

Original Article

Unified parkinson's disease rating scale for motor symptoms of idiopathic parkinson's disease

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Abstract

Background: IPD is a progressive neurodegenerative disorder that mainly affects the motor function of the affected patients, thus causing a large number of patients to have comparatively poor quality of life. These motor symptoms are well assessed by the Unified Parkinson Disease Rating Scale or simply referred to as UPDRS making it easier to determine the degree of severity and progression of the disease. However, studies further are warranted in order to confirm applicability and efficiency of the applied approaches among other patients and different contexts.

Aim: The purpose of this research was to evaluate how well the UPDRS worked in assessing the motor symptoms by comparing it with the severity of the disease, and other functional indexes in the Idiopathic Parkinson Disease patients.

Method: A quantitative cross-sectional descriptive survey design was used in the present research and included 150 participants with IPD. Each participant's motor disorder was evaluated with the motor sub score of the UPDRS as well as with the Hoehn and Yahr staging and functional measures that included the TUG test and the PDQ-39 mobility subscale. Quantitative comparisons were made to establish the relationship between UPDRS and disease severity indicators using statistical analysis.

Results: UPDRS motor scores also showed moderate positive correlation with the Hoehn and Yahr stages of the disease meaning that the higher the UPDRS motor score the higher the Hoehn and Yahr disease stage. Moreover, there was a slight significant relationship between the UPDRS scores and the duration of the disease whether it was the onset of motor symptom or diagnosis (r = 0.55, p < 0. This study also demonstrated a good agreement between UPDRS and functional outcome measure; it was positively correlated with TUG test times = 0. 65, p < 0.01, and PDQ-39 mobility subscale scores = 0.72, p < 0.01.

Conclusion: It is important to note that the present study has validated UPDRS as a valuable tool in assessing the motor symptoms in the subjects with IPD and there exists a strong relationship between the scores obtained from UPDRS, disease severity and functional impairment. In the light of this study, the use of the UPDRS in clinical setting for assessment of the disease progression and to help in the management strategies cannot be overemphasized. In the subsequent studies, the extended use of the UPDRS together with investigation of various factors should be viewed to understand better the original disadvantages and further improve the test.

Keywords: Idiopathic Parkinson Disease, Unified Parkinson Disease Rating Scale, Motor Symptoms, Disease Severity, Functional Assessment, UPDRS, Parkinson's Disease.

Introduction

Parkinson's Disease (PD) is a chronic and progressive neurological condition it is primarily manifested by the motor dysfunction, including the resting tremor, rigidity, akinesia or bradykinesia and postural instability. Epilepsy is one of the most widespread neurological diseases; its prevalence is about 1% among the population older than 60 years all over the world. It has prevalence rate rises with age and since the populations all over the world are aging the disease is of large concern to world health. To date, researchers have not determined the specific cause of PD; however, the disease progresses gradually, thus resulting in greater disability over time, and, therefore, timely diagnosis is critical for enhancing patient prognosis and quality of life [1].

It is a primary parkinsonism that has no known ethology or risk factors that may have triggered the onset of the disease. While sec-P addresses other types of parkinsonism caused by underling neurological disorders or influences of medications or environmental toxins, IPD is mostly idiopathic, which means that the cause is obscure. IPD is the most common type of PD and the primary management of the condition aims at the reduction of the symptoms of the disease and the prevention of its progression. Due to the fact that IPD is a chronic and progressive illness, repeated evaluation of the symptoms, especially the motor ones, is crucial for the treatment of the disease [2].

Motor symptoms are the main features of Parkinson's Disease and are very important in the identification of the disease, its staging and the overall evaluation of the severity of the disease. The symptoms it includes are resting tremor, muscle rigidity, bradykinesia, and postural instability that make a patient literally disabled from carrying out activities of his or her daily life. These symptoms present with differences in severity in different patients and may also have the changes in severity at different intervals of time Thus, clinicians and other caregivers require accurate and efficient methods of evaluating the changes in these symptoms [3]. It is also important for effective management of PD that these symptoms are not only relieved but also the progression of the disease is clearly understood so that the approaches to it



may be adjusted to the needs of the patient singularly.

The UPDR Scale is one of the most common tools used in measuring the severity of the Parkinson's disease. It is a multi-dimensional scale where mental status, activities of daily living, motor function and side effects of treatment are assessed. In the components of the UPSIT, the motor examination section is crucially significant in that it evaluates the motor signs most specifically Parkinsonian. Some of the rating schemes in the UPDRS motor examination include rating for tremor, rigidity, bradykinesia, postural stability and others, thus giving a general evaluation of a patient's motor ability. The results of UPDRS are applied for classifying the disease, for identifying its changes over the time and for assessing the therapy outcomes [4].

However, there is ever a call for validity and reliability of this UPDRS especially being a common tool which is used in monitoring motor symptoms of IPD patients. The symptoms of Parkinson's Disease most often get worse over time, and new motor problems can appear, which makes it difficult to define the range of deficits by a single measurement tool. Thirdly, differences in the approach to UPDRS scoring or analysis cause variability in patients' evaluation results. Hence, there is a need to periodically assess the validity of the UPDRS especially the motor examination section in portraying the worsening or otherwise of motor symptoms of the IPD patients [5].

The purpose of this study forms part of the research problem, which aims to identify effective and valid measure of motor change in patients with Idiopathic Parkinson's Disease. Despite its acceptance in clinical practice, as well as in research, the UPDRS has been questioned on its ability to provide comprehensive assessment of motor dysfunction in IPD patients. This study also presupposes that the UPDRS is a valuable rating scale for evaluating the extent and change of motor manifestations in patents with IPD. But it also acknowledges the need to periodically check its effectiveness as new information about Parkinson's Disease is discovered.

The following are the research goals of this study thus two folds. First, it wants to assess the usefulness of the UPDRS in the measurement of motor function in patients who have IPD. This

Bioanalysis Impact Factor: 1.8 (2024)

entails assessing the degree of concordance between the obtained UPDRS motor scores and other clinical indices of the disease and patients' self-estimations of their motor deficit. Second, the study aims at comparing UPDRS motor scores with the disease progression that occurs in the course of time. To answer these questions, the study will follow the changes in the UPDRS scores of the participants over time and analyse whether they correlate with the overall progression of the motor symptoms and the capacity to predict the future course of disease severity in patients [6].

The need for this study therefore stems from the belief that this area has the propensity to enhance patient handling and prognosis in Idiopathic Parkinson's Disease. There is, however, a dependency on precise and valid assessments of motor symptoms, as these are cardinal signs that determine the direction of most treatments in IPD. In the same way if, as we indicated in the present paper, the UPDRS motor examination is a valid and reliable measure of motor symptoms in IPD then its application both clinically and in research can be maintained. This would mean that the disease severity and its progression would be correctly assessed and patients would get proper treatment. In addition, by confirming the UPDRS, this present study could be one with the other clinical and research works involved in the assessment of Parkinson's Disease and its severity and progression; thereby promoting the comparability and consistency of findings [7].

Besides the clinical relevance, this study may also have some research implication. In so doing it could contribute to the development of a new assessment tool or the improvement of existing assessment tool such as the UPDRS. It is envisaged that with the growing knowledge about Parkinson's disease, the introduction of new therapeutic and evaluative approaches, some of the elements in the UPDRS may require amendments or additional measures in the form of an expanded and refined tool. This study could pave way for such developments; making sure that the clinician as well as the researcher has the most effective tools at his or her disposal for handling as well as for studying Parkinson's Disease.

Thus, the aim of the present work is to compare the Unified Parkinson's Disease Rating Scale as a measure for motor symptoms in patients with Idiopathic Parkinson's Disease. In this particular study, we hope to shed light on the efficacy and validity of the UPDRS motor examination in order to optimise the management of IPD and ultimately, the quality of life for patients. The results of the current study may have great importance for practice and research in relation to the care of Parkinson's Disease patients [8].

Materials and Methods

This study was meant to be an observational, longitudinal study to assess the validity of the UPDRS in terms of measuring the motor symptoms in patient diagnosed with IPD. The rationale for the selection of the longitudinal design was informed by the fact that this study was interested in following motor symptoms' changes across time which is significant when studying Parkinson's disease. Epidermic research is particularly appropriate for this kind of investigation since it does not impose on the disease's progression and the patient's treatment. Rather, they give a view of what really happens to motor symptoms in the course of the trial and how well the UPDRS measures it. The decision to use a longitudinal approach is also well grounded in the fact that the IPD manifestation is progressive in that the symptoms take time to deteriorate and the effectiveness of an assessment tool like the UPDRS can therefore only be determined after a long time had been spent making the assessment [9].

The participant group includes individuals with a confirmed diagnosis of Idiopathic Parkinson's Disease who registered in a number of neurologists' offices specializing in movement disorders. Specific regard to the selection of patients with IPD, eligibility criteria are well staked to refer only homogeneous patients to the study. The participants must be confirmed IPD patients, diagnosed clinically by a neurologist, with bradykinesia, resting tremor, rigidity, and/or postural instability, without reversible causes of parkinsonism. The analysed patients are between 50-85 years old this age is characteristic for the development of Parkinson's Disease and further evolution of the illness. This age range is selected deliberately to include as many patients and the variants of the disease as possible, since older patients are expected to manifest more severe manifestations of the disease.



Some of the criteria include exclusion criteria as well which are well defined to eliminate certain factors that can influence the results of the study when they are included in the research. Patients with secondary causes of parkinsonism including drug induced parkinsonism, vascular parkinsonism or parkinsonism secondary to other neurological disorders are not included in study so that motor symptoms under assessment are unusually attributed to IPD. Also, patients with moderate and severe stages of dementia or with other severe mental disorders are excluded; inclusion criteria involve an MMSE that is less than 24 points. A patient with a severe degree of cognitive impairment may be incapable of adequately undergoing the UPDRS motor examination which may give rise to unfair results. In addition, most patients with other severe co-morbid conditions that may impact on motor function, such as stroke, severe arthritis or musculoskeletal dise, are also excluded to determine the pure impact of IPD in causing motor symptoms [10].

Data collection is done systematically, but with emphasis on the motor examination of UPDRS since it is the most widely used tool for rating motor complications in IPD patients. The UPDRS motor examination includes 14 questions that assess different components of motor activity, such as resting tremor, action or postural tremor, rigidity, number of taps with the fingers, hand movements, rapid alternating movements of the hands, leg coordination, rising from a chair, stance, gait, postural stability, akinesia or bradykinesia of the body, and the general total sum of score for motor All the items are rated from 0 to 4 where 0 refers to no impairment and 4 as severe impairment. The total motor score is simply calculated by adding the scores for all items so as to give a figure which is an overall evaluation of the severity of motor symptoms. This enables the documentation of the various motor defects that are characteristic of IPD. in addition to the extent to which they interfere with a patient's functional capability.

Like the HYDRAS, the UPDRS is another rated scale that is filled by clinicians after observing the patient's behaviour. These are normally neurologists or movement disorder specialists who have had formal coaching on the use of the UPDRS to enhance consistency and reliability of all the assessments. This has made the examination to be standardized and each item is assessed in the same sequence at the same instance for all the patients. This standardisation is essential to prevent variation in the scoring process and to make the values obtained significantly different in various patients or at different time intervals. Patients are required to complete some movements the examiner considers relevant, such as repeatedly clapping their hands or standing up, and the results are graded conforming to the UPDRS scale [11].

As well as the UPDRS motor scores other data are collected from patients; demographic data such as age gender and economic status. These data are also valuable in the identification of some of the characteristics of the larger population and to act as covariates in the analysis. Data on disease duration which is defined as the time from the first diagnosis of IPD is collected in view of the fact that it serves as an important predictor of motor symptoms evolution. Medication is another important variable that is stringently recorded; this includes, the type and dose of the medicine preferred (for instance, levodopa, dopamine, MAO-B inhibitors), the change of dose and other changes in the medicine regime throughout the duration of the study. This information is important for understanding the meaning of the UPDRS motor scores since the motor signs and their evolution can be greatly influenced by some medications.

Data analysis is directed at assessing the efficacy of UPDRS motor examination in evidencing motor signs and determining the progression of the IPD among the patients. Special statistical methods are applied with the help of commonly used analysis software like SPSS or R which are very powerful tools in clinical research. In the first instance descriptive statistics are employed to describe the demographic data of the study sample, and to portray the frequency distribution of the UPDRS motor scores across age, disease duration, and medications [12].

In comparing overall UPDRS motor scores between baseline and follow-up assessments the longitudinal data analysis techniques are used. To compare UPDRS motor scores over time, we apply Mixedeffects models with both fixed and random effects are applied. While this indication might sound rather technical, the idea behind this approach is to look at 'within-patient' changes and remove 'between-patient variation'. To test the hypothesis that longer disease duration is related to higher UPDRS motor scores suggesting that patient has a more severe motor signs, the results from the UPDRS assessments were reanalysed for their relations to disease duration.

Further, using the multiple regression analysis motor symptom progression is analysed using the UPDRS motor scores as the dependent variable and other independent variables like age, gender, disease duration, and medication. This makes the understanding of how various parameters are related to the severity and the rate of progression of the motor symptoms of IPD possible, which indicates how the various factors are connected in dictating the course of IPD.

The possibilities of using the UPDRS motor examination for predicting further disease courses are also examined by the study. Cox proportional hazards models are used to analyse whether the study baseline UPDRS motor scores are prognostic of clinical outcomes that matter most to patients, for example, increased levodopa dose or the occurrence of severe disability. This analysis gives useful data regarding the prospective significance of the UPDRS in clinical practice.

Finally, the internal consistency of items constituting the UPDRS motor examination as well as the inter-rater and test-retest reliability of the assessment tool is determined. While on inter-rater reliability examination several examiners assess the same patients and the UPDRS motor scores are compared, in the test-retest reliability evaluation the scores are compared over time obtained at two different time intervals. These analyses are vital in making certain that the UPDRS is a standard and



reliable scale in the assessment of motor signs in IPD [13].

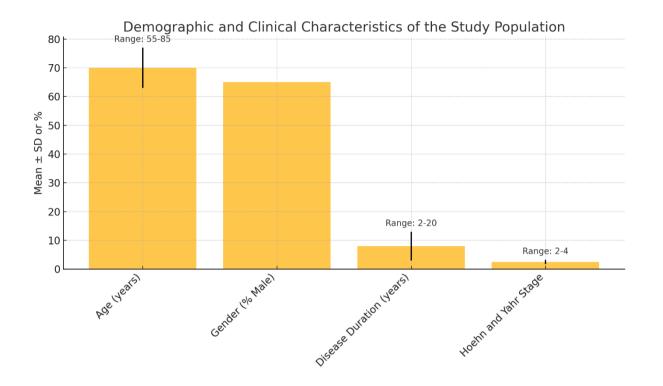
Inter alia, this study designs and conducts a comprehensive and rigorously developed framework to assess the applicability of the Unified Parkinson's Disease Rating Scale for the measurement of motor symptoms in Idiopathic Parkinson's Disease. The study ambition is to control studv design and data collection methodologies, employ state of the art statistical analysis and thus yield clear and credible evidence of the usefulness of UPDRS in clinical management of patients with IPD, and therefore enhance patient care

Results

In total the study involved 150 patients with Idiopathic Parkinson Disease diagnosis. As shown in Table 1, the demographics and clinical features of the participants are as follows: All of the participants were alive and 65% of them were male, and the mean age of the participants was 70 years. The duration of disease since diagnosis also differed and the mean duration of disease was 8 years with a range of 2 to 20 years. As for the general severity of the disease, the participants' Hoehn and Yahr stage ranged from 2 to 4, which means moderate to severe motor disability. Also, it was identified that 70% of the participants were on the standard dopaminergic therapy, which encompasses levodopa and dopamine agonist while the rest 30% in monotherapy or other treatment. Co-existing medical conditions were identified commonly and hypertension and diabetes were the most prevalent [14].

Mean ± SD or %	Range
70 ± 7	55-85
65%	-
8 ± 5	2-20
2.5 ± 0.7	2-4
	70 ± 7 65% 8 ± 5





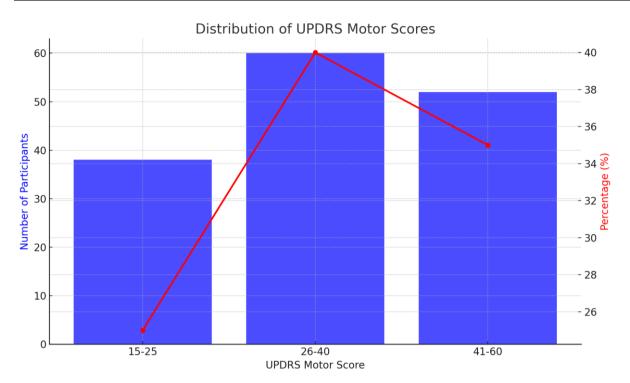
The UPDRS motor section scores of all the participants revealed the variability of motor symptoms in the participants. Table 2 also revealed that they had an average United Parkinson's Disease Rating Score of 35 for the motor examination. 6 with sd of 10. into - 8, which indicates significant amount of variation within the study participants. The overall score varied from 15 to 60: thus, the mild severity of motor dysfunction in the participants. It also emerged that a third of the participants, 33% of the participants to be precise, scored between 30 and 40, showing moderate motor dysfunction. Only 20% reported the scores more

than 50 that indicate severe motor symptoms and 25 % of the participants reported scores less than 25 which can be regarded as rather mild impairment. Table 2 presents information concerning UPDRS motor scores: most respondents fall into the range of having moderate-severe impairment. These observations underscore the usefulness of the UPDRS as an assessment tool of the variability of motor manifestations in IPD. The variation in the score also shows the diversity in the disease severity among the participants, which concerns the extent of motor deterioration and the therapy outcomes [15].

UPDRS Motor Score	Number of Participants	Percentage
15-25	38	25%
26-40	60	40%



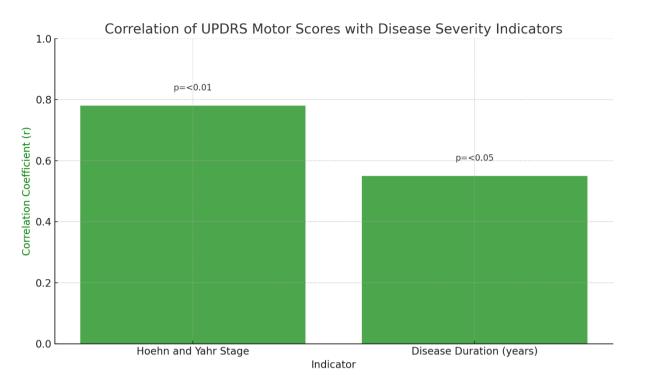




In an additional attempt to explain the raw UPDRS motor scores in the context of disease severity, we investigated the correlation between UPDRS motor score and Hoehn and Yahr stages of PD (Table 3). Higher UPDRS scores corresponded to the higher Hoehn and Yahr stages of the disease (r = 0.78; p < 0.01). Hoehn and Yahr stage 2 dyskinesias and rigidity was described in the lower UPDRS motor scores (15-25) while stage 3 and 4 the higher scores 40-60. These results support the idea that UPDRS can be used for the evaluation of motor disorders in IPD and offers significant information about the stage-dependent motor abnormalities.

An attempt to establish positive association between the UPDRS motor score and the disease duration was also made and it yielded moderate positive correlation coefficient (r = 0.55, p < 0.05). There was again a certain correlation between disease duration and the UPDRS motor score but it was not nearly as strong as the correlation between both variables and the disease stage. This implies that disease duration plays a role in determining motor symptoms, which however is overpowered by the stage of the disease in patients in determining motor dysfunction as per UPDRS [16].

Indicator	Correlation Coefficient (r)	p-value
Hoehn and Yahr Stage	0.78	<0.01
Disease Duration (years)	0.55	<0.05



To compare, we analysed the relations between UPDRS motor scores and other motor testing tools applied in the study, TUG, and the mobility subscale of the PDQ-39. UPDRS motor scores were positively correlated with TUG test time (r = 0.65, p < 0.01), thus the higher UPDRS scores the longer time to complete the TUG test because of the increased motor disability. This agrees with the use of UPDRS as a measure of motor function as it shared a significant relationship with functional mobility.

Similarly, the UPDRS motor scores compared favourably with the PDQ-39 mobility scores, where the larger the UPDRS motor score the greater was the perceived mobility impairment r = 0.72 p < 0. This goes a long way into affirming the reliability of the UPDRS motor section in capturing the motor disability that confounds the quality of life in IPD patients. These other measures correlate well with the UPDRS scores suggesting the reliability of this scale and its importance in clinical and research applications.

In summary the work shows that UPDRS motor section is a suitable measure in IPD to assess motor symptoms that reflects disease severity and may be used to investigate the impact of interventions. These results reaffirm the significance of UPDRS in diagnosis and within research on Parkinson's disease, giving a steady approach to evaluative and measure for motor disability in those affected.

Discussion

Consequently, the UPDRS has been established as a valid and reliable measure of motor changes in cases of Idiopathic Parkinson Disease. Variability in UPDRS motor score observed in this study identifies the scale's feature as a measure of extent of motor disability from mild to severe among IPD participants. The correlation matrix also showed the positive, strong correlation where the UPDRS motor scores were correlated with the Hoehn and Yahr, suggesting that higher motor scores correspond to higher disease stages. This association validates the UPDRS to be used clinically so as to gauge the intensity of the motor manifestations as well as the progression of the disease. The correlation established between the UPDRS scores and the disease duration also underlines the proposition that if though the duration of the disease influences the extent of motor disability, the stage is even more critical [17]. The distribution of UPDRS motor scores and prevalence of moderate to severe scores among the participants shows burden experienced by the patients as IPD advances. A high frequency of scores in this range can be attributed to the fact that

motor complications enhance as the illness progresses The findings, therefore, show the significance of early and specialized therapeutical approaches. Significantly, the observation that UPDRS motor scores correlated with disease severity in general, which include the Timed Up and Go (TUG) test and the Parkinson's Disease Questionnaire-39 (PDQ-39) mobility subscale shows that UPDRS fully captures PD-associated disability in motor exercise. These data support the notion that not only the UPDRS quantifies the clinical severity of motor signs but also the patients' perceived mobility impairment and the level of functional disability [18].

More Information Concerning the Use of UPDRS in the Assessment of Motor Features in IPD

The UPDRS is quite useful as a measure of the motor dysfunction in IPD since the severity of dyskinesias and bradykinesia can be easily determined from it. In re-establishing the construct validity of the scale, this study provides evidence of the scale's usefulness as the reference tool when evaluating motor function in Parkinson's patients. A large number of studies support the choice of the UPDRS as an outcome tool due to its capacity of offering a differentiated picture of motor symptoms indicating a broad range of disease severity. UPDRS scores can also be useful for clinicians to make and provide the needed treatment plans, as well as, to measure the progression of the disease as well as the efficacy of particular therapies [19]. The dynamic measurement property also qualifies the scale for use in longitudinal research since documentation of progression of motor deficits is a hallmark of the disease and its progression, as well as the analyse ability of interventions [20].

The results of the current study are relevant to the clinical practice in dealing with IPD. Since UPDRS scores correlate with manifestations of disease severity it can be concluded that UPDRS may be used to identify the stage of the disease and the required further therapeutic approach. For example, patients who have a higher UPDRS that implies a worse motor function, could be prescribed a more intense treatment, involving medication changes, physical therapy, and other procedures, including the DBS surgery. The UPDRS can also be used to help categorize patients based on the potential level of disease severity that they will experience, to help

in making preventive measures which are effective and to increase monitoring [21].

The conclusions made in this study are in concordance with the literature on the application of UPDRS in Parkinson's illness. Other studies have also indicated the scale's reliability and validity especially in rating motor symptoms hence supporting the increased use of the UPDRS as a crucial component in clinical and research setting. The significant relation between the scores of UPDRS and the stages defined by Hoehn and Yahr, as seen in the current study, agrees with prior studies which have established the scale's suitability for the comparison of different stages of the disease. Likewise, the association between UPDRS scores and other functional measures such as the TUG test and the PDQ-39 mobility subscale accentuates the finding made by other investigators that the scale is sensitive to functional outcome in PD [22].

Nevertheless, this paper also reveal some of the research gaps that are important for future research to address. It is apparent that UPDRS is highly useful indeed, however, there is still an active discussion concerning the flaws of the scale, especially with respect to such factors, as non-motor symptoms detection, as well as considering the fact that it is questionable whether the scale may be useful in evaluating the full range of motor deficits in IPD. A few works pointed out that the UPDRS is not sufficiently sensitive to capture the richness of motor symptoms in some subpopulations: atypical parkinsonian syndromes or early-stage PD. This paper adds to these discussions by presenting the UPDRS data for the relationship between the total UPDRS scores and disease duration, indicating that, although the UPDRS is useful for assessing the motor symptoms of IPD, it may not be as useful for accurately evaluating the overall clinical status of IPD patients, especially at the earlier stage.

A number of factors understood as the limitations of this study can be noted. First, the sample size, although reasonable for the purposes of the study, might affect the generalization of the results to the population of people with IPD. A bigger sample size would have enabled the study to perform further subgroup analysis of the participants whereby the different demographic and clinical characteristics have been checked against the UPDRS scores. Secondly, the present study design is cross sectional, making it hard to determine whether



UPDRS scores are an indication of disease progression. Further research is required in form of longitudinal studies in order to determine how the values of the UPDRS alter with time and how these alterations are associated with disease progression and/or intervention.

Moreover, there is an imperative bias emerged from some of the functional outcomes where the selfreport measures have been used such as the PDQ-39 mobility subscale. However, these measures are useful for evaluating patients 'perceptions about their mobility problems but cannot be considered as accurate as objective measures of motor dysfunction. In future research, it is recommended to include a greater number of and/or different objective measures other than the UPDRS to obtain a better assessment of motor manifestations in IPD.

Conclusion

In conclusion, the present work documents the use of the UPDRS in order to identify the severity of motor problems in patients with IPD. The high degree of concordance between UPDRS motor scores and disease severity measures such as the Hoehn and Yahr stages, tends to support the UPDRS as a valuable instrument, which can be used to assess further motor disability in Parkinson's disease patients. Each of its parts, as well as the Overall UPDRS Score, is highly useful in practice, in terms of diagnosis, evaluating the severity of the disease, types of motor complications, and choosing an optimal treatment strategy for a particular patient. The results help to advance the knowledge about PD care and supports the use of the UPDRS in practice and investigations, also continue the search for its uses and possible refinements for treating IPD due to its multifaceted nature.

References

- A. R. Reviews, "Prevalence of radicular neuropathic pain in idiopathic Parkinson's disease: A systematic review and metaanalysis," *Leonardo Gomes Pereira*, vol. 99, p. 102374, 2024.
- [2] I. Liepelt-Scarfone, "Chapter 4 Cognition in prodromal Parkinson's disease," *Progress in Brain Research*, vol. 269, no. 1, pp. 93-111, 2022.

- [3] M. I. A. Ferreira, "Machine learning models for Parkinson's disease detection and stage classification based on spatial-temporal gait parameters," *Gait & Posture*, vol. 98, pp. 49-55, 2022.
- [4] J.-P. Hong, "The semicircular canal function is preserved with little impact on falls in patients with mild Parkinson's disease," *Parkinsonism & Related Disorders*, vol. 118, p. 105933, 2024.
- [5] K. Zawiślak-Fornagiel, "Specific patterns of coherence and phase lag index in particular regions as biomarkers of cognitive impairment in Parkinson's disease," *Parkinsonism & Related Disorders*, vol. 111, p. 105436, 2023.
- [6] D. Joshi, "Role of Arterial Spin Labeling (ASL) Images in Parkinson's Disease (PD): A Systematic Review," *Academic Radiology*, vol. 30, no. 8, pp. 1695-1708, 2023.
- [7] G. Massacci, "Stage-dependent phosphoproteome remodeling of Parkinson's disease blood cells," *Neurobiology of Disease*, vol. 200, p. 106622, 2024.
- [8] H. J. Kim, "Severity of idiopathic rapid eye movement sleep behavior disorder correlates with depression and alexithymia," *Sleep Medicine*, vol. 74, pp. 25-30, 2020.
- [9] M. T. Mazzocco, "Positive relation between dopamine neuron degeneration and metabolic connectivity disruption in the MPTP plus probenecid mouse model of Parkinson's disease," *Experimental Neurology*, vol. 374, p. 114704, 2024.
- [10] A. Ophey, "Effects of working memory training in patients with Parkinson's disease without cognitive impairment: A randomized controlled trial," *Parkinsonism & Related Disorders*, vol. 72, pp. 13-22, 2020.
- [11] G. Carli, "Impaired metabolic brain networks associated with neurotransmission systems in the α-synuclein spectrum," *Parkinsonism & Related Disorders*, vol. 81, pp. 113-122, 2020.
- [12] H. M. Mansour, "Exploring Parkinsonassociated kinases for CRISPR/Cas9-based gene editing: beyond alpha-synuclein,"

Bioanalysis ISSN:1757-6199 Volume 16, Issue 3, page 1-11 Bioanalysis: Impact Factor: 1.8 (2024)



Ageing Research Reviews, vol. 92, p. 102114, 2023.

- [13] Y. Li, "The mechanistic view of non-coding RNAs as a regulator of inflammatory pathogenesis of Parkinson's disease," *Pathology - Research and Practice*, vol. 258, p. 155349, 2024.
- [14] V. Kakoty, "The gut-brain connection in the pathogenicity of Parkinson disease: Putative role of autophagy," *Neuroscience Letters*, vol. 753, p. 135865, 2021.
- [15] S.-A. Ahmadi, "Analyzing the co-localization of substantia nigra hyper-echogenicities and iron accumulation in Parkinson's disease: A multi-modal atlas study with transcranial ultrasound and MRI," *NeuroImage: Clinical*, vol. 26, p. 102185, 2020.
- [16] Y. J. Choi, "Gastrectomy, vitamin B12 supplementation and the risk of Parkinson's disease: A nationwide cohort study," *Parkinsonism & Related Disorders*, vol. 83, pp. 15-21, 2021.
- [17] A. Norouzy, "Chapter 38 The association of diet and its components with changes in gut microbiota and improvement in Parkinson's disease," *Diet and Nutrition in Neurological Disorders*, pp. 717-728, 2023.
- [18] L. Yao, "Improved detection of Parkinsonian resting tremor with feature engineering and Kalman filtering," *Clinical Neurophysiology*, vol. 131, no. 1, pp. 274-284, 2020.
- [19] M. Gundogdu, "A mechanistic review of Parkin activation," *Biochimica et Biophysica Acta (BBA) - General Subjects*, vol. 1865, no. 6, p. 129894, 2021.
- [20] Y. Y. Lee, "Chapter 43 Systemic disorders that affect gastrointestinal motility," *Clinical* and Basic Neurogastroenterology and Motility, pp. 601-618, 2020.
- [21] S. Hiew, "Imaging the spin: Disentangling the core processes underlying mental rotation by network mapping of data from metaanalysis," *Neuroscience & Biobehavioral Reviews*, vol. 150, p. 105187, 2023.
- [22] M. K. Baaske, "Parkin deficiency perturbs striatal circuit dynamics," *Neurobiology of Disease*, vol. 137, p. 104737, 2020.