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The relationship of pain and health-related quality of life in Korean patients with Parkinson's disease

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Background – Parkinson's disease (PD) is a chronic progressive neurodegenerative disorder. Increasing attention has been focused on the pain and health-related quality of life (HrQOL) in patients with PD. *Objective* – To evaluate the relationship between pain and the HrQOL in patients with PD. *Methods* – Eighty-two patients with PD were included and classified into two groups according to the presence of pain. The Hoehn and Yahr scale, the Unified Parkinson's Disease Rating Scale (UPDRS), the Modified Somatic Perception Questionnaire (MSPQ), the Zung Depression Inventory – Self-rating Depression Scale (SDS), the Visual Analogue Scale and the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) were administered. The factors influencing the pain, HrQOL and parkinsonian manifestations were evaluated. *Results* – The PD with pain group had higher UPDRS part III scores, lower SF-36 scores, higher SDS scores and higher MSPQ scores than the PD without pain group. The presence of pain, high Hoehn and Yahr stage, advanced age and somatic perception were the factors that had a negative effect on the physical component of the HrQOL. Depression and somatic perception were the most important predictive factors for the mental component of the HrQOL. Depression and poor parkinsonian motor abilities were the leading factors contributing to pain. *Conclusion* – Pain and depression were major detrimental factors affecting the physical and mental aspects of the HrQOL respectively. Therefore, the treatment of pain and depression can be important to improve the HrQOL.

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Introduction

Parkinson's disease (PD) is a common neurodegenerative disorder affecting 1.47% of the population over 60 years of age in Korea (1). Although pain is not a cardinal feature of PD, it has been a prevalent feature in the description of PD since James Parkinson first introduced PD in 1817. The prevalence of pain has been reported to range from 40% to 85% in patients with PD (2–6). In the early stages of PD, stiffness, rigidity and restless leg syndrome may provoke pain. In the advanced stages of PD, motor fluctuations and combined musculoskeletal or radicular problems may cause corresponding pain. On the other hand, primary sensory complaints unrelated to motor disability in patients with PD have also been described: these include aching, numbness, tingling, burning and sensations of vibration or a vague overall sensation of tension and discomfort. Such unexplained pain may be termed 'primary pain of a central origin' and thought to be caused by abnormalities in the basal ganglia related to pain encoding (7). As pain is a major contributing factor that can influence the health-related quality of life (HrQOL) in patients with various chronic neurologic diseases, measurement of pain is essential in comprehensive evaluations of patients with PD (8). In the case of PD,

the disease-specific measure, PDQ-39, has been widely used in recent years (9, 10). An increased interest in the HrQOL in patients with PD has led to many reports from well-designed studies that relate the impact of various factors to the HrQOL. However, most studies have addressed parkinsonian motor symptoms or depression rather than pain itself (11). Therefore, we hypothesized that pain, as well as parkinsonian manifestations and depression, could have a relationship with the HrQOL. We also determined the factors that contribute to pain, depression and the HrQOL in patients with PD.

Subjects and methods

Subjects

We recruited patients with PD from the Movement Disorders Unit of a university-affiliated hospital between January and April 2006. PD was defined according to the clinical diagnostic criteria of the UK Parkinson's Disease Society Brain Bank (12). We excluded patients who reported that they had a history of medical diseases, such as stroke, diabetes mellitus and arthritis, and prior surgery that might cause chronic pain. Patients who could not complete questionnaires because of cognitive impairment (Mini-Mental Status Examination < 24) were also excluded. Written informed consent was obtained from each patient. The Institutional Review Board at our hospital approved this study.

Clinical evaluation

Information on demographic data, including age, gender, age at disease onset and duration of disease, was obtained by patient interview and review of the medical records. Patients were examined during 'on' states by one movement specialist. The Hoehn and Yahr stage (13) was determined and the degree of motor impairment was assessed by Unified Parkinson's Disease Rating Scale (UPDRS) part III scores (14).

Self-questionnaires

All patients were asked to complete questionnaires with information on pain, the HrQOL, depression and somatic anxiety. A neurologist at the hospital assisted the patients in completing the questionnaires.

The pain intensity was evaluated using the Visual Analogue Scale (VAS; 15). Patients were asked to express their level of pain by marking a 100-mm horizontal line. A score of zero on the extreme left part of the line indicated no pain and a score of 100 on the extreme right part of the line indicated unbearable pain.

The Zung Depression Inventory – Self-rating Depression Scale (SDS) was used to evaluate depression. The scale consists of 20 items with scores ranging from 20 to 80, with a higher score indicating more severe depression (16). The somatic complaints were assessed by the Modified Somatic Perception Questionnaire (MSPQ; 17). This questionnaire is a 13-item scale designed to measure heightened somatic awareness or somatic anxiety in patients with chronic pain. The scores range from 0 to 39, with higher scores representing more somatic complaints.

The HrQOL in patients with PD was evaluated by the Korean version of the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36; 18–20). SF-36 measures eight aspects of health status, including physical functions, role limitations due to physical problems, bodily pain, general health, vitality, social functions, role limitations due to emotional problems and mental health as tested by 36 questions. After analyzing the eight dimensions separately, the data were used to compute Physical Component Summary (PCS) and Mental Component Summary (MCS) scores of the HrQOL using the equation provided by the Medical Outcomes Trust.

Classification of patients with PD

We categorized patients with PD into two groups based on the existence of pain. The PD with pain group was subdivided into a pain related to PD group and a pain unrelated to PD group using specifically designed criteria (Table 1). For the objective classification of groups, a scoring system was used. Pain related to PD was defined

Table 1 The six questions for the definition of the Parkinson's disease (PD)-related pain

1. Patient's own perception of relation between pain and PD (Do you think your pain is related to PD?)
2. A chronology of pain and PD (Was your pain experienced after parkinsonian symptom development?)
3. A response of pain to levodopa therapy (Was your pain relieved by levodopa therapy?)
4. The laterality of pain (Does the area or side of the pain correlate with the same side in which parkinsonian symptoms are more severe?)
5. The presence of motor complication-induced pain (Are there any pain related to the motor symptom fluctuation like dystonia or rigidity?)
6. No evidence of neuropathy or myopathy documented by electrodiagnostic study

as pain caused by the pathogenic mechanisms of PD. The characteristics of the pain related to PD were set as follows: (i) pain which the patient feels is related to PD; (ii) pain developing after the revelation of PD motor symptoms; (iii) pain relieved by levodopa therapy; (iv) pain induced by parkinsonian symptom fluctuation and (v) pain which lateralizes to the same side as the more severe parkinsonian symptoms. Conversely, pain unrelated to PD was defined as follows: (i) any type of pain which is not perceived to be related to PD by the patient; (ii) no chronologic relationship to the development of PD; (iii) no response to levodopa therapy; (iv) no influence from PD symptom fluctuation and (v) different lateralization compared with PD motor symptoms. As there is no clear relationship between PD and peripheral neuropathy or myopathy in terms of pathogenesis and clinical findings, neuropathies or myopathies confirmed by electrodiagnostic studies were classified as characteristics of pain unrelated to PD. Electrodiagnostic studies with nerve conduction studies and electromyography were performed using a Viking IV EMG machine (Viasys; Nicolet Biomedical, Madison, WI, USA), by one electromyographer who was certified by the American Board of Electrodiagnostic Medicine. With each item in the criteria scoring 0 or 1, patients with sum scores ≥ 3 were classified in the pain related to PD group. The patients who had sum scores <3 were classified in the pain unrelated to PD group.

Statistical methods

To identify and compare the baseline characteristics of pain and demographic data, a chi-squared test and the Mann–Whitney test were used, where appropriate. The Spearman rank correlation analysis was used to evaluate the correlation of the clinical status of parkinsonian symptoms and responses to the questionnaires related to pain, depression and the HrQOL. The Mann–Whitney test was performed to compare the clinical characteristics and responses to the questionnaires between patients with and without pain and between the pain related to PD group and the pain unrelated to PD group. We performed multiple stepwise linear regression analyses to assess the factors contributing to the HrQOL and pain in patients with PD. Statistical results with a value $P < 0.05$ were considered statistically significant. SPSS 10.0 (SPSS, Inc., Chicago, IL, USA) was used for the statistical analysis.

Results

Sample characteristics and demographic factors

One hundred and eleven patients with PD were enrolled in this study. Of the 111 patients, 29 were excluded due to diabetes mellitus (12 patients), arthritis (six patients) and incomplete studies when electrodiagnostic studies were declined (11 patients); 28 men and 54 women, with a mean age of 66.4 ± 8.7 years (range 45–83 years), participated in the study.

The median age at disease onset was 63.0 ± 9.44 years (range 40–81 years), and the mean duration of disease was 3.4 ± 2.7 years (range 1–12 years). The clinical characteristics and demographic data of the patients are presented in Table 2.

Prevalence and characteristics of pain

In the 82 patients, the prevalence of pain was 74% (61/82). The prevalence of pain differed between men and women [54% (15/28) in men and 85% (46/54) in women; $P < 0.01$]. Among the 61 patients with pain, 28 patients were categorized into the pain related to PD group and 33 patients were categorized into the pain unrelated to PD group. The mean value of the VAS score was 54.52 ± 28.69 in patients with pain. The mean value of the VAS score was higher in women (49.1 ± 32.4) than in men (24.9 ± 32.1; $P < 0.01$). The areas of pain were distributed as follows: the lower back (70%), knees or legs (28%), shoulders or arms (21%), neck (10%) and whole body (1%).

Table 2 Patient's demographics and clinical characteristics

Mean age (years)	66.4 (±8.7)
Gender (M:F)	28:54
Mean duration of disease (years)	3.4 (±2.7)
Mean age at onset (years)	63.0 (±9.4)
Hoehn and Yahr stage (% of patients)	
1	13.4
1.5	11.0
2	57.3
2.5	14.6
3	1.2
4	2.4
Unified Parkinson's Disease Rating Scale (UPDRS) part III score	12.6 (±8.4)
Visual Analogue Scale (VAS) score	40.6 (±34.4)
Zung depression inventory – Self-rating Depression Scale (SDS) score	44.0 (±9.4)
Modified Somatic Perception Questionnaire (MSPQ) score	23.2 (±6.2)

The correlation of pain, the HrQOL, depression and parkinsonian motor symptoms

The VAS score showed a moderate correlation with decreased HrQOL ($\gamma = -0.661$ for PCS and -0.371 for MCS), a moderate positive correlation with UPDRS part III scores ($\gamma = 0.493$; $P < 0.01$), more severe depression ($\gamma = 0.457$ for SDS) and more somatic complaints ($\gamma = 0.438$ for MSPQ; $P < 0.01$).

The PCS score from the HrQOL had a moderate negative correlation with age ($\gamma = -0.315$), Hoehn and Yahr stage ($\gamma = -0.404$) and UPDRS part III scores ($\gamma = -0.447$; $P < 0.01$). The MCS also had a moderate negative correlation with UPDRS part III scores ($\gamma = -0.316$; $P < 0.01$). However, the VAS, PCS, MCS and SDS did not correlate with disease duration.

Contributing factors to the HrQOL in patients with PD

To define the contributing factors to the HrQOL, multiple stepwise linear regression analysis was performed with PCS scores of the SF-36 serving as dependent variables, and the values with statistical significance (age, gender, Hoehn and Yahr stage, UPDRS part III scores, VAS scores, SDS scores and MSPQ scores) serving as explanatory variables. Pain estimated by VAS scores had the most detrimental impact on the QOL evaluated by PCS scores. The Hoehn and Yahr stage was the second most important explanatory variable affecting the PCS of QOL. Age and somatic perception were the next important explanatory variables ($r^2 = 0.572$; Table 3).

In addition, MCS scores from the SF-36 served as dependent variables and the values with statistical significance (UPDRS part III scores, VAS scores, SDS scores and MSPQ scores) were adopted as explanatory variables for the regression analysis. The most detrimental factors determined by the MCS of the SF-36, in order of importance, were depression and somatic perception, ($r^2 = 0.403$; Table 3).

Contributing factors to pain in patients with PD

Another multiple stepwise regression analysis was performed with VAS scores serving as the dependent variable, while gender, Hoehn and Yahr stage, UPDRS part III scores, SDS scores and MSPQ scores served as the independent variables. Pain, as evaluated by VAS scores, was significantly influenced by depression. Parkinsonian motor deficits, as evaluated by UPDRS part III scores, were the second leading cause of pain ($r^2 = 0.406$; Table 3).

Table 3 Difference between the PD with pain group and the PD without pain group (Mann–Whitney test)

	PD with pain group	PD without pain group	*P*-value
Age	67.30 (±8.87)	63.95 (±8.00)	NS
HY stage	2.00 (±0.25)*	2.00 (±0.50)*	NS
UPDRS part III	13.89 (±9.25)	8.76 (±3.39)	<0.01
VAS	54.52 (±28.69)	0.00 (±0.00)	<0.01
SDS	45.90 (±8.96)	38.43 (±8.68)	<0.01
MSPQ	24.62 (±6.27)	19.24 (±3.83)	<0.01
PCS	39.10 (±11.23)	49.24 (±6.57)	<0.01
PF	37.92 (±12.34)	50.52 (±7.13)	<0.01
RP	37.62 (±14.68)	48.11 (±10.02)	<0.01
BP	41.93 (±11.40)	55.86 (±9.46)	<0.01
GH	36.02 (±10.05)	44.13 (±9.81)	<0.01
MCS	40.21 (±15.40)	51.90 (±8.88)	<0.01
VT	40.73 (±12.45)	50.75 (±9.55)	<0.01
SF	42.01 (±14.74)	51.92 (±7.89)	<0.01
RE	38.10 (±17.09)	50.33 (±9.00)	<0.01
MH	38.47 (±16.14)	52.96 (±7.31)	<0.01

Values are represented as mean (±SD). NS, not significant; PD, Parkinson's disease; HY stage, Hoehn and Yahr stage; UPDRS part III, Unified Parkinson's Disease Rating Scale, part III score; VAS, Visual Analogue Scale score; SDS, Zung depression inventory – Self-rating Depression Scale; MSPQ, Modified Somatic Perception Questionnaire score; PCS, physical component summary of SF-36; PF, physical functioning; RP, pole-physical; BP, bodily pain; GH, general health; MCS, mental component summary of SF-36; VT, vitality; SF, social functioning; RE, role-emotional; MH, mental health.
*Median ± interquartile range.

Contributing factors to depression in patients with PD

With respect to depression, SDS scores were used as dependent variables, and the values with statistical significance (age, UPDRS part III scores, VAS scores, MSPQ scores, PCS scores and MCS scores) were used as dependent variables for the regression analysis. The MCS score from the SF-36 was the most detrimental factor on depression. The PCS score was the second leading cause of depression ($r^2 = 0.415$; Table 3).

Comparison of the subgroups

Unified Parkinson's Disease Rating Scale part III scores, VAS scores, MCS and PCS from the SF-36, SDS scores and MSPQ scores showed significant differences in comparisons between the PD with pain group and the PD without pain group (Table 4). However, among the patients in the pain group, there was no significant difference between the pain related to PD group and the pain unrelated to PD group (Table 5).

Discussion

Pain correlated with the HrQOL, PD motor symptoms and depression. Pain estimated by VAS scores had the most detrimental impact on

Table 4 The difference between the Parkinson's disease related pain and Parkinson's disease unrelated pain group (Mann–Whitney test)

	PD-related pain group Mean (±SD)	PD-unrelated pain group Mean (±SD)	*P*-value
Age (years)	65.64 (±8.71)	68.70 (±8.89)	NS
H&Y stage	2.00 (±0.38)*	2.00 (±0.50)*	NS
UPDRS part III	16.00 (±11.49)	2.09 (±6.47)	NS
VAS	55.89 (±29.77)	53.36 (±28.15)	NS
SDS	45.93 (±9.29)	45.88 (±8.81)	NS
MSPQ	24.82 (±5.31)	24.45 (±7.05)	NS
PCS	38.46 (±10.89)	39.64 (±11.65)	NS
PF	37.11 (±11.08)	38.60 (±13.45)	NS
RP	35.25 (±14.53)	39.64 (±14.74)	NS
BP	39.77 (±10.59)	43.77 (±11.89)	NS
GH	35.19 (±10.37)	36.73 (±9.88)	NS
MCS	36.34 (±15.94)	43.38 (±14.36)	NS
VT	39.04 (±12.08)	42.16 (±12.76)	NS
SF	38.54 (±15.58)	44.95 (±13.53)	NS
RE	34.50 (±16.88)	41.15 (±16.91)	NS
MH	35.02 (±16.02)	41.39 (±15.90)	NS

Values are represented as mean (±SD). NS, not significant; PD, Parkinson's disease; H&Y stage, Hoehn and Yahr stage; UPDRS part III, Unified Parkinson's Disease Rating Scale, part III score; VAS, Visual Analogue Scale score; SDS, Zung depression inventory – Self-rating Depression Scale; MSPQ, Modified Somatic Perception Questionnaire score; PCS, physical component summary of SF-36; PF, physical functioning; RP, pole-physical; BP, bodily pain; GH, general health; MCS, mental component summary of SF-36; VT, vitality; SF, social functioning; RE, role-emotional; MH, mental health.
*Median ± interquartile range.

Table 5 Contributing factors on the quality of life and pain in patients with PD

	Coefficient	*P*-value	r^2 (%)
PCS			57.2
Step 1. VAS	−0.154	1	
Step 2. H&Y stage	−5.984	<0.001	
Step 3. Age	−0.318	0.001	
Step 4. MSPQ	−0.325	0.029	
MCS			40.3
Step 1. SDS	−0.734	<0.000	
Step 2. MSPQ	−0.721	0.002	
VAS			40.6
Step 1. SDS	1.010	0.005	
Step 2. UPDRS part III	1.201	0.002	
Step 3. MSPQ	1.365	0.012	
Step 4. Gender	13.658	0.036	
SDS			41.5
Step 1. MCS	−0.330	<0.001	
Step 2. PCS	−0.256	0.001	

PCS, physical component summary of SF-36; MCS, Mental Component Summary of SF-36; VAS, Visual Analogue Scale; HY stage, Hoehn and Yahr stage; MSPQ, Modified Somatic Perception Questionnaire score; SDS, Zung depression inventory – Self-rating Depression Scale; UPDRS part III, Unified Parkinson's Disease Rating Scale, part III score.

the HrQOL evaluated by PCS scores, and depression had the most detrimental impact on the HrQOL evaluated by MCS scores. Therefore, we can deduce that relieving pain and depression could improve the HrQOL of patients with PD. In addition, pain evaluated by VAS scores was significantly influenced by depression and parkinsonian motor impairment evaluated by UPDRS part III scores, suggesting that proper management of depression and parkinsonian motor symptoms could help alleviate pain, hence further improve the HrQOL of patients with PD.

In our cross-sectional study, 74% of patients with PD experienced pain. Prior studies reported that the overall presence of pain in PD was estimated to be 40–85% (2–5). Variability of the prevalence is probably related to the inclusion criteria to define pain. One study with a low prevalence of pain included patients with pain related to PD only (4); however, another study with a high prevalence of pain included all patients with any kind of pain (6). In the present study, we included any type of pain, resulting in a high prevalence of pain in patients with PD. The prevalence of the pain related to PD was 34% and the prevalence of the pain unrelated to PD was 40%. Our results suggest that in about one-half of patients with PD with pain, the pain is directly related to the underlying pathogenic mechanism of PD or secondary to complications of parkinsonian motor symptoms.

We used criteria, including six items to discriminate the pain related to PD and the pain unrelated to PD (Table 1). Based on the previous report by Goetz et al. (3), we adopted the patient's own perception of pain in the criteria. We thought that the lateralization of pain identical to the side with worse parkinsonian symptoms or signs and the chronologic development of pain after PD symptom development would support the relationship of PD and pain. Pain associated with motor fluctuations or complications was also defined as the pain related to PD. Beyond the debate about levodopa therapy for pain, relieving pain by levodopa therapy is accepted as a characteristic of the pain related to PD (21). We also used an item referred to as 'no evidence of neuropathy or myopathy' that was confirmed by electrodiagnostic studies. We used an electrodiagnostic study, as it is more specific than MR imaging of the spine as a screening tool for musculoskeletal or radicular disorders. In addition, an electrodiagnostic study can be used to evaluate the current functional status of neuromuscular disease (22–24).

Although we tried to define the pain related to PD objectively by using six-item criteria, the differentiation of pain related to PD from pain unrelated to PD may not be perfect. However, this is a first trial to use objective tools for the differentiation of pain in patients with PD. Additional analysis revealed the relationship between

the chronology of pain development and pain lateralization in patients with PD. Patients who had pain after the onset of parkinsonian manifestations (25/82, 30.5%) had a tendency to have pain which had the same lateralization as the symptomatic side of PD (14/25, 56.0%; $P = 0.002$). These findings are supportive data for the detailed definition of the 'pain related to PD,' which was first devised in the current study.

Pain, high Hoehn and Yahr stage, advanced age and somatic perception were the variables that had detrimental effects on the HrQOL, as assessed by the physical component of the SF-36 in our study. The physical aspect of the HrQOL is mainly affected by motor disability in most neurologic disorders, especially disorders with prominent motor symptoms, such as multiple sclerosis, cerebellar ataxia, dystonia and hereditary peripheral neuropathy (25–28). In our present study, however, pain was the leading influential factor on the physical HrQOL of patients with PD, followed by the Hoehn and Yahr stage. Because most of the subjects were in an early stage of PD (82%, HY stage ≤ 2), the pain may have influenced the physical HrQOL, rather than the motor disability.

Our study showed that the PD with pain group had more severe parkinsonian motor symptoms, a poorer QOL, a higher frequency of depression, and more somatic complaints compared with the PD without pain group (Table 4). However, there were no significant differences identified between the pain related to PD group and the pain unrelated to PD group (Table 5). These results suggest that pain has a substantial impact on the motor and non-motor aspects of patients with PD regardless of the characteristics of pain.

The shortcoming of this study is the high rate of patients with early-stage PD, which possibly contributed to the low prevalence of pain related to motor complication or fluctuation (3.7%). The small sample size and predominance of women in our study could also limit the accurate assessment of the prevalence of pain in patients with PD. Another limitation was that patients with dementia were excluded from the enrolled subjects. It would be difficult to assess the pain in demented patients using a questionnaire. Another limitation of our study was that the SF-36 PCS and MCS have been found to be problematic for use in patients with different neurologic conditions (29–32). Therefore, we demonstrated not only two summary measures, but also the SF-36 subscales (Tables 4 and 5). Finally, the questionnaire for pain related to PD, which was used for assessing the categories of pain, has not been validated.

In conclusion, this study showed the impact of pain on the HrQOL of patients with PD. In addition, pain was significantly influenced by depression and parkinsonian motor impairment. Therefore, we suggest that not only the treatment of motor symptoms but also the alleviation of pain and depression should be emphasized in the management of PD patients to improve the HrQOL.

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