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Review

Quality of Life and Related Concepts in Parkinson’s Disease: A Systematic Review

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Abstract: Several studies have investigated the quality of life (QOL) of patients with Parkinson’s disease (PD). The purpose of this study was to review the conceptual and methodological quality of quality of life (QOL) studies among patients with PD and to identify factors associated with poor (HR)QOL. Computerized bibliographic databases were screened for publications from 1960 to January 2007. According to a list of predefined criteria, the methodological quality of the 61 studies was moderate. The term ‘QOL’ was often used inappropriately. In fact, almost all studies in this review actually assessed health status (HS) instead of QOL. The functioning of patients with PD on physical, social, and emotional domains is affected by PD. Their HS seems to be lower when compared to healthy persons or patients with other chronic diseases. HS studies augment the insight in self-perceived functioning. Therefore, HS is conceived as a valuable construct. However, QOL is also an important factor in health care. Attention towards QOL is needed in order to draw valid conclusions regarding a person’s subjective experience of well-being in a broad sense. In order to accomplish this, future studies should apply the QOL concept with more rigor, should use an adequate operational definition, and should employ sound measures. © 2007 Movement Disorder Society

Key words: Parkinson’s disease; quality of life; health-related quality of life; health status; systematic review.

INTRODUCTION

Nowadays, the physical consequences of PD are well described. 1 Therefore, the focus has shifted to the measurement of patient-based outcomes in order to assess (1) the impact of the disease and (2) the efficacy of inter-

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formulated by the World Health Organization Quality of Life Group (WHOQOL Group) follows this principle by defining QOL as “an individual’s perception of his/her position in life in the context of the culture and value systems in which he/she lives and in relation to his/her goals, expectations, standards and concerns. It is a broad-ranging concept incorporating in a complex way the person’s physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of the environment” (p. 1405).5

Some researchers have proposed the concept of HRQOL in order to narrow the QOL concept. HRQOL focuses on QOL in relation to the impact of disease and treatment on patients,6 the physical, emotional and social well-being after diagnosis and treatment,7 but also on a combination of objective functioning and more subjective perceptions of health.8 Thus, HRQOL is QOL, but less broadly formulated.9 Full consensus on a single definition of HRQOL remains illusive.10 On the one hand, many researchers and clinicians see HRQOL as a concept containing both objective and subjective dimensions (e.g. Ref. 8). In doing so, however, HRQOL is actually predominantly referring to perceived HS, as can be learned from an inspection of the items of some well-known HRQOL instruments like the SF-36 or the Nottingham Health profile.11 In contrast, others emphasize that HRQOL should reflect a purely subjective experience. For instance, Patrick and Erickson12 formally define HRQOL in terms of the value assigned to opportunities, perceptions, functional status, impairment and death, associated with events or conditions as influenced by disease, injuries, treatments or policy. In spite of the fact that some authors use the term HS to include HRQOL (e.g. Ref. 13) or the term HRQOL to include HS (e.g. Ref. 14), there is a growing agreement that the two concepts should be clearly distinguished.12 For instance, meta-analytic results indicate that, from the perspective of patients, HRQOL and HS are distinct constructs.2 Therefore, we are strongly in favor of the position not to use HRQOL as an umbrella term for various desired medical outcomes.15 HS refers to perceived health in terms of physical and mental symptomatology, social conditions or functions, not to internal experiences. HS represents the impact of health on one’s ability to perform a variety of physical, emotional and social activities.16 In contrast, QOL represents reflections of the way that patients “perceive and react to their health status and to other, nonmedical aspects of their lives” (p. 619).17 Therefore, HS is at best a factor that may influence (HR)QOL and therefore should be conceived of as a predictor of (HR)QOL, not as part of it.

In conclusion, HS refers to function levels, while QOL and HRQOL reflect internal experiences.9,16 As a consequence, HS questionnaires contain items about actual patients’ functioning (e.g., “Due to Parkinson’s disease, how often did you have problems walking half a mile?”), HRQOL questionnaires focus on the subjective evaluation of health (e.g., “How satisfied are you with your abilities?”), while QOL questionnaires exceed the health domain by focusing on the subjective evaluation of life as a whole (e.g., “How would you rate your overall quality of life?”). Therefore, HS questionnaires are often emphasizing the frequency of certain behaviors, feelings, or social activities. In contrast, (HR)QOL questionnaires use scales assessing the level of satisfaction with activities and life conditions.4

Almost 20 years ago, Mor and Guadagni18 compared the conceptualization and measurement of QOL with the tower of Babel. Recently, Schrag19 still had to conclude that assessments are often called QOL while in fact a much narrower concept was measured. Taking this into account, the purpose of the current study was to appraise the conceptual rigor in published (HR)QOL studies in the field of PD.

METHODS

Search Strategy

A computerized search of the literature for the period 1960 to January 2007 was performed in Pubmed (692 hits), PsychINFO (172 hits), the Cochrane Library (37 hits), and Web of Science (415 hits). The term “Parkinson’s disease” was used in combination with the key term “quality of life” (including the related terms “health-related quality of life” and “health status”). Reference lists of relevant retrieved studies were checked in order to identify additional published research that was not found in the computerized database searches. After applying the selection criteria (see later) to these articles and their reference articles, 61 studies remained.

Selection Criteria

All studies were included that met the following criteria: (1) the objective was to describe QOL in PD with QOL questionnaires and/or questionnaires on related concepts; (2) the study population either exclusively concerned Parkinson’s disease or included an identifiable and separately analyzed subgroup of patients with Parkinson’s disease; (3) QOL or related concepts were measured with a standardized questionnaire; (4) studies contain at least a physical, psychological and social dimension, reflecting the WHO definition of health20; (5) the article was a full report published in English, Dutch,
or German, and (6) studies were published in peer-reviewed journals. The primary objectives of the selected studies in this review were to evaluate (HR)QOL in PD, to relate demographic and/or clinical factors to (HR)QOL (Supp. Table 1), and to assess the influence on (HR)QOL of neurosurgery (Supp. Table 2) and medication (Supp. Table 3).

The described inclusion criteria were applied to the initial 1316 hits (of which 83 were duplicates). Sixty-eight articles met the criteria, based on titles of articles and abstracts. Hard copies were obtained of almost all studies. Not-retrieved studies\(^1\) could not be fairly judged and were excluded from this review. After inspection of the hard copies, 61 articles met our selection criteria and were included in this review.\(^2\) 82

The quality of studies is shown in the Supplemental Tables 1–4. The quality scores ranged from 6 (low quality) to 12 points (high quality). The mean quality score was 10. Methodological shortcomings mainly concerned the following items: the definition of (HR)QOL and/or HS (item A), reasons for choosing measurement instruments (item B), the distinction between (HR)QOL and HS (item C), also items based on a list of criteria, especially developed for reviewing QOL studies.\(^3\) The criteria are presented in Table 1.

Each item of a selected study, which met our criteria, was assigned one point. If an item did not meet a particular criterion or was described insufficiently or not at all, no point was assigned. The highest possible score was thus 17. Studies scoring 70% or more of the maximum attainable score (i.e. \( \geq 12 \) points) were considered to be of “high quality.” Studies scoring between 50% and 70% were rated as “moderate quality.” Studies scoring lower than 50% were considered as “low quality” studies.

Findings were consistent if \( \geq 75\% \) of the studies that investigated a particular factor showed the same direction of the association. We defined four levels of evidence\(^4\) (See Table 2).

### RESULTS

#### Study Characteristics

The main findings are summarized in Supplemental Tables 1–3, available online at http://www.interscience.wiley.com/jpages/0885-3185/suppmat.

In studies reporting the influence of neurosurgery on HS, the study size was often small. Overall, sample size ranged from five\(^5\) to 1020 patients.\(^6\)

Almost all studies were cross-sectional, except for 22 studies. Eighteen of these 22 studies were studying the effects of medical treatment on HS.

Most studies described at least two demographic and clinical variables of interest. Age and sex were the most frequently included demographic variables, while the clinical variables were commonly represented by the age at onset, duration of symptoms, medication use, scores on the Hoehn and Yahr scale (H&Y),\(^8\) the Unified Parkinson’s Disease Scale (UPDRS),\(^9\) and/or the Schwab and England scale.\(^10\)

#### Methodological Quality

The evaluation of the methodological quality of the 61 studies yielded the following results. There was disagreement (less than 5%) between the two reviewers when scoring the articles, mainly due to differences in applying the criteria B, F, and P. These disagreements were solved through discussion in a consensus meeting. The quality of studies is shown in the Supplemental Tables 1–4. The quality scores ranged from 6 (low quality) to 12 points (high quality). The mean quality score was 10. Methodological shortcomings mainly concerned the following items: the definition of (HR)QOL and/or HS (item A), reasons for choosing measurement instruments (item B), the distinction between (HR)QOL and HS (item C),

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\(^1\) Articles could not be ordered by Dutch libraries; authors involved were not reachable by e-mail.
potential prognostic factors (item G), participation and response rates for patient groups (item H), information about nonresponders versus responders (item I), study size (item J), longitudinal design (item L), a follow-up period of at least 6 months (item N), and the loss to follow-up (item O). In the next paragraphs, an overview is provided of our findings.

**Appraisal of the Conceptual Rigor of Published Studies**

More than half of the studies included in this review did not describe any of the QOL-specific criteria (A-C). Twenty-five studies discussed (HR)QOL by giving a full definition or by describing the characteristics of (HR)QOL, i.e., the importance of the patient’s view and/or the domains of QOL.

**TABLE 1. List of criteria for assessing the methodological quality of studies on quality of life among patients with Parkinson’s disease**

<table>
<thead>
<tr>
<th>Positive if with respect to QOL assessment</th>
</tr>
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<tbody>
<tr>
<td>A. A description is given of (HR)QOL and/or health status by describing at least the domains and/or the importance of the subjective experience of the patient.</td>
</tr>
<tr>
<td>B. A reason is given for choosing a certain questionnaire.</td>
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<tr>
<td>C. A distinction is made between (HR)QOL and HS.</td>
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<th>Study population</th>
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<tr>
<td>D. A description is included of at least two socio-demographic variables (e.g., age, sex, employment status, educational status, etc.).</td>
</tr>
<tr>
<td>E. A description is present of at least two clinical variables (e.g., duration of symptoms, use of medication, UPDRS score, etc.).</td>
</tr>
<tr>
<td>F. Inclusion and/or exclusion criteria are provided.</td>
</tr>
<tr>
<td>G. The study describes potential prognostic factors by using multivariate analyses or structural equation modeling.</td>
</tr>
<tr>
<td>H. Participation rates for patient groups are described and these rates are exceeding 75%.</td>
</tr>
<tr>
<td>I. Information is given about the ratio non-responders versus responders.</td>
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<table>
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<tr>
<th>Study design</th>
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<tr>
<td>J. The study size is consisting of at least 50 patients (arbitrarily chosen).</td>
</tr>
<tr>
<td>K. The collection of data is prospectively gathered.</td>
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<tr>
<td>L. The design is longitudinal (more than 1 year).</td>
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<tr>
<td>M. The process of data collection is described (e.g., interview or self-report, etc.).</td>
</tr>
<tr>
<td>N. The follow-up period is at least 6 months.</td>
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<tr>
<td>O. The loss to follow-up is &lt;20%.</td>
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<tr>
<th>Results</th>
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<tr>
<td>P. The results are compared between two groups or more (e.g., health population, groups with different severity of PD or age) and/or results are compared with at least two time points (e.g., longitudinally or pre- versus post-treatment).</td>
</tr>
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</table>

<table>
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<tr>
<th>Outcome measures</th>
</tr>
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<tbody>
<tr>
<td>Q. A psychometrically sound (health-related) quality of life or health status questionnaire is used.</td>
</tr>
</tbody>
</table>

One study made a distinction between (HR)QOL and HS. However, all studies claimed to measure (HR)QOL. According to the definitions as outlined in the introduction, all studies actually assessed HS, except for two studies. QOL was assessed by means of the World Health Organization Quality of Life instrument-BREF (WHOQOL-BREF) and the Schedule for Evaluation of Individual Quality of Life (SEIQoL). HS was measured by means of four generic and three disease-specific questionnaires. One study discussed HS by using several questionnaires covering the physical, psychological, and social domain.

Fourteen studies included reasons for choosing a specific measurement by stating that the questionnaire was widely used in the field of PD and/or by describing its adequate psychometrics. In our opinion, the description of a selection procedure should include more. Numerous HS instruments are available nowadays, all of them have adequate psychometrics (e.g., Ref. 91). Therefore, stating that a questionnaire is widely used does not rule out other potential questionnaires.

**Quality of Life Among Patients With Parkinson’s Disease**

Two studies examined the QOL in patients with PD by means of the WHOQOL-BREF and the SEIQoL. Schestatsky et al. found that the duration of disease was negatively associated with psychological health, while...
the severity of disease correlated negatively with perceived quality of social relationships. Lee et al. compared the PDQ-39 with the SEIQoL. The only predictor of QOL in patients with PD was depressive symptoms, while HS was predicted by disease stage, the number of symptoms, and depression.

Health Status Among Patients With Parkinson’s Disease

In the majority of studies, PD patients reported a diminished HS when compared with healthy controls and groups of patients with other diseases, like diabetes mellitus or multiple sclerosis. Gage et al. concluded that the HS in PD veterans was lower compared to depressive veterans and veterans with spinal cord injury, congestive heart failure, stroke, chronic low back pain, arthritis, diabetes mellitus, angina/coronary heart disease, and depressive persons. Only veterans with spinal cord injury reported a slightly lower level of physical functioning and depressed veterans scored lower on mental functioning when compared to veterans with PD.

Specific symptoms can be related to the diminishing experience of HS. Herlofson and Larsen studied the differences between PD patients by splitting the group in persons with and without fatigue. Patients with fatigue scored not only worse on physical functioning, but also on emotional and social functioning when compared with patients without fatigue. Sweating, another symptom reported by patients with PD, was studied by Swinn et al. They concluded—although no significant associations between sweating and HS were found—that excessive sweating can have a considerable impact on patients’ lives. Most patients felt uncomfortable, and some felt embarrassed or reported that they were limited in their social activities.

Another study investigated potential differences between younger patients and older patients with PD. Younger patients were experiencing more problems with respect to stigmatization, availability of social support, and cognitive functioning compared with the older ones.

HS After Neurosurgery

All studies among PD patients reported HS improvements after neurosurgery. In general, these studies found that patients improved on physical functioning (e.g., mobility, activities of daily living, and bodily discomfort), emotional functioning, and social functioning (e.g., stigmatization).

One study randomly assigned patients to either a transplant or a sham surgery. The investigators showed that there was a placebo effect, when persons thought that they had transplantation, but in fact had been assigned to the sham surgery. In all cases, those who thought that they had received the transplant reported better HS scores. They reported, for instance, more interaction in the social domain, compared to the “real” surgery group.

All studies used a prospective design. One study used a prospective as well as a retrospective design to describe the effects of neurosurgery on HS and reported inconsistent findings. In the prospective assessment, patients perceived a general improvement of their HS after surgery, while assessing retrospectively the same patients did not report significant HS improvements at all. In other words, they seem to overestimate their preoperative functioning.

HS and Use of Medication

Seven studies investigated HS in combination with specific medications. Different study designs were used. Two studies used a placebo group in order to determine the effect of tolcapone or rasagiline on HS. Both studies concluded that medication improved the HS of patients. The placebo-group showed no effects. Three studies found no significant improvements after drug treatments.

Predictors of HS

The predictors of demographic variables as well as disease characteristics were determined. More specifically, demographic (age, sex, education), psychological (depression, feelings of optimism, psychological adjustment, satisfaction with PD diagnosis), and disease variables (clinical stage/disease severity, use of medication, number of reported symptoms, the presence of specific symptoms, medication/neurosurgery) were investigated. Strong evidence was found for the predictive value of depressive symptoms and the level of independence in the domain of activities of daily functioning as measured by the Schwab and England scale. Fourteen studies investigated depression as predictor, all of them found evidence for its predictive value. Four studies assessed the ability to perform activities of daily functioning as a predictor of HS. Moderate evidence was found for the predictive value of self-reported insomnia, levodopa use/medication, and surgery. For instance, Caap-Ahlgren and Dehlin investigated the influence of insomnia on HS, because of its high prevalence rates. They found that patients who reported problems to fall...
asleep, a disturbed sleep, or early in the morning awakening, also reported poorer physical and emotional functioning as well as poorer general health. Predictors with weak evidence were, postural instability and gait function. Inconclusive evidence, that is, too few studies investigated the following predictors or inconsistent findings were reported, was found for the demographic variables: sex, age, and education. Disease related variables with a weak level of evidence were duration of disease, morbidity, motor complications/physical functioning, dyskinesia, bradykinesia, clinical fluctuations, pain, clinical stage/disease severity (H&Y), tremor, UPDRS, cognitive impairment, and number of reported symptoms. Other factors investigated for their prognostic value were expenses related to disease, psychological adjustment, satisfaction of the (explanation of the condition at) diagnosis of PD, mental health symptoms, and current feelings of optimism. A lot of variables provide inconclusive evidence for an association with HS. Therefore, more research is needed to draw more definite conclusions on these variables.

**DISCUSSION**

The purpose of the current study was to appraise the conceptual rigor in published QOL studies in the field of PD. Additionally, data was presented on factors associated with impaired outcome in PD.

In general, PD patients suffer from a wide range of symptoms, probably affecting QOL, but definitely influencing self-perceived HS as this review points out. Most studies claimed the assessment of (HR)QOL. However, according to the definitions used in this review, almost all studies actually reported results on HS. As outlined before, in HS studies, patients are asked to indicate their level of physical, emotional, and social functioning. Patients are not questioned on their life satisfaction nor on how much they are bothered by their limitations. Preliminary QOL findings suggest that the duration and the severity of disease are negatively influencing the QOL-domains Psychological Health and Social Relationships, respectively. Lee et al. asked patients to indicate those life-areas that were of eminent importance to them. They found that the majority of patients nominated family as the most important life area. In this study, QOL seems to be more determined by psychosocial issues than by physical ones. This idea was supported when the PDQ-39 and the SEIQOL were compared. The PDQ-39 domains that were predictive of the SEIQOL-index were the social support, cognitive impairment, and emotional domains. QOL of PD patients was predicted by depressive symptoms, while HS in this population was predicted by the stage of disease. With regard to HS, it can be concluded that PD patients experience a lower HS when compared to healthy controls or patients with other chronic diseases. Besides a declined functioning in the physical domain, patients also experience a diminished social and emotional functioning. Prudence is necessary when conclusions are drawn based on diminished functioning and its relation to QOL. Some studies found that QOL can be maintained or even improved when patients experience a life-threatening or progressive illness.

QOL is an important factor in health care, because it is thought to be influenced by the type of treatment the patient receives. When professionals advise patients regarding the (dis)advantages of a certain treatment modality, it is important to have knowledge of the results of QOL studies in PD and to know which factors are prognostic for a patient’s well-being. Several articles reported outcomes on potential predictors of HS. It seems that having depressive symptoms is a strong predictor for experiencing a lower HS. The same applies for being dependent on other persons. Overall, the level of evidence of potential predictors with regard to QOL was predominantly weak or even inconclusive.

There are several obvious shortcomings in the set of available studies. Demographic and clinical variables should be more extensively and uniformly described in future studies. Most frequently reported demographic variables were age and sex, while marital status, educational levels, and employment status, could also be possible predictors of HS, as well as QOL (e.g. Ref. ). Clinical variables are reported in various ways. In order to compare studies with each other, however, it will be necessary to have some form of uniformity. By the implementation of additional qualitatively good studies, more clarity with respect to the HS and QOL of patients with PD could be achieved.

Based on the works of Gill and Feinstein, Moons et al., Van der Steeg et al., we suggest implementation of the following recommendations when designing future studies. First, determine whether (HR)QOL or HS is the subject of interest. If the study objectives focus on merely the functional consequences of PD, the use of HS instruments is sufficient to answer the research question at hand. If the study aims to describe how much a patient with PD is bothered by these limitations in life, (HR)QOL instruments are needed. If both objectives are present, then both types of instruments should be represented in the test booklet. Second, provide an explicit definition of the concept of interest. Because a uniform definition of QOL does not exist and related concepts are often erroneously used interchangeably, it is
important to be very explicit about the employed concepts; not only for directing the study design, but also to give other scientists and clinicians insight in what is measured in the study. In addition, QOL measurements can only be evaluated if QOL is explicitly defined. Therefore, simply referring to the existence of a wide variety of definitions or describing relevant components of QOL is not enough to clarify the concept. Third, the selection of instruments should be based on systematic reasoning and, therefore, will depend on the study aims and the way (HR)QOL and/or HS is conceptualized. According to the definition of QOL used in this review, QOL can, for instance, be measured using the generic instruments World Health Organization Quality of Life—100 items (WHOQOL-100) and WHOQOL-BREF, SEIQOL or with a movement disorder-specific instrument, like the Questions of Life Satisfaction scale. Regularly, the rationale for using a specific questionnaire is that it is widely used. Of course, widely used instruments make comparison between studies a lot easier, but there are other aspects of importance when selecting an instrument. The first aspect is whether to choose a generic or PD-specific instrument. Both types of instruments have advantages and disadvantages (see for a detailed overview Patrick and Deyo). Make sure, by inspecting several questionnaires that may be used, that the selected questionnaires measure the concept you are interested in. It should also be kept in mind that instruments which measure a certain concept, like HS, differ considerably from one another. For example, cognitive functioning is only a topic in the Parkinson’s Disease questionnaire-39 items (PDQ-39) and Parkinson’s Disease Quality of Life (PDQL), while the Parkinson’s Impact scale (PIMS) and the Parkinson’s Disease Quality of Life scale (PDQUALIF) both assess financial consequences of PD, a facet that is lacking in other instruments. The final aspect is to inspect the psychometric properties of questionnaires. For instance, when one is interested in studying changes over time in PD, the sensitivity to change of an instrument should be adequate. In the end, the actual selection of questionnaires should systematically rule out other potential questionnaires. Fourth, when patients are eventually assessed on HS and/or (HR)QOL, and it comes to describing the outcomes in an article, it is of eminent importance to present the outcomes in accordance with the initially described definition and the instruments used. As stated above, all studies included in this review made no distinction between (HR)QOL en HS. Too often, a HS instrument is used, while the title of the article points out that the focus is on QOL. Finally, we would like to point out that criteria lists developed for reviewing articles and writing systematic review, such as used in this study, could provide guidelines to improve the quality of studies. Eventually, this makes that more definite conclusions can be drawn on variables of interest.

In conclusion, HS studies are well represented in the field of Parkinson’s disease. Attention towards QOL, however, is needed in order to draw conclusions on a person’s well-being.

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