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PDD-5S: A useful screening tool for Parkinson's disease dementia

Wei-Ju Lee [a, b, c], Shey-Lin Wu [d], Jie-Yuan Li [b, e], Chin-Chung Chen [f], Juei-Jueng Lin [g, h], Giia-Sheun Peng [i], Tsu-Kung Lin [j], Shuu-Jiun Wang [b, k], Rou-Shayn Chen [l, m], Yuan-Han Yang [n, o, p], Chon-Haw Tsai [q, r, s], Jung-Lung Hsu [l, m, t], Yi-Chu Liao [b, k], Shih-Pin Chen [b, k], Jong-Ling Fuh [b, k, *]

[a] Neurological Institute, Taichung Veterans General Hospital, Taichung, Taiwan
[b] Faculty of Medicine, National Yang-Ming University Schools of Medicine, Taipei, Taiwan
[c] Institute of Clinical Medicine, National Yang-Ming University Schools of Medicine, Taipei, Taiwan
[d] Department of Neurology, Changhua Christian Hospital, Changhua, Taiwan
[e] Division of Neurology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan
[f] Department of Neurology, Shung Ho Hospital, Taipei Medical University, New Taipei City, Taiwan
[g] Department of Neurology, Chushang Show-Chwan Hospital, Nantou, Taiwan
[h] Department of Neurology, Chung-Shan University Hospital, Taichung, Taiwan
[i] Department of Neurology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan
[j] Department of Neurology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan
[k] Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan
[l] Department of Neurology, Chang Gung Memorial Hospital, Taipei, Taiwan
[m] Chang Gung University College of Medicine, Taipei, Taiwan
[n] Department of Neurology, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan
[o] Department of and Master's Program in Neurology, Faculty of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan
[p] Department of Neurology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung Taiwan
[q] Department of Neurology, China Medical University Hospital, Taichung, Taiwan
[r] School of Medicine, Medical College, China Medical University, Taichung, Taiwan
[s] Graduate Institute of Neural and Cognitive Sciences, China Medical University, Taichung, Taiwan
[t] Institute of Biomedical Engineering, National Taiwan University, Taipei, Taiwan

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ABSTRACT

Introduction: Parkinson's disease dementia (PDD) contributes to poor quality of life and increases the mortality risk. Early detection and diagnosis of PDD are essential for clinical care.
Methods: We recruited patients with idiopathic Parkinson's disease (PD), who underwent clinical assessments and neuropsychological tests, at 12 teaching hospitals in Taiwan. Probable PDD was diagnosed according to the Movement Disorder Society Task Force clinical criteria. Using binary logistic regression, we selected significant items from an original 30-item informant questionnaire. We utilized these items, along with a simple cognitive test, to discriminate between PDD and nondemented PD (PD-ND).
Results: Among the 265 PD patients (156 men, 109 women, mean age 71.9 ± 9.1 years), 102 and 163 patients were diagnosed with probable PDD and PD-ND, respectively. The mean education of participants was 8.8 ± 5.3 years, and the mean disease duration was 5.5 ± 5.4 years. When the patients fulfilled either of the following criteria: (1) a score ≥ 3 for the five endorsed screening questions, (2) a score of 1–2 for the five above screening questions combined with a score ≤ 10 items for category verbal fluency, the sensitivity and specificity of the PDD screening tool were 80.4% and 80.4%, respectively. The area under the receiver operating characteristic curve (AUC) was 0.804. We tested this screening tool in another 137 unrelated PD patients and the sensitivity, specificity, and AUC were 77.4%, 96.4%, and 0.869, respectively.
Conclusion: The "PDD-5S" is a brief and useful screening tool for PDD.

* Corresponding author. Neurological Institute, Taipei Veterans General Hospital, Taipei, 112, Taiwan.
E-mail address: jlfuh@vghtpe.gov.tw (J.-L. Fuh).

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1. Introduction

Dementia is an important complication of Parkinson's disease (PD) because dementia in PD contributes to poor quality of life and increases the mortality risk [1,2]. Early detection and diagnosis of Parkinson's disease dementia (PDD) are essential for clinical care. However, PDD may be underdiagnosed in neurological clinics [3], which may be partially due to the lack of a brief screening tool that discriminates between dementia in PD patients and normal cognition.

Current clinical PDD diagnoses follow the recommendations of the Movement Disorder Society Task Force [4,5]. An algorithm was developed [5] based on the current diagnosis tools. A clinical validation study of this diagnostic algorithm showed only 46.7% sensitivity for a PDD diagnosis compared with the full neuropsychological assessment [6]. Impairment of activities of daily living (ADLs) in PD patients not attributed to motor or autonomic symptoms is a major criterion used to diagnose PDD. However, determining this value is challenging during clinical practice [4,5]. PDD cannot be correctly diagnosed by brief procedures; instead, a comprehensive evaluation, including neuropsychological tests and clinical interviews, is necessary [3,6]. The length of time needed for a standard PDD diagnosis is a major limitation. Therefore, clinical physicians need a brief tool to screen potential PDD patients.

Some previous studies focused on the screening tests for dementia in PD patients, for example, PDD-Short Screen (PDD-SS) [7] and Mini-mental Parkinson (MMP) [8]. However, the PDD-SS takes 5–7 min to be administered because it includes four tests and five screening questions [7]. The administration time and too many steps of PDD-SS might be the major limitations to use as a brief screening test. The MMP cannot detect the functional decline from previous levels because it does not include the informant-based questionnaire [8].

In this study, we aimed to establish a brief PDD screening tool which can be administered less than 5 min and is useful in routine clinical practice at outpatient services. Due to the brief period available to screen patients in clinical practice, several trade-offs that sacrifice the specificity and sensitivity of the screening tool may have to be made to detect dementia and enable the screening instrument to be completed in the short time of a few minutes. In this paper, we use the term “screening” to refer to an opportunistic case finding in a clinical setting (especially primary care), as opposed to the epidemiologic sense of screening asymptomatic individuals in the community. Employment of this screening method may be the first step in screening PDD patients by general practitioners and neurologists and for the diagnosis of PDD in future research studies.

2. Methods

2.1. Study participants

Study participants were already enrolled in the Dementia Registry of Parkinson's Disease (DRPD) study in Taiwan. Consecutive patients with idiopathic PD with or without cognitive decline were enrolled at 12 teaching hospitals in Taiwan [3]. All subjects had been diagnosed with PD according to the UK Parkinson's Disease Society Brain Bank criteria [9]. Other inclusion criteria included age at onset greater than 50 years, no depressive disorder (Geriatric Depressive Scale [10] score < 6), and the caregiver was available to provide collateral history. Patients who had developed dementia within 1 year after PD onset or who had other diseases that could impair cognition (e.g., stroke, hydrocephalus, epilepsy, or major depressive disorder) were excluded. We also excluded the patients who received deep brain stimulation and who took anticholinergics, cholinesterase inhibitors and NMDA inhibitors. Patients with motor fluctuations were enrolled during the “on’” state. The age, sex, years of education, and length of time since PD diagnosis were recorded for each patient. Another unrelated group of PD patients with or without cognitive decline according to the same inclusion and exclusion criteria were recruited from one teaching hospital to re-evaluate and validate the screening tool. The study protocol was approved by the institutional review boards of each hospital. Informed consent was signed by all patients and patients' relatives (caregivers) together.

2.2. Clinical evaluation and procedures

Experienced neurologists in 12 teaching hospitals conducted independent patient and caregiver interviews to determine the significant impairment of ADLs that cannot be attributed to motor or autonomic symptoms, which is one of the major criteria for diagnosing PDD [3]. The PD stage was evaluated by the modified Hoehn and Yahr (H & Y) Scale [11]. Motor symptoms were assessed using the motor part of the Unified Parkinson's Disease Rating Scale (UPDRS) [12]. General cognitive functioning was evaluated by the Mini-Mental State Examination (MMSE) [13] and Montreal Cognitive Assessment (MoCA) [14]. In accordance with the summary of tests at level II testing for PDD diagnosis by the Movement Disorder Task Force [5], we evaluated four cognitive domains, as follows: attention and working memory (digit span) [15], memory (12-item word recall test) [16], executive function (category verbal fluency) [17], and visuospatial function (5-point scale for cube copying [18] and 16-point [19] scale for clock drawing). Significant ADLs impairment was assessed by neurologists during interviews. Impairment of at least two cognitive domains was assessed by neuropsychiatric test batteries that had suitable and previously reported cut-off values [14,16,18,20]. Probable PDD was diagnosed according to the clinical criteria [4].

2.3. Screening tool development

We developed a brief PDD assessment tool, PDD-5S, which includes both a performance-based assessment of the patient and a brief informant interview. The list of screening questionnaires was developed on the basis of literature reviews and our experience conducting patient and informant interviews. Initially, we developed a 30-item questionnaire primarily adopted from the informant questionnaire on cognitive decline in the elderly (IQCODE) [21] and AD8 [22] (see Supplement 1). The following three response options were provided for each question in the questionnaire: no change, deterioration, and unknown. The initial 30-item questionnaire was administered by trained study assistants to all PD patient caregivers, and the neurologists who performed the clinical interviews were blinded to the results.

We performed statistical analysis (for detail, see Statistical analysis) to select significant items from the 30-item questionnaire. To improve its ability to distinguish between patients with PDD and nondemented PD (PD-ND), we next introduced one of following simple cognitive tests which were suggested for diagnosing PDD at level I by Movement Disorder Society Task Force [5]: category verbal fluency, 3-word recall of the MMSE, serial 7's of the MMSE, and drawing of the MMSE pentagons. We analyzed the diagnostic value when combining the screening questionnaire with one of the simple cognitive tests results.

After establishing the final screening instrument, we administered the instrument to another unrelated group of PD patients for validation. Besides, we selected 30 patients randomly and measured test-retest reliability during the 2 weeks interval. Clinicians, who were blinded to the PDD-5S results, diagnosed the