Risk factors for sleep disorders in patients undergoing peritoneal dialysis

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Abstract

Sleep disorders in patients with end-stage renal disease are common but have rarely been reported in previous studies. Therefore, we examined the prevalence of sleep disorders and the risk factors for declining sleep quality in patients undergoing peritoneal dialysis (PD). A multicenter prospective cohort study was conducted at five PD centers across different provinces in China. A total of 449 patients who underwent PD between March to November 2013 were enrolled. Demographic data, laboratory indicators, presence of depression, and sleep assessment data were collected. Sleep questionnaires reflecting five categories of sleep disorders, namely, insomnia, restless legs syndrome, excessive daytime sleepiness, possible narcolepsy, and sleepwalking and nightmares, were administered at baseline and at 24 months postoperatively. Sleep disorders were diagnosed when a patient had at least one sleep problem. At baseline, 335 (74.6%) patients had at least one type of sleep disorder. Depression, diabetes mellitus (DM), and male were found to be associated with the presence of a sleep disorder. At follow-up, the prevalence of insomnia, restless legs syndrome, and excessive daytime sleepiness had significantly increased in 285 patients. Furthermore, cardiovascular disease (CVD) was found to be associated with the presence of sleep disorders in patients with one or more disorders at baseline, whereas a low serum albumin level was found to be associated with sleep disorders in patients without any sleep disorders at baseline. The prevalence of sleep disorders was relatively high among PD patients at baseline and increased after the 2-year follow-up. Depression, DM, and male were associated with all sleep disorders at baseline. CVD was associated with the presence of a sleep disorder at baseline and worse sleep quality at the 2-year follow-up; whereas a low serum albumin level was associated with the risk of acquiring a sleep disorder at the 2-year follow-up among patients with normal sleep status at baseline.

Keywords Peritoneal dialysis · Sleep disorders · Sleep quality · End-stage renal disease

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Introduction

Given the increasing prevalence of end-stage renal disease (ESRD) and its associated burden on health, it is urgent to improve the clinical outcomes and quality of life of patients with ESRD [1]. Patients with ESRD, especially those undergoing dialysis, have significantly higher rates of sleep disorders than the general population [2]. The prevalence of sleep disorders varies between 50% and ≥ 80% in patients with ESRD, depending on the methodology used [2–5]. A Hong Kong study reported a high prevalence of sleep symptoms among patients undergoing continuous ambulatory peritoneal dialysis [6], including sleep maintenance insomnia (60%), sleep onset insomnia (73%), restless legs syndrome (62%), pruritus (71%), daytime sleepiness (77%), and frequent awakening (69%). Dialysis patients with sleep

disorders are prone to have a poorer quality of life and increased morbidity (including cardiovascular events, such as stroke and myocardial infarction) and mortality as well as poor mental capacity and task performance [5, 7].

Previous studies have reported that advanced age, hyperphosphatemia, and depression are risk factors for sleep disorders in patients on dialysis [4, 8]. Recent reviews have shown sex-based differences in the two most common sleep disorders, insomnia and restless legs syndrome. However, studies on sex-based differences in sleep disorders are limited [9].

Restless legs syndrome, depression, and low serum albumin levels are risk factors for sleep disorders among patients undergoing peritoneal dialysis (PD) [10]. However, evidence on the prevalence of and risk factors for sleep disorders in previous studies was inconsistent [4, 8–10]. Moreover, there are limited studies on sleep disorders and related factors in the PD population. Therefore, we conducted a multicenter, prospective cohort study with a 2-year follow-up to examine the risk factors for sleep disorders in patients undergoing PD.

Materials and methods

Recruitment

This study was part of a multicenter, longitudinal cohort study on sleep quality conducted at five PD centers across different provinces in China. Data from each center were collected using a strict quality control framework. Data on demographic characteristics, comorbidities, and biochemistry findings, along with assessments of depression and sleep disorders, were collected at baseline. All participants were followed up for 2 years prospectively.

Biochemical levels, depression, and sleep quality were repeatedly measured in patients with PD between March and November 2015. We had no private access to information that could identify individual participants during or after data collection. The study was approved by the Ethics Committee of Peking University First Hospital [Approval Number 2013 (587)]. Patients provided written informed consent for the collection of their information from the hospital's database and its analysis.

Patients with PD were enrolled between March and November 2013. The inclusion criteria were as follows: ≥ 18 years of age, undergoing PD for at least 3 months, clinically stable, and able to complete all required measurements and questionnaires. Patients with a systemic infection, acute cardiovascular event, active hepatitis or cancer, surgery or trauma in the month prior to the study, or any other conditions that would interfere with their participation in the study (e.g., severe impairment of eyesight, language

incompatibility, illiteracy, mental disturbance (pre-existing dementia or confusion, various mental disorders), or upper-limb disability] were excluded from the study. All participants received conventional glucose-based, lactate-buffered PD solutions (Ultrabag, Baxter Healthcare, Guangzhou, China).

Clinical characteristics

We recorded the participants' demographics and comorbidities, including age, sex, duration of PD, educational level, body mass index, systolic and diastolic blood pressure, primary kidney disease, the presence of diabetes mellitus (DM), and history of cardiovascular disease (CVD). CVD was recorded if one of the following conditions was present: angina, class III–IV congestive heart failure (New York Heart Association), transient ischemic attack, history of myocardial infarction or cerebrovascular accident, or peripheral arterial disease [11].

Laboratory measures

The biochemical indices were recorded as the mean of the measurements taken during the previous 3 months, including serum sodium, albumin, calcium, phosphate, triglycerides, total cholesterol, high-sensitivity C-reactive protein (hs-CRP), and hemoglobin. Biochemical profiles were tested using an automatic Hitachi chemistry analyzer.

Depression status and sleep assessment

Assessments of depression and sleep disorders were performed individually in a separate room by a member of the medical staff. The questionnaire was evaluated by a doctor and a patient in a separate, quiet, dimly lit room, with the purpose of allowing the patient to fully relax and avoid tension. The medical staff had previously received two 4-hour theoretical training sessions and one 2-hour on-the-spot practice session related to the assessment of the mental health questionnaire. Depression was assessed using Zung's Self-rating Depression Scale [12], which has been validated in the general Chinese population and with patients with various medical illnesses using a cut-off score of 53. The sleep quality questionnaire assessed five major categories of sleep disorders: insomnia, restless legs syndrome, excessive daytime sleepiness, possible narcolepsy, and sleepwalking and nightmares.

The diagnosis of insomnia was determined using five questions from the Diagnostic and Statistical Manual-IV (1994). Question 1 assessed difficulty in falling asleep. Question 2 assessed frequent awakening with difficulty in falling asleep once again. Question 3 assessed early morning wakefulness. Patients were considered to have

insomnia if they responded to any of questions 1–3. Question 4 assessed the frequency of tiredness consequent to sleep loss. Question 5 assessed the frequency of mood effects consequent to sleep loss [4]. A response of “three times or more per week” for questions 4 and 5 was defined as the cut-off point for positive responses.

Restless legs syndrome was defined based on the criteria and rating scale developed by the International Restless Legs Syndrome Study Group. Higher total scores indicated more severe disease [13]. Specifically, participants were asked: (1) Did you ever experience a desire to move your legs or arms because of discomfort or disagreeable sensations? If so, (2) Did you sometimes feel the need to move to relieve discomfort, for example by walking, or to relieve the discomfort by rubbing your legs? (3) Were these symptoms worse when you were at rest, with at least temporary relief by activity? (4) Were these symptoms worse later in the day or at night than in the morning? Patients who answered “yes” to these four questions were considered to have RLS.

Daytime sleepiness was assessed using the Epworth Sleepiness Scale [14], covering eight questions that included sleeping while sitting and reading, sleeping while watching TV, sleeping while sitting, inactive in a public place (e.g., a theater or a meeting), sleeping while as a passenger in a car for an hour without a break, sleeping while lying down to rest in the afternoon when circumstances permit sleeping while sitting and talking to someone, sleeping while sitting quietly after a lunch without alcohol, sleeping while in a car stopped for a few minutes due to traffic. Responses to each item were assessed using a four-point Likert scale: 0 = would never doze, 1 = slight chance of dozing, 2 = moderate chance of dozing, and 3 = high chance of dozing. Patients with a score ≥ 10 were considered to have excessive daytime sleepiness. The validity and reliability of the Chinese version of the Epworth Sleepiness Scale have been demonstrated in patients with PD [15].

Possible narcolepsy was evaluated using the minimal clinical criteria of the International Classification of Sleep Disorders (ICSD-1990) [16], which inquires whether the patient has both (1) recurrent daytime naps or lapses into sleep occur almost daily for at least 3 months, and (2) sudden bilateral loss of postural muscle tone occurs in association with intense emotion (cataplexy).

Sleepwalking and nightmares were assessed using Hatoum’s nighttime disturbances questionnaire [17], which included experiences of leg jerks, sleepwalking, nightmares, bed wetting, and falling off the bed. Any one of these five categories can be diagnosed as sleep disorders [4]. Our participants were divided into two groups according to their responses to the questionnaires: patients with at least one sleep disorder (SD+ group) and those without any sleep disorders (SD- group).

Definition of survival outcomes

Cardiovascular death was defined as death due to congestive heart failure, myocardial infarction, arrhythmia, stroke, sudden death, and peritoneal arterial disease.

Statistical analysis

Continuous variables are presented as mean $\pm$ standard deviation, except for the duration of PD, hs-CRP, and residual renal function, which are presented as medians and interquartile ranges because they were highly skewed. Categorical variables are presented as frequencies and counts. Two independent *t* test, the Mann–Whitney *U* test, and the chi-square test were used to compare between-group differences in characteristics at baseline (first survey), and the paired *t* test and Wilcoxon’s signed-rank test were used to compare differences in the measures of sleep disorders between baseline (first survey) and the 2-year follow-up (second survey).

Multivariate logistic regression was used to analyze the association between sleep disorders and clinical characteristics at baseline. Variables reported to be associated with sleep disorders in previous studies were entered into the regression models as covariates, including demographic data (age and sex), comorbidity status (DM, CVD, and depression status), and laboratory parameters (serum albumin, phosphate, and hs-CRP); odds ratios and 95% confidence intervals were calculated. Univariate and multivariate logistic regression analyses were used to analyze the risk factors for changes in general sleep quality at the 2-year follow-up. The abovementioned confounders were included in the models as covariates.

Cox survival analysis was used to explore the association between sleep disorders and outcomes, such as all-cause and cardiovascular mortality. The level of significance for all statistical tests was set at 0.05. All analyses were performed using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL). This study addressed Zhang YH’s study [18].

Results

Baseline characteristics and follow-up

In our study, the longest follow-up period was 36 months, the shortest was 26 months, and the average was 30 ± 1 months.

Of the 667 patients who were eligible for the study, 493 (73.9%) provided their consent to participate. Of these 493 patients, 449 (91.1%) completed the baseline sleep disorder assessment. At baseline, 335 patients (74.6%) were diagnosed with sleep disorders. Compared with patients without sleep disorders, patients with sleep disorders were older ($P = 0.036$) and had a higher prevalence of DM ($P = 0.002$),

CVD ($P=0.018$), and depression ($P<0.01$). They also had higher phosphate levels ($P=0.006$). However, there were no differences in sex, PD duration, level of education, body mass index, mean arterial pressure, hemoglobin, serum albumin, triglycerides, total cholesterol, serum sodium, or calcium (Table 1).

During the 2-year follow-up period, 42 patients died, 57 switched to hemodialysis, 24 opted for kidney transplantation, 21 refused to participate, and 20 patients could not complete the questionnaires for various reasons, for example, severe loss of eyesight, language incompatibility, upper-limb disability, or being lost to follow-up in the second survey. A total of 164 patients were excluded during the follow-up period (Fig. 1). The remaining 285 patients were repeatedly assessed for sleep quality. The basic and clinical characteristics of the drop-outs and those followed up in the whole study were compared, as shown in Table S1. The prevalence of DM and possible narcolepsy and serum hs-CRP levels were significantly higher in the excluded group ($P=0.009$,

0.044, and 0.045, respectively). No significant differences were found in other demographic or biochemical data between the two groups (Table S1). Merlino et al. reported that sleep disorders were significantly associated with DM, which may weaken the correlations between diabetes and sleep disorders in the second survey [4]. However, DM was not confirmed as a significant and independent predictor of sleep disorders. Our study also showed that serum hs-CRP levels were higher in participants dropping out ($P=0.045$). A Greek study found that CRP was related to insomnia but not to other categories of sleep disorders [19].

Changes in sleep measures during the follow-up period

During the follow-up period, the prevalence of sleep disorders increased from 73.3% (209/285) to 81.8% (233/285). Our assessment revealed the presence of general sleep disorders (72.6%), insomnia (23.5%), restless legs syndrome

Table 1 Differences in clinical characteristics between PD patients with and without sleep disorders ($N=449$)

Variables	Total	SD+ group	SD – group	P value
N (%)	449 (100)	335 (74.6)	114 (25.4)	–
Age (years)	51.79 ± 14.24	52.61 ± 13.99	49.38 ± 14.74	0.036
Male (%)	227 (50.6)	186 (55.5)	52 (45.6)	0.067
PD duration (months)	25.17 (11.13,49.32)	26.03 (11.90,50.23)	24.25 (12.17,43.23)	0.999
Comorbidity				
DM (%)	106 (23.6)	91 (27.2)	15 (13.2)	0.002
Cardiovascular disease (%)	94 (20.9)	79 (23.6)	15 (13.2)	0.018
Depression status (%)	242 (50.5)	190 (56.7)	37 (32.5)	<0.001
Level of education				
Elementary school or lower (%)	82 (18.3)	60 (17.9)	22 (19.3)	0.524
Middle school (%)	132 (29.4)	100 (29.9)	32 (28.1)	
High school (%)	136 (30.3)	106 (31.6)	30 (26.3)	
Above high school (%)	99 (22.0)	69 (20.6)	30 (26.3)	
Body-mass index (kg/m ²)	22.89 ± 3.52	23.04 ± 3.42	22.45 ± 3.80	0.117
Mean arterial pressure (mmHg)	100.16 ± 12.93	100.45 ± 13.19	99.30 ± 12.17	0.414
Hemoglobin (g/L)	104.58 ± 17.66	104.01 ± 17.55	106.25 ± 17.96	0.242
Serum albumin (g/L)	36.09 ± 5.58	35.82 ± 5.47	36.89 ± 5.83	0.070
Triglycerides (mmol/L)	1.98 ± 1.34	1.93 ± 1.29	2.13 ± 1.49	0.207
Total cholesterol (mmol/L)	4.75 ± 1.12	4.70 ± 1.09	4.90 ± 1.17	0.089
Serum sodium (mmol/L)	139.01 ± 7.11	139.45 ± 3.14	137.71 ± 12.99	0.158
Calcium (mmol/L)	2.27 ± 0.24	2.26 ± 0.24	2.28 ± 0.26	0.655
Phosphate (mmol/L)	1.65 ± 0.42	1.68 ± 0.45	1.57 ± 0.35	0.006
hs-CRP (mg/L)	2.86 (0.92,8.64)	3.07 (0.99,8.84)	2.39 (0.67,6.80)	0.090
RRF (ml/min)	2.18 (0.00,5.67)	2.07 (0.00,5.42)	2.68 (0.48,6.37)	0.111
Total Kt/V	1.90 ± 0.41	1.88 ± 0.39	1.96 ± 0.46	0.094
Total Ccr (L/w/1.73 m ²)	58.34 ± 17.63	57.67 ± 16.83	60.36 ± 19.79	0.164

PD peritoneal dialysis; DM diabetes mellitus; BMI body mass index; hs-CRP high-sensitivity C-reactive protein; RRF residual renal function; Kt/V urea clearance per week; Ccr creatinine clearance per week; SD+ presence of sleep disorders at baseline; SD– absence of sleep disorders at baseline

Fig. 1 Flow chart of study

(44.0%), excessive daytime sleepiness (40.5%), possible narcolepsy (3.2%), and sleepwalking and nightmares (19.9%) at baseline. We observed poorer health outcomes at the 2-year follow-up among patients with insomnia ($P=0.002$), restless legs syndrome ($P=0.044$), and excessive daytime sleepiness ($P=0.001$). The prevalence of possible narcolepsy, sleepwalking, and nightmares did not differ significantly between baseline and the 2-year follow-up (Fig. 2).

Risk factors for sleep disorders at baseline and follow-up

Depression was significantly associated with general sleep disorders and all specific sleep disorders measured

at baseline. DM was related to general sleep disorders and restless legs syndrome; a low serum albumin level was also associated with restless legs syndrome. Advanced age was positively associated with insomnia. Men had a higher possibility of excessive daytime sleepiness, which was approximately twice as common in men than in women (Table 2).

Of the 285 patients who completed the baseline and follow-up assessments, 209 patients had sleep disorders at baseline, 29 of whom returned to normal sleep at follow-up. In contrast, of the 76 patients who had normal sleep at baseline, 53 patients developed sleep disorders at the follow-up survey. A low serum albumin level was a significant risk factor for sleep disorders, with a 1 g/L reduction

Fig. 2 Comparison of sleep disorder prevalence

in serum albumin increasing the risk of sleep disorders by 16% (Tables 3 and 4).

Sleep disorders and outcomes

By the end of the study, 45 patients had switched to hemodialysis and 46 patients died, 26 of whom died of cardiac disease. In total, there were 104 hospitalizations during the follow-up period. Univariate and multivariate Cox survival analyses found that sleep disorders failed to predict poor health outcomes, such as first hospitalization, transition to hemodialysis, all-cause mortality, or cardiovascular mortality (Table 5).

Discussion

This prospective study, which included a large sample of patients undergoing PD at five centers, found that 74.6% (335/449) had sleep disorders and 56.7% of those with sleep disorders had depression. Depression and DM were positively associated with sleep disorders at baseline, and a higher risk of sleep disorders was reported in men (Table 2). At the 2-year follow-up, the incidence of sleep disorders increased from 73.3% (209/285) to 81.8% (233/285), with insomnia increasing from 23.2% to 33.7%, restless legs syndrome increased from 38.6 to 46.0%, and excessive daytime sleepiness increased from 43.9 to 55.4%. The prevalence of possible narcolepsy, sleepwalking, and nightmares at the 2-year follow-up did not significantly differ from baseline. More importantly, our study found that CVD was a risk factor for normal sleep status at the 2-year follow-up among patients with sleep disorders at baseline, whereas a low serum albumin level was a risk factor for sleep disorders at the 2-year follow-up among patients with normal sleep status at baseline. This may provide a theoretical basis for nephrologists to improve the prognosis of patients with PD by implementing interventions to improve sleep on the basis of the abovementioned risk factors.

We found that depression was significantly associated with general sleep disorders and all specific sleep disorders measured at baseline. Previous studies have found that depression affects many aspects of quality of life and sleep quality [20–22], and Peterson and Benca have provided physiological evidence that depression can independently cause sleep disorders [23]. It is possible that depression affects various parts of sleep. Recent polysomnography studies by Lee et al. have found an association between depression and insomnia [24], and an association between depression and restless legs syndrome has also been found in other studies [25–27]. Depression has been shown to be a risk

Table 2 Associations between sleep disorders and baseline clinical characteristics based on multivariate logistic regression ($N=449$)

Variable	Sleep disorders		Insomnia		Restless legs syndrome		Excessive day-time sleepiness		Possible narcolepsy		Sleepwalking and nightmares	
	OR	P	OR	P	OR	P	OR	P	OR	P	OR	P
Age (y)	1.007	0.438	1.020	0.047	1.014	0.123	0.998	0.776	0.987	0.452	0.991	0.371
Male	1.688	0.028	0.797	0.366	0.829	0.414	1.725	0.009	2.073	0.160	0.609	0.059
Diabetes mellitus	1.908	0.049	1.318	0.337	1.834	0.028	1.550	0.085	0.553	0.390	1.493	0.188
Cardiovascular disease (%)	1.460	0.261	1.088	0.781	1.661	0.073	1.641	0.067	1.601	0.425	1.404	0.280
Depression status (%)	2.551	<0.001	2.678	<0.001	2.987	<0.001	2.260	<0.001	3.950	0.018	2.917	<0.001
Serum albumin (g/L)	0.968	0.152	0.973	0.241	0.945	0.012	0.993	0.714	0.936	0.113	1.001	0.971
Phosphate (mmol/L)	1.723	0.072	3.340	<0.001	1.245	0.427	0.786	0.341	2.054	0.148	1.193	0.564
hs-CRP (mg/L)	1.005	0.546	1.006	0.441	1.012	0.129	1.009	0.181	0.996	0.763	1.004	0.583

OR odds ratio; *hs-CRP* high-sensitivity C-reactive protein

Table 3 Univariate logistic regression results for normal sleep status at the 2-year follow-up ($n = 29$) among patients with sleep disorders at baseline ($n = 209$)

Variable	OR (95% CI)	<i>P</i> value
Age (y)	1.014 (0.984, 1.045)	0.364
Male (%)	0.650 (0.295, 1.430)	0.284
Diabetes mellitus (%)	1.575 (0.665, 3.728)	0.301
Cardiovascular disease (%)	0.114 (0.015, 0.861)	0.035
Depression status (%)	0.516 (0.233, 1.143)	0.103
Serum albumin (g/L)	1.031 (0.956, 1.111)	0.429
Phosphate (mmol/L)	1.141 (0.502, 2.597)	0.753
hs-CRP (mg/L)	0.970 (0.923, 1.020)	0.237

OR odds ratio; *hs-CRP* high-sensitivity C-reactive protein

Table 4 Univariate logistic regression results for sleep disorders at the 2-year follow-up ($n = 53$) among patients with normal sleep status at baseline ($n = 76$)

Variable	OR (95% CI)	<i>P</i> value
Age (y)	0.994 (0.962, 1.027)	0.709
Male (%)	1.161 (0.433, 3.109)	0.767
Diabetes mellitus (%)	1.094 (0.196, 6.197)	0.919
Cardiovascular disease (%)	1.867 (0.364, 9.563)	0.454
Depression status (%)	1.500 (0.503, 4.471)	0.467
Serum albumin (g/L)	0.862 (0.774, 0.960)	0.007
Phosphate (mmol/L)	0.396 (0.090, 1.748)	0.221
hs-CRP (mg/L)	1.057 (0.924, 1.209)	0.418

OR odds ratio; *hs-CRP* high-sensitivity C-reactive protein

Table 5 Association between sleep disorders and poor outcomes based on Cox survival analysis ($N = 449$)

Outcomes	HR (95% CI) for sleep disorders	
	Univariate	Multivariate
First hospitalization	1.347 (0.841, 2.158)	1.155 (0.561, 2.380)
	0.215	0.696
Transition to HD	1.591 (0.741, 3.417)	1.554 (0.445, 5.427)
	0.234	0.490
All-cause mortality	1.427 (0.689, 2.956)	1.159 (0.376, 3.574)
	0.339	0.798
Cardiovascular mortality	1.152 (0.463, 2.870)	0.831 (0.195, 3.543)
	0.760	0.803

The multivariate model was adjusted for age, gender, diabetes mellitus, cardiovascular disease, depression status, serum albumin, phosphate, and hs-CRP

HR hazard ratio

factor for excessive daytime sleepiness [28, 29]. Christopher et al. demonstrated that nightmares were significantly associated with depressive symptoms [30], although this needs to

be confirmed using polysomnography. In addition, depression was found to be an independent risk factor for cognitive impairment and decline in our previous studies [18, 31], which may be associated with reduced adherence to treatment and decreased well-being. Although some studies have found that antidepressants improve sleep [32, 33], there are opposing opinions on the effects of antidepressants on sleep because iatrogenic sleep disorders can be caused or exacerbated with the use of antidepressants [34, 35]. Additionally, serotonergic antidepressants can induce or worsen several sleep disorders, such as restless legs syndrome [36]. Studies have shown that self-management and cognitive behavioral therapy can improve depression and quality of life in patients with chronic kidney disease [37, 38], and routine screening and timely interventions for depression might become a new strategy for preventing sleep disorders in PD patients.

In our study, DM was found to be a risk factor for general sleep disorders and restless legs syndrome. There may be interactions between sleep disorders and glucose metabolism. A Chinese study confirmed that patients with prediabetes and newly diagnosed diabetes had significantly worse sleep quality than those with normal glucose tolerance [39]. Another study found that DM was associated with restless legs syndrome, as prolonged sleep may increase the probability of developing insulin resistance and metabolic disturbances [40]. A recent study found that exenatide, a hypoglycemic drug, improved wakefulness and reduced daytime sleepiness in obese patients with DM [41]. Further studies need to focus on the effects of glucose control on sleep among patients with DM.

Our study suggests that men are at a greater risk of sleep disorders than women. Contrary to our results, a meta-analysis found that women are more likely to have insomnia than men [42]. Further large-scale studies are needed to clarify these sex-based differences in sleep disorders.

Our study also found that patients with CVD had an increased risk of sleep deterioration at the 2-year follow-up among PD patients with sleep disorders at baseline. Few studies have been conducted on patients with PD to determine the underlying mechanisms. However, we can speculate several possible mechanisms. First, there are some common risk factors for CVD and sleep disorders. For example, obesity is one of the usual risk factors for CVD. Recent studies have shown that CVD and restless legs syndrome also have a common pathogenesis [43]. Second, when a patient's blood flow increases in the supine position at night, it can lead to an acute episode of CVD. Patients often need to sit up and breathe to improve dyspnea, which, in turn, affects sleep. Finally, to reduce the volume load during the acute phase of CVD, it is often necessary to enhance diuretic or PD treatment, and frequent urination and exchange of peritoneal dialysate also affect a patient's sleep.

We found that a low serum albumin level was an independent risk factor for sleep disorders in patients with normal sleep at baseline. Similarly, previous studies have shown that malnutrition and low serum albumin levels are independent predictors of sleep disturbance in patients undergoing continuous ambulatory PD [10, 44]. Malnutrition and inflammation are common comorbid conditions in PD patients [45], and we presume that they may jointly affect patients' sleep. Moreover, malnutrition and inflammation tend to occur concurrently in dialysis patients, which has been called "malnutrition inflammation complex syndrome". Comorbidity, oxidative and carbonyl stress, nutrient loss through dialysis, anorexia and low nutrient intake, uremic toxins, decreased clearance of inflammatory cytokines, volume overload, and dialysis-related factors are possible causes of malnutrition inflammation complex syndrome [46, 47]. Therefore, it is essential to pay attention to patients' nutritional status.

Our study has several strengths. First, studies exploring sleep disorders among patients with PD are limited. Our study not only evaluated changes in sleep disorders over a 2-year period but also investigated factors of sleep disorders in patients with PD. Second, we investigated a full range of specific sleep disorders, including five different classes of symptoms. Finally, confounders that were reported by previous studies were controlled using logistic regression models in our study. Moreover, our questionnaires have been widely used and were perfectly understandable and convenient for patients to complete in comparison to polysomnographic recordings.

However, several limitations of this study should be acknowledged. First, given the relatively small number of endpoint events, the power of the regression analysis in our study was limited. Thus, the associations between sleep disorders and poor outcomes could not be determined. Future studies with larger sample sizes and longer observation periods are warranted to further explore the association between sleep disorders and poor outcomes. Second, selection bias was inevitable because approximately 40% of the participants who completed the baseline assessment did not complete the second assessment. Since patients who dropped out of the study tended to be sicker at baseline, this could have resulted in an underestimation of sleep quality over time. Third, sleep apnea is a common type of sleep disorder in patients with ESRD; however, we did not use overnight polysomnography to diagnose obstructive sleep apnea and verified the validity of the sleep questionnaires. Future studies that focus on the quantitative sleep data and quality of sleep, documented using polysomnography, would be helpful. Fourth, the use of sleeping pills was not recorded in our study, which may have led to false negatives in the second assessment.

In conclusion, we observed a high prevalence of sleep disorders in patients receiving PD treatment. Depression, DM, and male were associated with sleep disorders at baseline. CVD predicted worsening sleep disorders for normal sleep status at the 2-year follow-up among patients with sleep disorders at baseline, while low serum albumin levels predicted worsening sleep disorders among patients with normal sleep status at baseline. To reduce the prevalence of sleep disorders, physicians and other healthcare professionals should pay close attention to psychological changes in patients undergoing PD and strive to control blood glucose, improve nutrition, and actively prevent and treat CVD.

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Author contributions Research idea and study design: DJ, LGL; data acquisition: LGL, ZQN, ZYL, XZY, LJL, RYP, WQ, DLP, ZZX, HL; statistical analysis: LGL, ZQN, DJ; revision: LGL, ZQN, HL; supervision or mentorship: DJ. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions on the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

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Compliance with ethical standards

Conflict of interest The authors have no conflict of interest to declare.

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