Systematic review and meta-analysis of the quality-of-life of patients with Parkinson's disease

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Abstract

Background: Parkinson's disease can adversely affect the quality-of-life.

Aims: We conducted a systematic review and meta-analysis of global literature on the quality-of-life of patients with Parkinson's disease and examined the association between patient characteristics and quality-of-life.

Methods: We searched Embase, PubMed, Scopus and Web of Science from January 2000 to January 2020. We included articles published in English that used the Parkinson's disease questionnaire to estimate the quality-of-life score and to identify the determinants of quality-of-life in patients with Parkinson's disease.

Results: In total, 41 studies with data from 4060 patients who had Parkinson's disease met our inclusion criteria. The overall quality-of-life score was 32.37 (95% confidence intervals (CI): 28.72–36.01). Age and duration of disease were inversely related to quality-of-life ($P < 0.001$). South America had the highest score on the questionnaire (39.73, 95% CI: 28.66–50.79, $P < 0.001$), indicating the lowest quality-of-life of patients with Parkinson's disease. Of the 6 World Health Organization regions, the Eastern Mediterranean Region had the highest score (36.28, 95% CI: 23.44–49.13, $P < 0.001$).

Conclusion: Although the global score in patients with Parkinson's disease indicated an acceptable quality-of-life, there is a possibility for improvements. The findings of this study can inform evidence-based strategies by health policymakers and clinicians to enhance the quality-of-life of patients with Parkinson's disease.

Keywords: quality-of-life, Parkinson's disease, neurodegenerative disorder, systematic review, meta-analysis, global review.

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Introduction

Parkinson's disease is one of the most common neurodegenerative disorders *(1)* and the second most common disease of the nervous system after Alzheimer disease. It affects more than 10 million people worldwide *(2–5)*. It is a chronic and progressive disease that affects the dopaminergic neurons in a specific area of the brain, called the substantia nigra *(6,7)*. The etiology of Parkinson's disease is still unknown, but genetic factors (in 10–15% of all patients with the disease) and environmental stimuli influence the development of the disease *(8,9)*.

At the onset of the disease, the body appears to be physically damaged and most of the obvious symptoms are movement-related – difficulty in walking, speaking and even using the hands. In later stages, cognitive and behavioural problems may appear and sleep disorders may arise which negatively affect patients' quality-of-life (QOL). Other conditions, including depression, severe fatigue, difficulty in mobility and speech, will exacerbate the patient's medical condition *(10,11)*. Decreased QOL not only affects the course of a patient's treatment negatively, but it also lowers life expectancy among people with Parkinson's disease *(10)*.

QOL has become an important issue in healthcare research, patient management policies and provision of effective medical interventions with sustainable effects. WHO defines health-related QOL as "an individual's perception of the impact of health and disease on the physical, mental and social aspects of life" *(12)*. Parkinson's disease can cause pain and limitations in daily activities *(10,13)*, which have a substantial and long-lasting effect on the body. Factors such as self-image, satisfaction with life and interaction with other people are adversely affected in patients with Parkinson disease and result in decreased QOL *(14,15)*.

As QOL is affected by complex multidimensional factors, it is crucial to identify its determinants *(16–19)* so as to improve QOL as much as possible for patients with

Parkinson's disease. In fact, QOL is mainly dependent on physical health and self-efficacy *(20,21)*. Many studies have examined the QOL of patients with Parkinson's disease *(22,23)*, but most did not consider the contribution of factors such as age, sex, disease duration and disease severity. This lack of data makes it difficult to draw evidence-based conclusions about how demographic factors and patient characteristics contribute to QOL. Thus, in this study, we conducted a systematic review and meta-analysis of the literature on QOL of patients with Parkinson's disease to examine the association between patient characteristics and QOL in people with the disease.

Methods

This systematic review and meta-analysis was registered in PROSPERO database (registration code: CRD42020177015). The review is reported according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) (Figure 1) *(24)*.

Databases searched and search terms

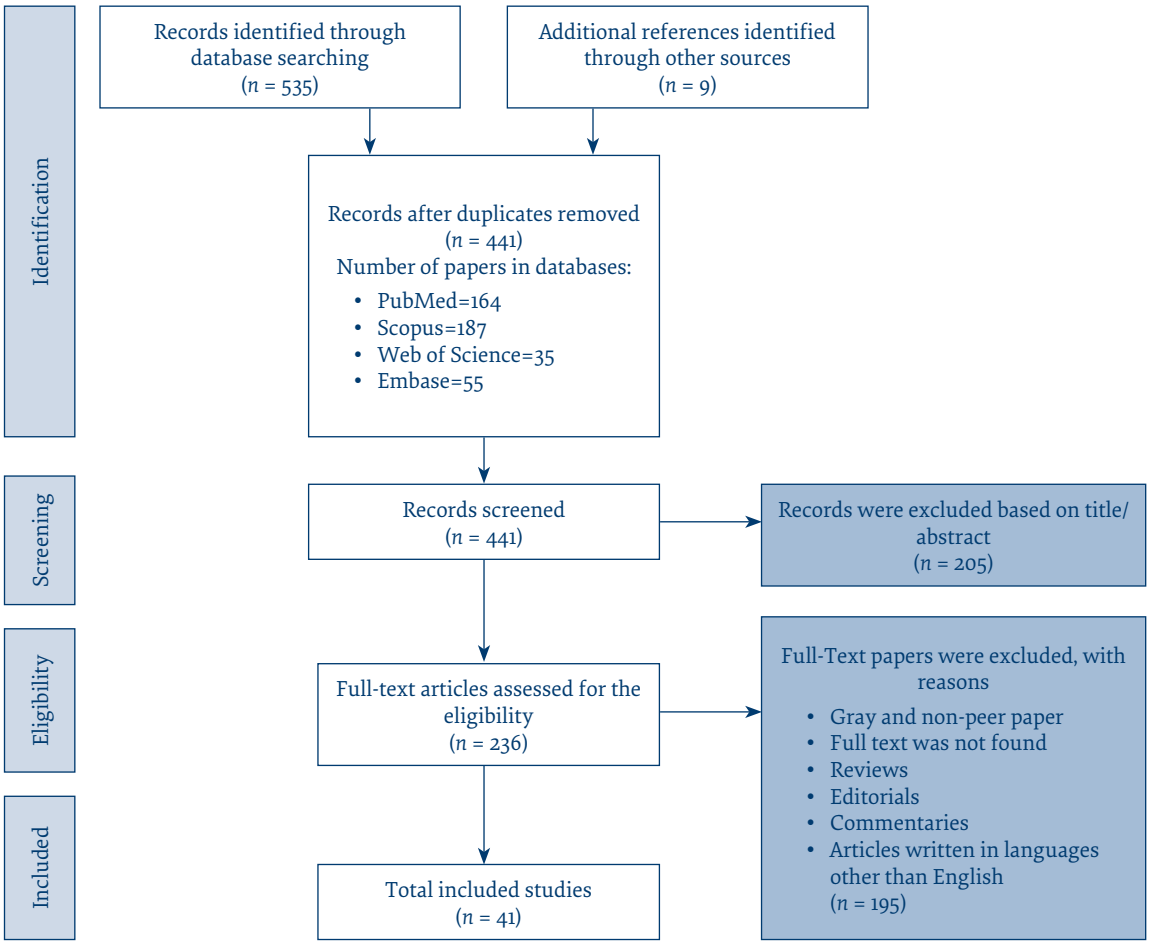
We undertook a systematic search of Embase, PubMed, Scopus and Web of Science from January 2000 to January 2020. We also searched Google Scholar using search terms: ((quality of life [Title/Abstract] OR health related quality of life [Title/Abstract] OR HRQOL [Title/Abstract]) AND (Parkinson [Title/Abstract] OR Parkinson's disease [Title/Abstract] OR Idiopathic Parkinson's disease [Title/Abstract] OR Lowy body Parkinson Disease [Title/Abstract])).

Inclusion and exclusion criteria

We included articles that used the PDQ-39 *(25)* to estimate the QOL score or identify the determinants of QOL among patients with Parkinson's Disease. The PDQ-39 is a self-report instrument widely used to understand disease-related health status and QOL. The 39-item PDQ evaluates the frequency of difficulties patients with Parkinson's disease experience in eight domains: daily activities, emotional well-being, stigmatization, social support, cognition, communication, and bodily discomfort. In this questionnaire, the score of each item is between 0 and 100, and the closer this score is to zero, the better the person's QOL.

The other inclusion criteria were: original articles with full text available; observational prospective, descriptive, cross-sectional, case-study or cohort study design; published in English; and conducted between January 2000 and January 2020. Studies were excluded if they were not in English, and were published before January 2000 or after January 2020. Randomized controlled trials, editorials, commentaries, expert opinions, theses,

Figure 1 PRISMA flow diagram of selection of articles for the systematic review



reports, book chapters, case–control studies and case-series were excluded. Papers on evaluation of treatment effects, medication approaches and clinical decision-making were excluded.

Articles retrieved

From the search, 535 articles were identified. Our additional search in Google Scholar resulted in retrieval of 9 articles. After removing duplicates, 441 articles remained, of which 187 (42%) were retrieved from SCOPUS, 164 (37%) from PubMed, 55 (12%) from Embase and 35 (8%) from Web of Science. After screening the titles and abstracts of the records, 205 publications were excluded. The full texts of the remaining 236 articles were screened for eligibility based on the inclusion and exclusion criteria, of which 195 were excluded. Thus, 41 articles were included in the review.

Studies which incorporated quantitative data on QOL in patients with Parkinson's disease or determinants of QOL, such as demographic factors, disease duration and disease severity, were included in the review. References of articles and conference abstracts included were also searched to find any eligible data to be add to the review. After applying the inclusion and exclusion criteria, 41 studies were selected (Figure 1).

Data extraction

Two investigators extracted data independently and in case of disagreement, a third reviewer resolved the differences. We developed a data extraction form which included author's name, publication date, research setting, study design, study findings (QOL determinants, total QOL score among patients with Parkinson disease, and level of anxiety and depression, emotional well-being, stigma, social support, cognition, communication, discomfort, and mobility .

Quality assessment

The quality of included articles was assessed using the Newcastle-Ottawa Scale, a standardized instrument for assessing the quality of observational studies *(26)*. To reduce bias, two independent reviewers assessed the quality of the studies; in case of disagreement, a third investigator resolved the discrepancy. The Newcastle-Ottawa Scale examines the quality of articles based on the definition of cases, introduction of cases, selection of controls, definition of controls, comparability of cases and controls, and exposure and outcome. Reported and unreported items are scored 1 and 0, respectively. The sum of scores assigned to reported items was considered as the total quality score of each article. The highest and lowest scores on the Newcastle-Ottawa Scale for each article were 10 (best quality) and 0 (lowest quality). In our review, articles with scores < 4 were considered low quality.

Statistical analysis

We used random-effects analyses (Der Simonian and Laird) for the meta-analysis to estimate the mean effect size and variability across studies. The results are reported at a 95% confidence level, meta-regression analysis was determined on the basis of publication date and sample size. We carried out sensitivity analyses to confirm the stability of the results. We conducted subgroup analyses for all the items of PDQ-39, sex, publication date, study setting and sample size. Duration of illness, age and publication date were used for the cumulative meta-analysis. We used the Egger test to measure publication bias and analyzed the data using comprehensive Meta-Analysis and Stata version 14 software.

Results

Our findings are reported based on the PRISMA checklist. After extraction of the main data from the 41 articles, the total number of patients with Parkinson's disease was 4060 and their total QOL score was 32.37 (95% Cl: 28.72–36.01).

The total scores for each item of the PDQ-39 were: daily activities 39.97 (95% Cl: 35.23 to 44.71); cognition 32.00 (95% Cl: 28.57 to 35.43); communication 27.97 (95% Cl: 24.07 to 31.87); discomfort 38.86 (95% Cl: 34.60 to 43.11); emotional well-being 36.03 (95% Cl: 32.46 to 39.61); mobility 42.49 (95% Cl: 37.12 to 47.86); social support 20.22 (95% Cl: 16.26 to 24.18); and stigma: 30.31 (95% Cl: 26.76 to 33.86) (Table 1).

Table 1 Quality-of-life of patients with Parkinson disease based on the PDQ-39

Domain	Mean (95% CI)	Variance	z	P
PDQ-39 summary index	32.37 (28.72 to 36.01)	3.46	17.40	< 0.001
Daily activities	39.97 (35.23 to 44.71)	5.85	16.52	< 0.001
Cognition	32.00 (28.57 to 35.43)	3.06	18.28	< 0.001
Communication	27.97 (24.07 to 31.87)	3.96	14.05	< 0.001
Discomfort	38.86 (34.60 to 43.11)	4.72	17.88	< 0.001
Emotional well-being	36.03 (32.46 to 39.61)	3.33	19.75	< 0.001
Mobility	42.49 (37.12 to 47.86)	7.51	15.51	< 0.001
Social support	20.22 (16.26 to 24.18)	4.08	10.01	< 0.001
Stigma	30.31 (26.76 to 33.86)	3.28	16.74	< 0.001

PDQ-39 = Parkinson's disease questionnaire 39; CI = confidence intervals.

Analysis by sex

We found a significant relationship between sex and QOL in patients with Parkinson's disease indicating that the disease was more common in men (PDQ-39 summary index: 3.32; 95% Cl: 2.04 to 4.60) (Table 2). Items that had negative association with gender included daily activities: −1.48 (95% Cl: −2.98 to 0.03), cognition: −0.20 (95% Cl: −1.42 to 1.02), emotional well-being −5.32 (95% Cl: −6.58 to 4.06), mobility −2.75 (95% Cl: −4.34 to 1.17 , social support−3.24 (95% Cl: −4.29 to 2.18), and stigma − 3.84 (95% Cl: −5.26 to 2.42). On the other hand, items that had positive association included communication 0.99 (95% Cl: −0.34 to 2.31) and discomfort 0.87 (95% Cl: −0.54 to 2.27) which were more common in men (Table 2)

Analysis by age and disease duration

There was a significant direct correlation between QOL and age in patients with Parkinson's disease ($P < 0.001$): PDQ-39-summary index 0.62 (95% Cl: 0.54 to 0.70). Thus for a one-year increase in patient's age, QOL score would decrease by 0.61 (Table 3).

There was a significant direct relationship between the duration of Parkinson's disease and QOL in patients ($P < 0.001$). Thus for a one-year increase in disease duration, the QOL score decreased by 0.13 (95% Cl: 0.12 to 0.14) (Table 3).

Analysis by location

The scores of all items of the PDQ-39 questionnaire were highest in South America (39.73; 95% Cl: 28.66 to 50.79) and lowest in Australia (20.9; 95% Cl: 1.89 to 39.91) (Table 4).

For the WHO regions, the Eastern Mediterranean Region had the highest score for the PDQ-39 summary index (36.28; 95% Cl: 23.44 to 49.13) and the Western Pacific Region had the lowest score (27.60; 95 % Cl: 20.71 to 34.49) (Table 4).

No studies were found for the WHO Africa Region.

Other sub-group analyses

Anxiety and depression affected the QOL of patients with Parkinson disease. The mean PDQ-39 scores in cases of anxiety and depression were 16.57 (95% CI: 7.60 to 25.53) and 5.87 (95% CI: 3.83 to 7.91) respectively.

Discussion

Our results based on the PDQ-39 showed that estimated QOL in patients with Parkinson's disease was 32.37. Based on the literature, there is no agreed range of scores to evaluate QOL by the PDQ-39. Thus, we categorized patient QOL into four levels based on information from the expert interviews, namely: 0–20 (good QOL); 21–40 (acceptable QOL); 41–60 (poor QOL) and more than 60 (very poor QOL). Our estimated QOL of 32.37 indicates that the QOL overall was in the acceptable range.

The total PDQ-39 score was highest in South America (39.73), which was close to the poor QOL range. Comparing the status of different countries in South America, the QOL in Brazil was estimated to be 45.00 *(27)*, indicating a poor QOL. The scores on daily living, mobility and emotional well-being were high in South America resulting in poor QOL. In Asia, the QOL was estimated at 32.97 in the Philippines *(20)* and 16.80 in China *(28)* because most of the items used in this study had good scores. In Europe, the QOL score in the United Kingdom of Great Britain and Northern Ireland was 17.10 *(29)* also indicating a good QOL, while it was 45.83 in Serbia *(30)* showing a poor QOL. The good QOL in some countries, such as China and the United Kingdom, is probably due to their advanced healthcare systems that provide easy and sufficient access to high-quality healthcare services. In North and Central America, Mexico had a QOL score of 33.52 *(31)* and the United States a QOL score of 27.11 *(32)*. Australia achieved a QOL score of 20.90, showing better QOL among people with Parkinson's disease than other continents *(33)*.

We also evaluated the QOL scores in different regions of WHO: the Eastern Mediterranean Region had the highest score (36.28) and the Western Pacific Region had the lowest score (27.60), indicating better environments for people with Parkinson's disease in the Western Pacific and hence better QOL, probably due to this region's economic development *(34)*.

Our study showed a significant inverse association between patients' age and QOL, meaning that increased

Table 2 Meta regression analysis of the PDQ-39 according to sex in each item

Domain	Point estimate (95% CI)	SE	*z*-	*P*
PDQ-39 summary index	3.31827 (2.03506 to 4.60148)	0.65471	5.06829	< 0.001
Daily activities	−1.47668 (−2.98136 to 0.03)	0.76771	−1.92349	0.054
Cognition	−0.19938 (−1.42382 to 1.02507)	0.62473	−0.31914	0.750
Communication	0.98636 (−0.33747 to 2.31019)	0.67543	1.46033	0.144
Discomfort	0.86691 (−0.53901 to 2.27283)	0.71732	1.20854	0.227
Emotional well-being	−5.32240 (−6.58400 to −4.06080)	0.64369	−8.26863	< 0.001
Mobility	−2.75428 (−4.33509 to −1.17346)	0.80655	−3.41488	< 0.001
Social support	−3.23721 (−4.29122 to −2.18320)	0.53777	−6.01970	< 0.001
Stigma	−3.83633 (−5.25750 to −2.41516)	0.72510	−5.29075	< 0.001

PDQ = Parkinson disease questionnaire; CI = confidence intervals; SE: standard error.

Table 3 Meta regression analysis of the PDQ-39 overall according to age and duration of disease

Subgroup	Point estimate (95% CI)	SE	z	P
Age	0.6199 (0.5356 to 0.7042)	0.0430	14.4147	< 0.001
Duration of disease	0.1293 (0.1166 to 0.1421)	0.0065	19.8745	< 0.001

PDQ = Parkinson disease questionnaire; CI = confidence intervals; SE = standard error.

Table 4 Meta regression analysis of the PDQ-39 overall according to continent and WHO region

	Effect size	Null test (2-tail)		Heterogeneity			
Variable	Pooled mean (95% CI)	z	P	Q	df (Q)	P	I^2
Total	32.37 (28.72 to 36.01)	17.40	< 0.001	2050.17	26	< 0.001	98.73
Continent							
Africa	37.50 (18.21 to 56.79)	3.81	< 0.001	0.00	0	> 0.05	0.00
South America	39.73 (28.66 to 50.79)	7.04	< 0.001	29.40	2	< 0.001	93.20
Asia	29.69 (22.42 to 36.95)	8.00	< 0.001	374.76	6	< 0.001	98.40
Australia	20.90 (1.89 to 39.91)	2.15	0.03	0.00	0	> 0.05	0.00
Europe	32.94 (27.59 to 38.29)	12.07	< 0.001	1285.71	12	< 0.001	99.07
North America	30.33 (16.77 to 43.89)	4.38	< 0.001	8.45	1	< 0.001	88.16
WHO region							
Eastern Mediterranean	36.28 (23.44 to 49.13)	5.54	< 0.001	1.21	1	> 0.05	17.49
European	32.92 (27.85 to 37.99)	12.72	< 0.001	1285.71	12	< 0.001	99.07
American	35.97 (27.85 to 44.10)	8.68	< 0.001	74.53	4	< 0.001	94.63
Western Pacific	27.60 (20.71 to 34.49)	7.85	< 0.001	270.53	6	< 0.001	97.78

PDQ = Parkinson disease questionnaire; WHO = World Health Organization; CI = confidence intervals; Df = degrees of freedom.

age had a negative impact on an individual's QOL. Another study reported that ageing had a negative effect on QOL and that younger patients had a higher QOL because of their active lifestyle and mobility *(35)*. However, in another study, no significant association between PDQ-39 score and age was reported *(31)*. Despite such discrepancies, it seems logical that ageing would negatively affect QOL because of the limitations it imposes on patients' mobility and active daily life *(36)*.

We found a significant inverse relationship between duration of disease and QOL, so that the longer the duration of Parkinson's disease, the lower the QOL score. A 2012 study reported this inverse relationship *(37)*, and other studies reported no significant relationship between duration of Parkinson disease and QOL *(31,38)*. Our results suggest that the duration of disease does not only affects QOL negatively, but also all the items of PDQ-39 questionnaire.

Regarding sex, men were more at risk of severe Parkinson's disease than women. Thus, women appeared to have a better QOL than men overall. However, we found different outcomes for the domains: men had poorer QOL for communication and discomfort, while women had more difficulties with daily activities, stigma, emotional well-being, mobility and cognition *(39)*. Other studies found that QOL scores in female patients were higher than males indicating a lower QOL *(40)*. A 2018 study concluded that men had higher scores (lower QOL) for mobility and discomfort, while women had higher scores for emotional well-being, stigma, cognition and communication *(32)*.

We found that anxiety and depression influenced the QOL of patients with Parkinson's disease, with anxiety having the greater effect on patients' QOL. A study in Poland considered that depression was the most important factor influencing QOL and patients with untreated depression had poorer QOL *(41)*. Another study mentioned depression as a determining factor for QOL, and anxiety as the second most common factor influencing QOL *(27)*. A 2018 study also highlighted the important role of depression and anxiety in QOL among patients with Parkinson's disease *(20)*.

A limitation of our study is that data from some countries were not available. Thus, studies in these countries were needed. Other limitations of the study were the lack of full text, lack of free access to, and low quality of some articles.

This study provides useful information about the effect of sex, age, duration of illness and psychological disorders, on the QOL of patients with Parkinson's disease. This information can be used by health policy-makers and clinicians for evidence-based strategies to improve the QOL of patients with Parkinson's disease who face problems with mobility, emotional well-being, daily living activities, stigma, social support, cognition, communication and discomfort.

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Analyse systématique et méta-analyse de la qualité de vie des patients atteints de la maladie de Parkinson au niveau mondial

Résumé

Contexte : La maladie de Parkinson peut avoir un impact négatif sur la qualité de vie.

Objectifs : Nous avons réalisé une analyse systématique et une méta-analyse de la littérature mondiale sur la qualité de vie des patients atteints de la maladie de Parkinson et avons examiné l'association entre les caractéristiques des patients et la qualité de vie.

Méthodes : Nous avons effectué des recherches dans Embase, PubMed, Scopus et Web of Science sur la période allant de janvier 2000 à janvier 2020. Nous avons inclus des articles publiés en anglais qui ont eu recours au questionnaire sur la maladie de Parkinson pour estimer le score de qualité de vie et identifier les déterminants de la qualité de vie chez les patients atteints de cette maladie.

Résultats : Au total, 41 études comportant des données sur 4060 patients atteints de la maladie de Parkinson répondaient à nos critères d'inclusion. Le score global de qualité de vie était de 32,37 [intervalles de confiance (IC) à 95 % : 28,72-36,01]. L'âge et la durée de la maladie étaient inversement liés à la qualité de vie ($p < 0,001$). L'Amérique du Sud a obtenu le score le plus élevé au questionnaire (39,73, IC à 95 % : 28,66-50,79, $p < 0,001$), révélant ainsi la plus faible qualité de vie des patients atteints de la maladie de Parkinson. Parmi les six Régions de l'Organisation mondiale de la Santé, la Région de la Méditerranée orientale a obtenu le score le plus élevé (36,28, IC à 95 % : 23,44-49,13, $p < 0,001$).

Conclusion : Même si le score global des patients atteints de la maladie de Parkinson indiquait une qualité de vie acceptable, il est toujours possible de l'améliorer. Les résultats de la présente étude peuvent permettre aux responsables de l'élaboration des politiques en matière de santé et aux cliniciens de mettre en place des stratégies fondées sur des données probantes pour renforcer la qualité de vie des patients atteints de la maladie de Parkinson.

استعراض منهجي عالمي وتحليل تلوي لجودة حياة مرضى باركنسون (الشلل الرعَّاش)

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الخلاصة

الخلفية: يؤثر مرض باركنسون (الشلل الرعَّاش) سلبًا على نوعية الحياة.

الأهداف: هدفت هذه الدراسة الى إجراء مراجعة منهجية وتحليلًا تلويًّا للأدبيات عالميًّا بشأن جودة حياة مرضى باركنسون (الشلل الرعَّاش)، ودراسة العلاقة بين خصائص المريض وجودة الحياة.

طرق البحث: أجرينا بحثًا في قواعد البيانات في Embase وPubMed وScopus وWeb of Science طوال المدة من يناير 2000 إلى يناير 2020. وضمت الدراسة مقالات منشورة باللغة الإنجليزية استخدمت استبيان مرض باركنسون (الشلل الرعَّاش)، لتقدير درجة جودة الحياة والوقوف على محددات جودة الحياة للمرضى المصابين بمرض باركنسون (الشلل الرعَّاش).

النتائج: إجمالًا، استوفت 41 دراسة تحتوي على بيانات من 4060 مريضًا مصابًا بمرض باركنسون معايير الإدراج لدينا. وبلغت الدرجة الإجمالية لجودة الحياة 32.37 (فاصل الثقة 95٪: 28.72–36.01). وكان عمر المريض ومدة الإصابة بالمرض مرتبطين ارتباطًا عكسيًّا بجودة الحياة (القيمة الاحتمالية < 0.001). ونالت أمريكا الجنوبية أعلى درجة بالاستبيان (39.73، فاصل الثقة 95٪: 50.79 – 28.66، القيمة الاحتمالية < 0.001)، الأمر الذي يشير إلى أدنى جودة لحياة المرضى المصابين بمرض باركنسون (الشلل الرعَّاش). ومن بين أقاليم منظمة الصحة العالمية الستة، نال إقليم شرق المتوسط أعلى درجة (36.28، فاصل الثقة 95٪ 23.44–49.13؛ القيمة الاحتمالية < 0.001).

الاستنتاجات: رغم أن المعدل العالمي الذي حصل عليه المرضى المصابون بمرض باركنسون (الشلل الرعَّاش) يشير إلى جودة حياة مقبولة، فإنه ثمة إمكانية لتحسينها. ويمكن الاسترشاد بنتائج هذه الدراسة في صوغ الاستراتيجيات المسندة بالدلائل التي يضعها صناع السياسات الصحية والأطباء السريريون لتعزيز جودة حياة المرضى المصابين بمرض باركنسون (الشلل الرعَّاش).

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