Y stage, more impairment on all domains, more disability and a lower HRQoL.

domain. The impairment domains depressive symptoms, psychiatric complications, motor symptoms, and autonomic dysfunction explained 58% of the variance in the PS domain. The disability domains ADL and PS and the impairment domains pain and depressive symptoms together explained 43% of the variance in the HRQoL. Two impairment domains that did not significantly contribute to this model were cognitive dysfunction and night-time sleep problems.

Table 2. Outcome measures

Domain	Outcome measure (scale range)	Mean (SD)
Impairments		
Motor symptoms	SPES/SCOPA-MS (0-42)	13.1 (4.6)
Motor complications	SPES/SCOPA-MC (0-12)	1.6 (2.4)
Cognitive dysfunction	SCOPA-COG (0-43)	26.2 (5.9)
Depressive symptoms	BDI (0-63)	9.8 (6.3)
Autonomic dysfunction	SCOPA-AUT (0-69)	17.5 (8.4)
Psychiatric complications	SCOPA-PC (0-18)	2.0 (1.9)
Night-time sleep problems	SCOPA-SLEEP NS (0-15)	4.4 (3.7)
Daytime sleepiness	SCOPA-SLEEP DS (0-18)	4.7 (3.7)
Pain	VAS-PAIN (0-100)	28.8 (25.2)
Disabilities		
ADL	SPES/SCOPA-ADL (0-21)	8.6 (3.3)
Psychosocial function	SCOPA-PS (0-33)	8.4 (4.9)
Global measures of health		
Health related Quality of Life	EQ-VAS (0-100)	67.8 (14.2)

SPES/SCOPA-MC: SPES/SCOPA motor complications; BDI: Beck Depression Inventory; SCOPA-PC: SCOPA-Psychiatric Complications; SCOPA-SLEEP NS: SCOPA-SLEEP Night-time sleep; SCOPA-SLEEP DS: SCOPA-SLEEP Daytime sleepiness; SPES/SCOPA-ADL: SPES/SCOPA Activities of Daily Living; SCOPA-PS: SCOPA-Psychosocial functioning; EQ-VAS: EuroQol-Visual Analogue Scale

Table 3. Pearson correlation matrix of impairment and disability domains and health-related quality of life

	EQ-VAS	SPES/SCOPA-ADL	SCOPA-PS
SPES/SCOPA-MS	-0.33 ¹	0.67 ¹	0.42 ¹
SPES/SCOPA-MC	-0.28 ¹	0.37 ¹	0.26 ¹
SCOPA-COG	0.24 ¹	-0.27 ¹	-0.20 ¹
BDI	-0.56 ¹	0.31 ¹	0.69 ¹
SCOPA-AUT	-0.40 ¹	0.54 ¹	0.57 ¹
SCOPA-PC	-0.31 ¹	0.38 ¹	0.42 ¹
SCOPA-SLEEP NS	-0.33 ¹	0.16 ²	0.38 ¹
SCOPA-SLEEP DS	-0.19 ¹	0.32 ¹	0.28 ¹
VAS-PAIN	-0.28 ¹	0.18 ¹	0.18 ¹
SPES/SCOPA-ADL	-0.42 ¹	-	0.51 ¹
SCOPA-PS	-0.59 ¹	0.51 ¹	-

¹: correlation is significant at the 0.001 level

²: correlation is significant at the 0.01 level

SPES/SCOPA-MC: SPES/SCOPA-motor complications; BDI: Beck Depression Inventory;

SCOPA-PC: SCOPA-Psychiatric Complications; SCOPA-SLEEP NS: SCOPA-SLEEP Night-time sleep; SCOPA-SLEEP DS: SCOPA-SLEEP Daytime sleepiness; SPES/SCOPA-ADL:

SPES/SCOPA-Activities of Daily Living; SCOPA-PS: SCOPA-Psychosocial functioning;

EQ-VAS: EuroQol-Visual Analogue Scale

To evaluate if the exclusion of subjects with missing values contributed to removal of cognition and sleep from the model, we compared the groups with T-tests and calculated correlations with the EQ-VAS for both groups. Patients excluded from the analysis had significant lower SCOPA-COG scores (20.8 (7.2) versus 26.2 (5.9) $p=0.000$) and higher SCOPA-SLEEP NS scores (6.0 (4.0) versus 4.4 (3.7) $p=0.010$). However, the correlation between SCOPA-COG and EQ-VAS was the same for both groups, $r=0.24$, whereas the correlation between the SCOPA-SLEEP NS and EQ-VAS was lower for the group that was excluded ($r=-0.33$ versus $r=-0.08$).

Model evaluation

The overall fit of the final model that encompassed only the significant paths was assessed using EQS. The χ^2 test was significant, which was expected given the large sample size. The other fit indices, however, fulfilled the cut-off criteria of a good model fit (Table 4). Except for depressive symptoms and pain, which have a direct influence on HRQoL, most impairment domains have an indirect relation through the disability level (Figure 1).

Table 4. Summary of final model fit statistics

χ^2 (df)	27.808 (12) p=0.006
NFI	0.979
NNFI	0.955
CFI	0.988
SRMR	0.021
RMSEA (90% CI)	0.059 (0.030-0.088)

χ^2 : model chi-square value; df: model degrees of freedom; NFI: Bentler-Bonett normed fit index; NNFI: Bentler-Bonett non-normed fit index; CFI: Bentler's comparative fit index; SRMR: standardized root mean square residual; RMSEA: root mean square error of approximation; CI: confidence interval around RMSEA

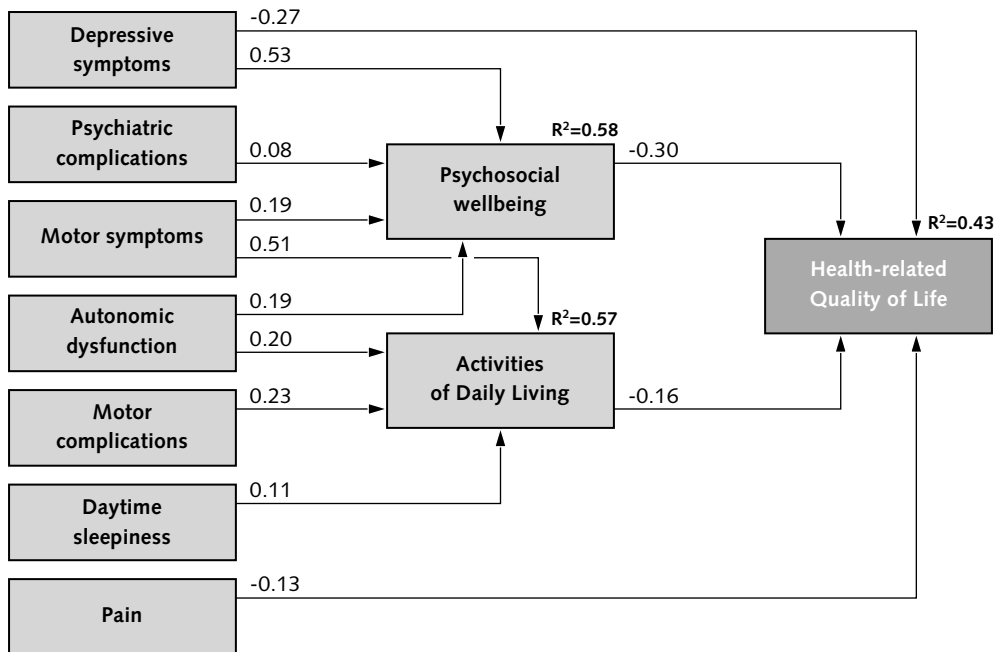
Depressive symptoms had the largest contribution to HRQoL, which was established through a direct relation with HRQoL and an indirect relation via the PS domain. Motor symptoms and autonomic dysfunction had indirect relations with HRQoL through both the PS and ADL domains. The indirect relation from psychiatric complications occurred through the PS domain, whereas the indirect relation of daytime sleepiness and motor complications occurred through the ADL domain.

Model evaluation with subdomains

“Axial symptoms” was the only motor subdomain that contributed significantly to the PS domain and explained 31% of the variance. All three motor subdomains contributed significantly to the ADL domain explaining 60% of the variance, in which

axial symptoms had the largest contribution and tremor the smallest contribution. Both motor fluctuations and dyskinesias contributed significantly to the ADL domain, explaining 14% of the variance. Only the subdomains GI, UR and PM of autonomic dysfunction contributed significantly to the ADL domain, and explained 32% of the variance. The subdomains GI, TR, UR, and CV contributed significantly to the PS domain, explaining 33% of the variance in the PS domain. The GI and UR subdomains were the most important contributors to both the PS and ADL domain.

Figure 1. Model of health-related quality of life in PD



All path coefficients are statistically significant at $p=0.05$. Covariances between impairment domains are not shown for reason of readability.

Model evaluation in subgroups

The path analysis was also performed in two subgroups based on disease duration (disease duration shorter or longer than 10 years) and two subgroups based on age at onset (age at onset under or above 50 years) (Table 5). The models that emerged for

each group were very similar. Compared to the model that was based on all patients, the models for all four groups (the two subgroups based on age at onset and the two subgroups based on disease duration) lost the contribution of psychiatric complications to PS, and for all but the group of patients with age onset under 50 years, lost the contribution of DS to ADL (Table 5). Differences consisted of the loss of a significant direct relation from pain and ADL to HRQoL in patients with a disease duration longer than 10 years. In the group of patients with an age at onset under 50 years, a direct relation from ADL to HRQoL was also not found, but a direct relation from motor complications to HRQoL was present. In addition to the contribution of motor symptoms, motor complications, and autonomic dysfunction to ADL that was shared by all subgroups, DS was included for patients with an age at onset under 50 years, whereas psychiatric complications was present in patients with an age at onset above 50 years.

Table 5. Significant domains in path analysis in PD subgroups

	Disease duration		Age onset	
	< 10 year	> 10 year	< 50 year	> 50 year
N	205	173	204	174
PS	Depression	Depression	Depression	Depression
	Autonomic	Autonomic	Motor	Autonomic
	Motor	Motor	Autonomic	Motor
	R² = 0.64	R² = 0.51	R² = 0.62	R² = 0.56
ADL	Motor	Motor	Motor	Motor
	Autonomic	Autonomic	MC	Autonomic
	MC	MC	Autonomic	MC
			DS	PC
	R² = 0.44	R² = 0.58	R² = 0.56	R² = 0.59
HRQoL	PS	PS	PS	PS
	Depression	Depression	Depression	ADL
	Pain		MC	Depression
	ADL		Pain	Pain
	R² = 0.44	R² = 0.40	R² = 0.42	R² = 0.51

PS: Psychosocial functioning; ADL: Activities of Daily Living; HRQoL: Health-related quality of life; MC: motor complications; PC: Psychiatric complications; DS: daytime sleepiness

Discussion

HRQoL represents the overall experienced impact of the disease and its consequences on a person's wellbeing. Some diseases are expressed in one impairment domain, and their impact on disability and HRQoL is generally straightforward. PD, however, is characterized by a broad spectrum of primary disease-related motor and non-motor manifestations. On top of these primary PD-related impairments, medical interventions may induce motor or psychiatric complications or DS. The impact of PD on patients' HRQoL is thus determined by the complex interaction of the motor and non-motor symptoms of the disease, the consequences of therapy and the functional consequences of the disease. This study shows that HRQoL in PD can be described by a good fitting model that disentangles the contributions of components in the pathway that links impairments and disabilities to HRQoL. Interestingly, on the disability level, the influence of the PS domain on HRQoL was larger than that of the ADL domain, underscoring the importance of psychosocial functioning in HRQoL of patients with PD.

Most impairments exerted an indirect influence on HRQoL through one or both of the disability domains. Pain was the only impairment domain with only a direct influence on HRQoL and its impact on HRQoL has been reported earlier.⁵ In line with other studies²⁸⁻³⁰, our study highlights that depressive symptoms had the largest contribution to HRQoL, which was portrayed in our model by a direct influence on HRQoL as well as an indirect influence through the PS domain. As depressive symptoms have now been highlighted repeatedly as the main contributor to HRQoL in PD, it remains surprising that in both patient management and trials, depression is insufficiently prioritized. Both daytime sleepiness and motor complications were only related to ADL whereas autonomic dysfunction contributed to both physical (ADL) and psychosocial (PS) functioning. Within the autonomic domain, gastrointestinal and urinary symptoms had the largest influence on HRQoL. Within the motor complications, both motor fluctuations and dyskinesias were significant contributors to HRQoL.

Motor symptoms had only indirect relations with HRQoL through both disability domains, and its total contribution to HRQoL was less than that of depression. Of motor symptoms, axial symptoms had the largest influence on both psychosocial and physical functioning. Motor symptoms and ADL, which until recently dominated the content of assessment scales in PD, were not the main contributors to HRQoL in patients with PD. However, it is important to keep in mind that dopaminergic replacement therapy aiming to alleviate part of the motor symptoms is the mainstay treatment of PD. It can be assumed that the contributions to the total model on HRQoL in PD would have been different, if this treatment had not been available. The impact of dopaminergic therapy on the model is further underscored by our finding that "axial symptoms", which are mainly of non-dopaminergic origin, had the largest influence on both the PS and ADL domains.

Neither cognition nor night-time sleep, contributed to HRQoL. Consistent with former studies^{31,32}, the univariate correlations between HRQoL and night-time sleep problems ($r=-0.33$), and between HRQoL and cognitive dysfunction ($r=0.24$) were significant, but their influence disappeared in the final model. It is likely that the strong association between night-time sleep problems and depressive symptoms ($r=0.49$) resulted in the exclusion of night-time sleep problems from the model.³³ The finding that cognition does not play a role in HRQoL is surprising, but robust, as two other studies have revealed similar results in multiple linear regression analysis.^{34,35} Contrary to night-time sleep problems, cognitive dysfunction was in this study not strongly correlated to other domains of PD (all $r < 0.40$) and therefore the question remains how this finding can be explained. One explanation could be that cognitive decline was of little importance in this cohort. Patients with more cognitive impairment could have been excluded because of missing values. Although patients excluded from the analysis were indeed more cognitively impaired, they also had a worse HRQoL and the correlation between cognition and HRQoL was the same in both groups. Although cognition is impaired in 33% of the cohort as compared to age- and education-matched controls³⁶, only 9% of the patients had an MMSE score < 24 .

It would be possible that the fact that the EQ-VAS is self-administered makes the data in cognitively impaired patients less valid. However, an independent samples T-test showed that the mean (SD) values of the EQ-VAS of the MMSE \geq 24 group (68.8 (13.4)) differs significantly from the MMSE $<$ 24 group (57.7 (17.3) $p=0.000$). As the cognitive impaired group exhibited a significantly worse HRQoL, as would be expected, the validity of the assessments appears to be in order. Another explanation could be that the cognitive assessment describes the current cognitive status and this does not automatically reflect cognitive decline since the premorbid variance of normal cognition is large. For most other domains, like motor symptoms or psychiatric complications, a score of zero is expected before the onset of PD and a higher score therefore implies more severe problems. A longitudinal study that assesses the influence of change in cognition in relation to change in HRQoL is necessary to obtain more insight in this issue.

The HRQoL model that was constructed appears robust, as it largely remained the same when evaluated in subgroups with a short and long disease duration and with a lower and higher age at onset. Depressive symptoms, psychosocial well-being, and autonomic dysfunction apparently remain important contributors to HRQoL along the course of the disease. The most prominent difference between the models of the two subgroups based on disease duration and the subgroup based on lower age at onset is the lack of a significant contribution of ADL to HRQoL in patients with a long disease duration.

We chose to use a generic instrument because we were specifically interested in overall HRQoL. Several disease specific HRQoL measures for PD have been developed to measure aspects of health that are of particular concern to patients with PD, for instance the Parkinson's Disease Questionnaire (PDQ-39).³⁷ However, because such measures encompass items that address specific aspects associated with PD, this would thereby increase the association between HRQoL and these clinical domains. In view of the objectives of this study, we therefore used a generic instrument, the EQ-VAS. The EQ-VAS has been extensively validated, is easy to complete, and has been found useful in a PD population.³⁸

A limitation of the study was the selective exclusion of patients with too many missing values. In addition, the stratification of the cohort based on age at onset and disease duration and the high recruitment of patients from academic hospitals (57%) may make the group less representative of the PD community. However, separate analyses in groups based on disease duration and age at onset did not show clear differences in the models. Apparently, even though the severity of the problems may differ between the groups, the relation between domains remain constant. Furthermore, the remaining group of patients was still large and reflected the full spectrum of PD, with a mean disease duration of 10 years and disease stages ranging from H&Y stage 1 to 5. The model incorporates only disease-specific aspects that explain 43% of the variance in HRQoL. This implies that other aspects not incorporated in the model play a role as well. Educational level, mastery, or psychological adjustment have indeed been described to impact on HRQoL in PD.^{34,39,40} Incorporating more variables in the model would, on the one hand, increase the amount of explained variance but conversely decrease the comprehensibility of the model. The main objective of this study was to evaluate the contribution of disease-specific factors to HRQoL, so as to highlight issues that require further attention in the management of patients with PD. Indeed, multiple factors affect HRQoL in patients with PD on symptomatic treatment. Research is warranted to develop and evaluate management strategies for the aspects that currently impact on HRQoL as psychosocial well-being, depressive symptoms, axial motor symptoms, gastrointestinal symptoms, and urinary symptoms. These findings call for a multi-disciplinary approach in the care of these features.

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