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Original Investigation

Depression and Cognitive Impairment in Peritoneal Dialysis: A Multicenter Cross-sectional Study

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Background: Depression and cognitive impairment have been identified as independent risk factors for mortality in peritoneal dialysis (PD) patients. The relationship between depression and global and specific cognitive functions in PD patients was investigated in this study.

Study Design: Multicenter cross-sectional study.

Setting & Participants: 458 clinically stable patients, drawn from 5 PD units, who performed PD for at least 3 months were enrolled.

Predictor: Depression, defined as depression severity index score > 0.5 using the Zung Self-rating Depression Scale.

Outcomes: Global and specific cognitive impairment. Global cognitive function was measured using the Modified Mini-Mental State Examination (3MS), Trail-Making Test forms A and B for executive function, and subtests of the Battery for the Assessment of Neuropsychological Status for immediate and delayed memory, visuospatial skills, and language ability.

Results: Prevalences of depression and cognitive impairment evaluated by the 3MS were 52% and 28.4%, respectively. Patients with mild or moderate/severe depression had higher prevalences of general cognitive impairment, executive dysfunction, and impaired immediate and delayed memory. After adjusting for demographics, comorbid conditions, and clinical parameters, depression scores were independently associated with lower 3MS scores, lower immediate and delayed memory and language ability scores, and longer completion times of Trails A and B. Even mild depression was independently associated with higher risk for cognitive impairment, executive dysfunction, and impaired immediate and delayed memory after multivariable adjustments.

Limitations: The causal relationship between depression and cognitive impairment could not be determined, and the potential copathogenesis behind depression and cognitive impairment was not fully investigated.

Conclusions: Even mild depression is closely associated with global and specific cognitive impairment in PD patients.

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INDEX WORDS: Peritoneal dialysis (PD); depression; cognitive impairment; cognitive dysfunction; executive dysfunction; executive impairment; end-stage renal disease (ESRD); chronic kidney disease (CKD).

For peritoneal dialysis (PD) as a home care therapy, patients must be able to self-monitor and self-manage their treatment[1]; therefore, it is dependent on adequate cognitive function.[2] Unfortunately, the prevalence of cognitive impairment is high, at 27% to 67% in patients with end-stage renal disease.[3-6] Cognitive impairment has been shown to be an independent predictor of mortality[3] and technique survival[7] in dialysis patients. It is therefore critical to explore risk factors for cognitive impairment in this population.

Depression is another common phenomenon in patients with chronic kidney disease (CKD), reaching a prevalence of 39.3% in patients with end-stage renal disease.[8] Depression is closely associated with decreased quality of life[9] and is predictive of higher mortality in dialysis-dependent and non–dialysis-dependent patients with CKD.[10-14] For PD patients, the presence of depression is also associated with increased risk for PD-associated peritonitis.[15] The effect of depression on cognitive function, such as executive function, memory, attention, and psychomotor speed, has been recognized in the general population.[16-18] By contrast, there are limited data for this issue concerning patients with CKD, with some data showing only a close relationship between depression and cognitive function in older adults with CKD[19] and

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patients on maintenance hemodialysis therapy.[20-22] To our knowledge, the association of depression and cognitive function has not been explored in PD patients in previous publications.

In this multicenter cross-sectional study, we aimed to investigate associations between depression and general and specific cognitive function in PD patients.

METHODS

Study Design and Participants

Five PD centers from 5 provinces (Beijing, Heilongjiang, Hebei, Anhui, and Guangdong) located at 4 geographical regions (north, northwest, east, and south) in China participated this multicenter cross-sectional study. All these centers have physicians and nurses trained in treating PD patients. Data from each center were collected within a strict quality control framework and further inspected and optimized to ensure the integrity and accuracy of the database. All study investigators and staff members completed a training program that taught them the methods and processes of the study. A manual of detailed instructions for data collection was distributed. The ethics committee of Peking University First Hospital approved the study. Patients gave written consent for their information to be stored on the hospital database and to be used in research.

This study enrolled prevalent PD patients from March 2013 until March 2014. Inclusion criteria for participants were as follows: 18 years or older, had been undergoing PD for 3 or more months and clinically stable, and able to undergo all measurements and questionnaires as required. Patients were excluded if they had a systemic infection, acute cardiovascular events, active hepatitis or cancer, surgery, or trauma in the month prior to the study, and all other study-obstructive conditions such as severe eyesight loss, language incompatibility, illiteracy, mental disturbance (preexisting dementia or confusion, and various mental disorders), and upper-limb disability. All participants received conventional glucose-based lactate-buffered PD solutions (Ultrabag; Baxter Healthcare). Continuous ambulatory PD was the only modality for all participants.

Clinical Characteristics

Demographics and comorbid conditions were recorded, including age, sex, education level, PD vintage, body mass index (BMI), systolic and diastolic blood pressure, primary kidney disease, the presence of diabetes mellitus (DM), and history of cardiovascular disease (CVD). Mean arterial pressure was calculated. Level of education was recorded as the highest school level at which a diploma was received (ie, elementary school or lower, middle school, high school, or above high school). If one or more of the following conditions was present, CVD was recorded: angina, congestive heart failure (New York Heart Association class III-IV), transient ischemic attack, history of myocardial infarction or cerebrovascular accident, and peripheral arterial disease.[23] Cerebrovascular accident was recorded separately.

Laboratory Methods

After overnight fasting while continuing PD therapy, participants had their venous blood sampled for routine and biochemical measurements. Biochemical data (including serum sodium, serum albumin, calcium, phosphate, triglycerides, total cholesterol, high-sensitivity C-reactive protein (hs-CRP), and hemoglobin) were gathered using an automatic Hitachi chemistry analyzer, and the mean value of measurements taken over the preceding 3 months was calculated. Residual kidney function was defined as the mean of residual creatinine and urea clearance from a 24-hour urine collection. Dialysis adequacy was defined as total Kt/V and creatinine clearance.

Cognitive Function and Depression Status

The Modified Mini-Mental State Examination (3MS)[24] was used to test overall cognitive function. In previously published observational studies of cognitive function, global cognitive impairment has been defined as a score less than 80 on the 3MS test.[6,25-27] Because mean scores on the 3MS vary by education, we used a 3MS cutoff point of less than 75 for individuals with less than a high school education and a 3MS cutoff point of less than 80 for individuals with a high school education.[26]

Specific cognitive functions measured were executive function (by the Trail-Making Test, forms A [Trails A] and B [Trails B]), immediate memory, delayed memory, visuospatial skill, and language ability by subtests of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Trails A and B[28] were to test executive function including decision making and processing speed. Executive dysfunction was defined as Trails A score more than 75 seconds and Trails B score more than 180 seconds.[29-31] In addition, subtests of RBANS were adopted to assess immediate memory (list learning and story memory), delayed memory (list recall, list recognition, story recall, and figure recall), visuospatial skill (figure copy), and language ability (picture naming and semantic fluency).[32] The reliability and validity of RBANS have already been established in Shanghai and Beijing populations.[33,34] Raw scores were transferred to age-standardized T scores for all subtests of RBANS. T scores less than 1 standard deviation below the published mean in an education-grouped Chinese population were identified as impaired for each test.[35] Depression status was assessed by using the Zung Self-rating Depression Scale. Depression was diagnosed if the depression severity index was greater than 0.5; this includes mild (index of 0.5-0.59) and moderate/severe depression (index $\geq$ 0.6).[36] The Zung Self-rating Depression Scale has been verified in the Chinese general population and in various medical illnesses.

Assessments of cognitive function and depression status were performed in a separate room with 1 medical staff to 1 patient. In total, 4 medical staff members participated in this study as observers and all completed a training program that taught them the methods and processes to ensure the integrity and accuracy of the assessment.

Statistical Analysis

Continuous data were presented as mean $\pm$ standard deviation except for PD vintage, residual kidney function, and hs-CRP level, which were presented as median with interquartile range due to high skew. Categorical variables were presented as proportions. Patients were divided into 3 groups: no depression, mild depression, and moderate/severe depression. One-way analysis of variance, Kruskal-Wallis, or χ^2 test was used to compare differences in demographic and biochemistry data and parameters of general and specific cognitive function between groups.

Correlations of depression scores, demographic and clinical characteristics, and parameters of cognitive function were examined by using univariable correlation analysis. Then depression scores were examined with their independent relationship with cognitive functions by multivariable linear regression analysis adjusting for recognized confounders. Three models of linear regression analysis models were built to explore the relationship between depression and cognitive function as assessed by 3MS, Trails A and B, immediate memory, delayed memory, visuospatial skill, and language ability. Model 1 included depression scores, demographic and comorbid condition status (age, sex, education level, BMI, DM, and CVD). Model 2 included depression scores, mean arterial pressure, and laboratory parameters (serum albumin, sodium, total cholesterol, hs-CRP, and residual kidney function). Model 3 included all variables in Models 1 and 2. Next, 3 models of multivariable logistic regression analyses were also performed