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ORIGINAL RESEARCH

Autonomic Nervous Regulation was Associated with Sleep Quality Among Peritoneal Dialysis Patients

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Background: The issue of compromised sleep quality among patients with end-stage kidney disease (ESKD), particularly those undergoing peritoneal dialysis (PD), is notably pronounced. Dialysis patients exhibit significant alterations in cardiac autonomic nerve activity. However, the relationship between autonomic nervous system activity and sleep remains inadequately elucidated.

Methods: This cross-sectional study enrolled adult maintenance PD patients in our center. The Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep quality. Heart rate variability (HRV) and Skin sympathetic nerve activity (SKNA) parameters were recorded to reflect autonerve activity responses or regulation capacity.

Results: A total of 73 PD patients participated in this study, with a prevalence of poor sleep quality at 38.4%. Serum creatinine (1157.0±294.3 vs 969.6±353.4 mmHg, p = 0.022) and phosphorus levels (2.1±0.5 vs 1.7±0.5 mmHg, p = 0.002) were higher in the poor sleep quality group compared to the good group. Linear regression analyses indicated that PSQI scores were associated with SKNA (β, −2.54; 95% CI, −4.90 to −0.19; P=0.035), standard deviation of all sinus RR intervals (SDNN) (β, −0.05; 95% CI, −0.09 to −0.01; P=0.015), and SD2 (β, −0.04; 95% CI, −0.07 to −0.01; P=0.018).

Conclusion: Poor sleep quality in PD patients may be associated with longer dialysis vintage, higher BMI, higher diastolic blood pressure, and higher level of serum uremic toxin, and affected by cardiac autonomic nerve function disorder.

Keywords: peritoneal dialysis, end-stage kidney disease, skin sympathetic nerve activity, heart rate variability, autonomic nervous system, sleep quality

Introduction

Various patients with chronic kidney disease (CKD) suffered sleep disturbances, which include struggling to get asleep or stay asleep, waking up prematurely, experiencing unsatisfactory sleep, or not feeling refreshed after sleeping. Sleep disturbances are diagnosed clinically and can be assessed using different patient questionnaires such as the Pittsburgh Sleep Quality Index. The reported incidence of sleep disturbances in individuals with CKD varies between 38 and 70%,[1,2] far surpassing the prevalence in the general population, which ranges from 15% to 35%.

Sleep disturbances in individuals with CKD may result in heightened tiredness, excessive daytime drowsiness, impaired daily performance, and a decline in health-related quality of life.[3,4] In a cohort of 11,351 patients from the Dialysis Outcomes and Practice Patterns Study, the presence of sleep disturbances was associated with a higher all-cause mortality rate. Specifically, the relative risk of mortality was 16% higher in patients with sleep disturbances than in those without.[3]

Sleep disturbances in CKD are multifactorial and can be attributed to a variety of factors, such as uraemia, medications, melancholy, elevated parathyroid hormone levels, bone pain, and pruritus. Additionally, poor sleep habits and frequent napping during dialysis contributed factors.[5] In two small RCTs, cool dialysate for hemodialysis patients

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decreased time to sleep start, lengthened sleep duration, and improved sleep quality. This improvement may have been caused by a decrease in nocturnal sympathetic activity and an enhanced ability of the body to dissipate heat.[6,7]

The significance of sympathetic activation in the development and progression of chronic kidney disease is well known. Similarly, progressive renal failure induces an exaggerated sympathetic activation, which culminates in a vicious cycle.[8] Autonomic nervous regulation refers to the equilibrium between sympathetic and parasympathetic nervous system processes. Heart rate variability (HRV) is one such classical indicator, which describes the reaction of cardiac postjunctional sinoatrial receptors to fluctuations in sympathetic and vagal activity, rather than the direct measurements of nerve output.[9] Decreased HRV parameters the standard deviation of all sinus RR intervals (SDNN) and SD of 5-min average of normal R-R intervals (SDANN), has proved to be negatively correlated with all-cause mortality in CKD-5 patients.[10]

Skin sympathetic nerve activity (SKNA) has emerged as a novel, noninvasive parameter that accurately represents real-time cardiac sympathetic nerve activity.[11,12] This parameter has been extensively employed as a predictor of sympathetic tone in patients with cardiac arrhythmogenesis, acute myocardial infarction, sleep apnea, and neurologic recovery.[13–17] The elevation of SKNA during hemodialysis was also observed in previous study using a noninvasive approach. Additionally, a decrease in the HR-aSKNA correlation was observed in the high interdialytic weight gain subgroup.[18]

The causes of poor sleep quality in peritoneal dialysis (PD) patients have not been completely understood and may be multifactorial. We designed this cross-sectional study to explore the sleep quality in PD patients, and its correlation with cardiac autonomic nerve function, including SKNA and HRV.

Methods

Study Design and Participants

This cross-sectional study enrolled patients undergoing maintenance PD from August 2020 to November 2020, which was approved by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University hospital. All the participants provided written informed consent. The inclusion criteria were described as follows: aged 18 years or older, having undergone regular dialysis for at least 3 months, and being able to finish examinations and questionnaires as required. The exclusion criteria included 1) presence of fever, infection, pregnancy, or diabetes; 2) severe hepatic or pulmonary diseases, malignant tumors, or mental disorders; 3) episodes of acute cardio-cerebral vascular incident, or a major surgical procedure within the past 3 months. 4) refused the recordings.

Clinical and Laboratory Data

This study recorded demographics, comorbid conditions, and drug usage, including gender, age, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate, dialysis vintage, history of hypertension, and stroke history, and current antihypertensive and mineral medications. Laboratory blood examinations were selected near the date of sleep quality evaluation and SKNA and single-lead electrocardiogram (ECG) recordings, including serum hemoglobin, glucose, creatinine, urea, weekly total KT/V, total cholesterol, triglyceride, albumin, calcium, phosphorus, and iPTH.

Assessments of Sleep Quality

The Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep quality and sleep disturbance over the past one month. The scale includes 19 items that generate 7 domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. For each domain, the score ranges from 0 to 3, with lower scores indicating better sleep quality. The abnormal sleep in each domain was defined as the score ≥2. The poor sleep quality was defined as the global PSQI score > 7.[19,20]

Heart Rate Variability Analysis

HRV analysis was performed with the PhysioNet Cardiovascular Signal Toolbox.[21] Beat-to-beat RR intervals were extracted and quantified using time domain analysis, frequency domain analysis, and nonlinear analysis.[18] The time domain analysis consists of SDNN, the square root of the mean square of differences between adjacent normal to normal intervals (RMSSD), acceleration capacity (AC), and deceleration capacity (DC). The frequency domain analysis included

total power (TP), high-frequency power (HF), low-frequency power (LF), and the ratio of low to highfrequency power (LF/HF). The nonlinear analysis included SD1, SD2, SD1/SD2, and sample entropy (SampEn).

Skin Sympathetic Nerve Activity Recordings and Data Processing

Each patient underwent continuous recording for 5 minutes during PD.[18] A bespoke device was used to simultaneously record SKNA and single-lead ECG signals,[22] which was compatible with the PowerLab system. As illustrated in the schematic representation, three electrodes were positioned (3M™ Red Dot Monitoring Electrode, #2570) in the left subclavian, right subclavian, and right lower abdomen regions, respectively. The sampling rate was 4000 hz. Patients were asked to remain in the supine position and to avoid unnecessary movements during recording. The use of electronic instruments, which could cause signal artefacts, was avoided during recording.

SKNA was derived from the raw data signals, which were subjected to bandpass filtering at 500–1000 hz. Subsequently, three quartiles were calculated as Q1, Q2, and Q3. We defined the deviations of Q1 and Q3 as interquartile ranges (IQRs). Outliers were excluded if they fell below Q1-1.5 * IQR or above Q3+1.5 * IQR. Next, we calculated the mean voltage of skin sympathetic nerve activity (aSKNA).

Statistical Analysis

Continuous data with a normal distribution are presented as the means ± standard deviation and were analyzed by Student's *t*-test. The data with high skew are presented as the median and interquartile range and were analyzed by the Mann–Whitney test. Categorical data were presented as proportions and analyzed by the chi-square test and Fisher's exact test. Pearson's coefficient test assessed correlations between variables. Variables with $P < 0.10$ in the univariate analyses were selected as adjusted variables for the multivariable linear regression analyses, which were performed to explore the association between the sleep quality with HRV and SKNA variables. The SPSS 21.0 statistical package (IBM Corporation, Armonk, NY) was used for all analyses, and a value of $P < 0.05$ was considered statistically significant. G*Power ver. 3.1.9.4 software was conducted to estimate sample size. Further, the fit curve of sleep quality with various HRV and SKNA variables was performed with Origin (Originlab Corporation, Northampton, MA).

Results

Characteristics of Study Participants

A total of 73 PD patients with a mean dialysis vintage of 36.0 months were enrolled in this study. Flow chart of patient enrollment were showed in Figure 1. Their mean age was 46.4±13.2 years and 31 (42.5%) of them were male. The participants were divided into two groups: 45 patients with good sleep quality (global PSQI score ≤7), and 28 patients with poor sleep quality (global PSQI score >7). The totally prevalence of poor sleep quality was 38.4%. The PSQI scale has high reliability and validity. The overall Cronbach's α coefficient of the scale items was higher than 0.8. The fitting effect of the structural model was good (the goodness of fit index was higher than 0.9). The prevalence of abnormal specific sleep domains were 30.1% for subjective sleep quality, 41.1% for sleep latency, 37.0% for sleep duration, 31.5% for sleep efficiency, 19.2% for sleep disturbance, 13.7% for sleep medication use, and 27.4% for daytime dysfunction (Figure 2).

Clinical Characteristics of PD Patients with Good or Poor Sleep Quality

The gender and age were comparable in two groups. The patients in poor sleep quality group had higher diastolic blood pressure (93.8±12.6 vs 87.1±12.6 mmHg, $p = 0.035$) and longer dialysis vintage (52.0 [24.0, 87.0] vs 31.0 [14.3, 53.3] months, $p = 0.035$) than those in good sleep quality group. The level of serum creatinine (1157.0±294.3 vs 969.6 ±353.4 mmHg, $p = 0.022$) and phosphorus (2.1±0.5 vs 1.7±0.5 mmHg, $p = 0.002$) was higher in poor sleep quality group than good group (Table 1).

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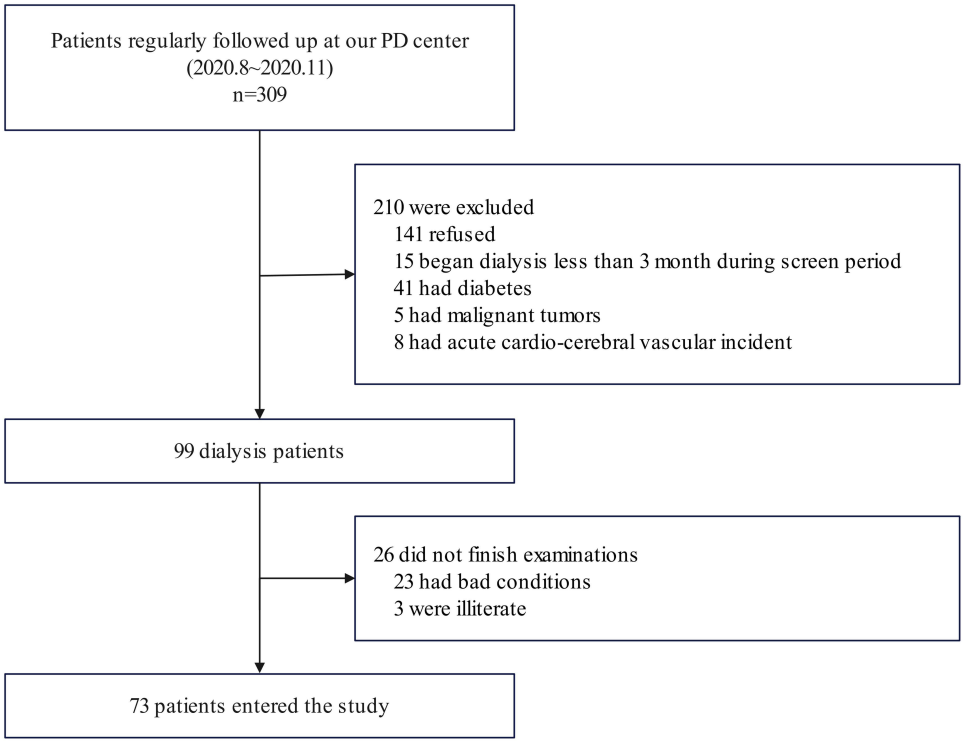

Figure 1 Flow Chart of Patient Enrollment.

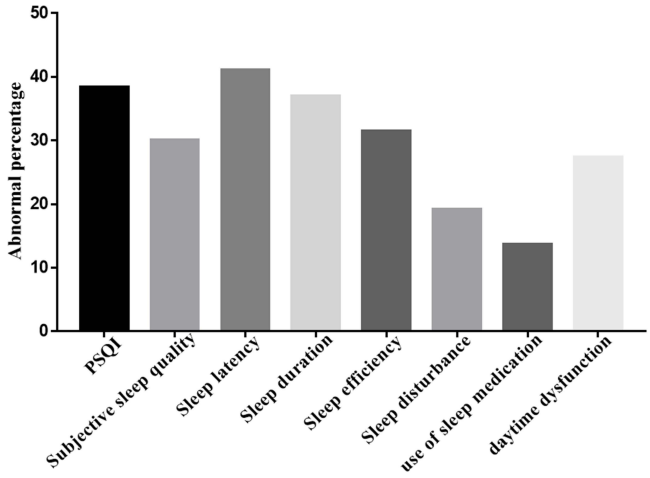

Figure 2 The percentage of PD patients with global and subdomain sleep quality impairment.

Autonomic Nerve Activity in PD Patients with Good or Poor Sleep Quality

We compared SKNA and HRV parameters between two sleep quality groups. SKNA value in the good sleep quality group was significantly higher than that in the poor group (1.2±0.3 vs 1.5±0.5 μV, p=0.002). Several HRV indices were also significantly higher in good sleep quality group, including SDNN (29.9 [18.4, 59.5] vs 23.6 [15.2, 32.7] ms, p=0.035), TP (836.4 [429.7, 3891.7] vs 589.6 [244.6, 1118.5], p=0.041), LF (247.5 [93.1, 813.9] vs 121.3 [37.1, 270.8], p=0.040), SD1 (23.1±22.1 vs 13.5±8.2, p=0.011) and SD2 (51.6±39.1 vs 32.8±17.9, p=0.007) (Table 2).

Table 1 Comparison of PD Patients with Good Sleep Quality or Poor Sleep Quality

	Total (n=73)	Good Sleep Quality (PSQI Score ≤ 7) (n=45)	Poor Sleep Quality (PSQI Score > 7) (n=28)	P value
Gender (male)	31 (42.5%)	19 (42.2%)	12 (42.9%)	0.957
Age (years)	46.4±13.2	46.9±14.4	45.4±11.3	0.647
BMI (kg/m2)	22.1±3.5	21.5±3.4	23.1±3.6	0.068
Systolic BP (mmHg)	138.6±23.8	136.1±20.4	142.9±28.5	0.248
Diastolic BP (mmHg)	89.6±12.9	87.1±12.6	93.8±12.6	0.035
Heart rate (per minute)	75.4 (66.0 to 87.9)	74.0 (64.7 to 87.7)	78.3 (67.0 to 91.1)	0.212
Dialysis vintage(months)	36.0 (18.0 to 61.0)	31.0 (14.3 to 53.3)	52.0 (24.0 to 87.0)	0.035
Hypertension	69 (94.5%)	42 (93.3%)	27 (96.4%)	1.000
Stroke	3 (4.1%)	1 (2.2%)	2 (7.1%)	0.554
ACEI/ARB	40 (54.8%)	23 (51.1%)	17 (60.7%)	0.423
β-receptor blocker	41 (56.2%)	25 (55.6%)	16 (57.1%)	0.894
Phosphate binders	46 (63.0%)	31 (68.9%)	15 (53.6%)	0.187
Active vitamin D sterols	25 (34.2%)	14 (31.1%)	11 (39.3%)	0.474
Cinacalcet	6 (8.2%)	2 (4.4%)	4 (14.3%)	0.195
Hemoglobin (g/L)	107.1±16.1	105.7±16.7	109.4±15.0	0.345
Glucose (mmol/L)	4.6 (4.2 to 4.9)	4.6 (4.2 to 5.2)	4.5 (4.2 to 4.8)	0.263
Creatinine (μmol/L)	1041.5±342.4	969.6±353.4	1157.0±294.3	0.022
Urea (mmol/L)	20.8±5.3	19.9±5.4	22.2±4.9	0.078
Weekly total KT/V	1.9±0.5	1.9±0.5	1.9±0.3	0.954
Total cholesterol (mmol/L)	4.6±1.1	4.5±1.1	4.8±1.1	0.299
Triglyceride (mmol/L)	2.4±1.7	2.2±1.3	2.7±2.1	0.210
Albumin (g/L)	38.2±3.9	38.3±4.6	37.9±2.7	0.635
Calcium (mmol/L)	2.4±0.2	2.4±0.2	2.4±0.2	0.752
Phosphorus (mmol/L)	1.8±0.5	1.7±0.5	2.1±0.5	0.002
iPTH (pg/mL)	249.0 (105.7 to 356.7)	195.4 (100.7 to 344.9)	271.1 (157.2 to 400.5)	0.177

Abbreviations: PD, peritoneal dialysis; PSQI, Pittsburgh Sleep Quality Index; BMI, body mass index; BP, blood pressure; ACEI/ARB, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers; iPTH, intact parathyroid hormone.

Table 2 Comparison of SKNA and HRV Parameters Characteristics Between Different Sleep Quality Groups

	Total (n=73)	Good Sleep Quality (PSQI Score ≤ 7) (n=45)	Poor Sleep Quality (PSQI Score > 7) (n=28)	P value
SKNA	1.4±0.5	1.5±0.5	1.2±0.3	0.002
Time domain measures				
SDNN	25.1 (17.3 to 47.7)	29.9 (18.4 to 59.5)	23.6 (15.2 to 32.7)	0.035
RMSSD	18.3 (10.9 to 30.1)	21.0 (10.7 to 40.3)	16.7 (11.3 to 24.9)	0.177
| AC |	5.0±3.2	5.5±3.5	4.2±2.5	0.089
DC	4.7±3.2	5.2±3.4	4.0±2.7	0.127
Frequency domain measures				
TP	777.3 (379.2 to 2579.1)	836.4 (429.7 to 3891.7)	589.6 (244.6 to 1118.5)	0.041
LF	165.2 (70.4 to 521.1)	247.5 (93.1 to 813.9)	121.3 (37.1 to 270.8)	0.040
HF	116.3 (38.4 to 274.0)	161.8 (38.4 to 551.6)	75.2 (33.9 to 197.6)	0.079
LF/HF	1.3 (0.7 to 2.9)	1.3 (0.7 to 3.1)	1.5 (0.6 to 2.9)	0.968

(*Continued*)

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Table 2 (Continued).

	Total (n=73)	Good Sleep Quality (PSQI Score ≤ 7) (n=45)	Poor Sleep Quality (PSQI Score > 7) (n=28)	P value
Nonlinear				
SD1	19.4±18.6	23.1±22.1	13.5±8.2	0.011
SD2	44.4±33.8	51.6±39.1	32.8±17.9	0.007
SD1/SD2	0.5±0.4	0.5±0.5	0.4±0.2	0.698
SampEn	1.4±0.4	1.4±0.4	1.5±0.4	0.264

Abbreviations: SKNA, skin sympathetic nerve activity; HRV, heart rate variability; |AC|, absolute value of acceleration capacity.

Correlation Analysis Between Autonomic Nerve Activities and Sleep Quality

Pearson's coefficient test was firstly used to assess the correlations between SKNA, HRV parameters and sleep quality, including global and each subdomain scores.

Correlation analysis showed that SKNA was negatively correlated with almost all sleep quality scores. Many HRV indices were correlated with various kinds of sleep quality domain (Table 3). The fit curve showed that PD patients demonstrated decrease in PSQI scores with SKNA (Figure 3A). A linear correlation was found in SKNA and SDNN (P=0.024) (Figure 3B). Figure 4 showed the fit curve of sleep quality with various HRV variables. The linear correlation was significant negative between PSQI scores and various HRV indices, including four time domain HRV indices, LF, SD1, and SD2 (Figure 4A–D, F, I and J).

Further, linear regression analyses were performed to explore the association of autonomic nerve activity variables with sleep quality (Table 4). Various HRV indices and SKNA were significantly associated with impaired PSQI scores in crude model. In model 1 adjusting for gender, age and dialysis vintage, PSQI scores showed a negative association with SKNA, SDNN, |AC|, DC, and SD2. Model 2 was adjusted for the variables entered into model 1, and BMI, DBP, serum creatinine, and serum phosphorus. Results from model 2 showed that PSQI scores were still negatively associated with SKNA (β, −2.54; 95% CI, −4.90 to −0.19; P=0.035), SDNN (β, −0.05; 95% CI, −0.09 to −0.01; P=0.015), and SD2 (β, −0.04; 95% CI, −0.07 to −0.01; P=0.018).

Table 3 Univariable Correlation Analysis Between SKNA, HRV Parameters and Sleep Quality

	PSQI		Subjective Sleep Quality		Sleep Latency		Sleep Duration		Habitual Sleep Efficiency		Sleep Disturbances		Use of Sleep Medication		Daytime Dysfunction	
	r	p	r	p	r	p	r	p	r	p	r	P	r	p	r	p
SKNA	−0.387	0.001	−0.307	0.008	−0.244	0.037	−0.295	0.011	−0.228	0.053	−0.339	0.003	−0.281	0.016	−0.288	0.014
SDNN	−0.341	0.003	−0.347	0.003	−0.22	0.062	−0.204	0.084	−0.252	0.032	−0.328	0.005	−0.204	0.083	−0.207	0.079
RMSSD	−0.26	0.027	−0.254	0.030	−0.117	0.326	−0.174	0.142	−0.227	0.054	−0.248	0.034	−0.174	0.141	−0.14	0.236
| AC |	−0.279	0.017	−0.139	0.242	−0.268	0.022	−0.262	0.025	−0.276	0.018	−0.154	0.193	−0.176	0.137	−0.109	0.357
DC	−0.268	0.022	−0.084	0.478	−0.245	0.037	−0.287	0.014	−0.306	0.009	−0.11	0.354	−0.206	0.081	−0.072	0.542
TP	−0.226	0.054	−0.27	0.021	−0.119	0.316	−0.081	0.493	−0.155	0.191	−0.279	0.017	−0.143	0.226	−0.153	0.197
LF	−0.236	0.044	−0.241	0.040	−0.143	0.228	−0.113	0.34	−0.151	0.202	−0.268	0.022	−0.188	0.111	−0.146	0.219
HF	−0.171	0.147	−0.231	0.049	−0.046	0.701	−0.014	0.91	−0.128	0.282	−0.263	0.024	−0.119	0.315	−0.134	0.259
LF/HF	0.066	0.577	−0.008	0.947	−0.019	0.87	0.112	0.347	0.105	0.379	−0.007	0.951	0.086	0.468	0.029	0.807
SD1	−0.26	0.027	−0.254	0.03	−0.117	0.326	−0.173	0.142	−0.227	0.054	−0.249	0.034	−0.174	0.141	−0.14	0.236
SD2	−0.337	0.004	−0.351	0.002	−0.228	0.053	−0.187	0.113	−0.235	0.046	−0.333	0.004	−0.194	0.099	−0.218	0.064
SD1/SD2	−0.004	0.972	0.06	0.615	0.055	0.642	−0.095	0.425	−0.067	0.573	0.061	0.608	−0.077	0.516	0.08	0.5
SampEn	0.151	0.204	0.304	0.009	0.089	0.456	0.094	0.427	−0.036	0.763	0.202	0.087	−0.014	0.907	0.157	0.185

Abbreviations: SKNA, skin sympathetic nerve activity; HRV, heart rate variability; |AC|, absolute value of acceleration capacity.

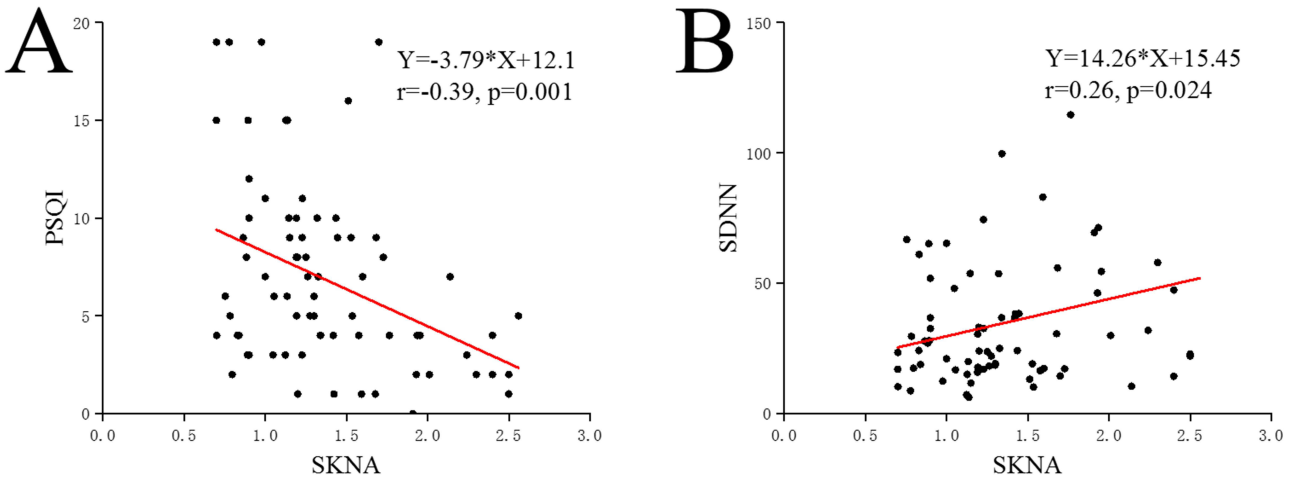

Figure 3 The correlation of SKNA with PSQI and SDNN. (**A**) The correlation of SKNA with PSQI. (**B**) The correlation of SKNA with SDNN.

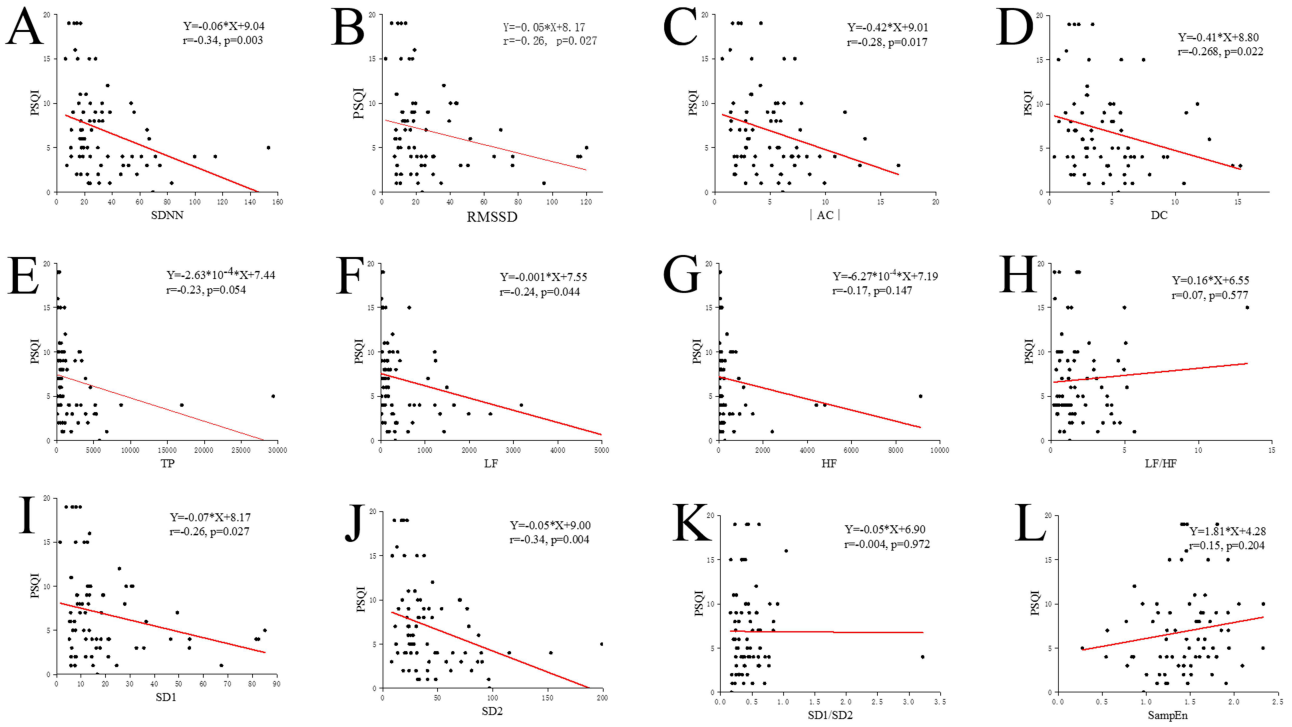

Figure 4 The correlation of various HRV parameters with PSQI. (**A**) The correlation of SDNN with PSQI. (**B**) The correlation of RMSSD with PSQI. (**C**) The correlation of |AC| with PSQI. (**D**) The correlation of DC with PSQI. (**E**) The correlation of TP with PSQI. (**F**) The correlation of LF with PSQI. (**G**) The correlation of HF with PSQI. (**H**) The correlation of LF/HF with PSQI. (**I**) The correlation of SD1 with PSQI. (**J**) The correlation of SD2 with PSQI. (**K**) The correlation of SD1/SD2 with PSQI. (**L**) The correlation of SampEn with PSQI.

Discussion

Our study demonstrated the high prevalence of poor sleep quality in PD patients (38.4%), and the most prominent manifestation of poor sleep quality were sleep latency and sleep duration. Our study showed the PD patients with poor sleep quality had longer dialysis vintage, higher BMI, higher diastolic blood pressure, and higher level of serum uremic toxin, such as creatinine, urea, and phosphorus. PSQI scores of PD patients in this study showed negative association with SDNN, SD2, and SKNA in linear regression analyses.

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Table 4 Univariate and Multivariate Linear Regression Analysis of SKNA, HRV Parameters and Sleep Quality

	Crude		Model 1		Model 2	
	β (95% CI)	P value	β (95% CI)	P value	β (95% CI)	P value
SKNA	−3.79 (−5.93 to −1.66)	0.001	−3.45 (−5.70 to −1.19)	0.003	−2.54 (−4.90 to −0.19)	0.035
Time domain measures						
SDNN (ms)	−0.06 (−0.10 to −0.02)	0.003	−0.05 (−0.09 to −0.01)	0.017	−0.05 (−0.09 to −0.01)	0.015
RMSSD (ms)	−0.05 (−0.09 to −0.01)	0.027	−0.04 (−0.09 to 0.00)	0.074	−0.04 (−0.08 to 0.00)	0.072
| AC |	−0.42 (−0.77 to −0.08)	0.017	−0.42 (−0.77 to −0.08)	0.016	−0.27 (−0.64 to 0.09)	0.137
DC	−0.41 (−0.76 to −0.06)	0.022	−0.39 (−0.74 to −0.05)	0.025	−0.24 (−0.61 to 0.12)	0.19
Frequency domain measures						
TP	0.00 (−0.00 to 0.00)	0.054	0.00 (0.00 to 0.00)	0.153	0.00 (0.00 to 0.00)	0.087
LF	−0.00 (−0.00 to 0.00)	0.044	−0.00 (−0.00 to 0.00)	0.128	−0.00 (−0.00 to 0.00)	0.104
HF	−0.00 (−0.00 to 0.00)	0.147	0.00 (−0.00 to 0.00)	0.336	−0.00 (−0.00 to 0.00)	0.181
LF/HF	0.16 (−0.41 to 0.73)	0.577	0.20 (−0.37 to 0.78)	0.484	−0.14 (−0.75 to 0.47)	0.647
Nonlinear						
SD1	−0.07 (−0.13 to −0.01)	0.027	−0.06 (−0.12 to 0.01)	0.074	−0.06 (−0.12 to 0.01)	0.072
SD2	−0.05 (−0.08 to −0.02)	0.004	−0.04 (−0.07 to −0.01)	0.019	−0.04 (−0.07 to −0.01)	0.018
SD1/SD2	−0.05 (−3.02 to 2.92)	0.972	−0.11 (−3.17 to 2.94)	0.941	0.15 (−2.85 to 3.15)	0.919
SampEn	1.81 (−1.00 to 4.62)	0.204	1.06 (−1.80 to 3.91)	0.462	1.96 (−0.87 to 4.79)	0.172

Notes: Crude: unadjusted. Model 1: adjusted for gender, age, and dialysis vintage. Model 2: adjusted for the variables in model 1, and BMI, DBP, serum creatinine, and serum phosphorus.
Abbreviations: SKNA, skin sympathetic nerve activity; HRV, heart rate variability; CI, confidence interval; |AC|, absolute value of acceleration capacity.

PD is an economical and uncomplicated method of replacing kidney function in individuals suffering from end-stage kidney disease (ESKD). PD has a notable rate of initial survival and maintains the remaining renal function. ESKD directly impairs sleep quality, and the additional physical and psychological difficulties experienced by patients undergoing PD exacerbate sleep disturbances.[23] Sleep difficulties subsequently have a substantial influence on the quality of life in PD patients, in a vicious circle. In one study including both PD and HD patients, 61.5% patients had poor sleep quality and patients with a PSQI score > 7 had a 2.96-fold increased risk of all-cause mortality.[24]

Previous study demonstrated that poor sleep quality was independently correlated with long dialysis duration, low albumin level, and high calcium×phosphorus product in patients undergoing PD.[25] Gender, education level, employment engagement, family support, anxiety, depression, and physical activity were identified as factors that had a correlation with sleep quality. There was a favorable correlation between anxiety and depression ratings and sleep quality.[26] Uremic toxin in PD patients may result in uremia-induced neuropathy or myopathy, decreased chemosensitivity, and hypervolemia, leading to sleep disturbances. Hyperphosphatemia may be associated with secondary hyperparathyroidism, uremic pruritus, bone pain, coronary artery calcification, and increased cardiovascular disease risk, all of which might have an impact on the sleep quality of PD patients.[27,28]

The correlation between sleep quality and nutritional status in PD patients is still unsure. Many studies showed individuals who were overweight exhibited inferior sleep quality in comparison to those who were of normal weight.[29,30] Meanwhile, malnutrition can contribute to poor sleep quality by influencing hormones and inflammatory levels.[31] The PSQI score was observed to have a negative correlation with serum albumin level, and exhibiting a positive correlation with the malnutrition–inflammation score.[32] Therefore, it is essential to achieve a balanced nutritional status.

This study's most striking finding reveals the correlation between autonomic nervous activity and sleep quality in patients undergoing peritoneal dialysis. The sympathetic and parasympathetic nerves together constitute the autonomic nervous system, which regulates physiological activities of organs through a delicate balance of antagonism and coordination. Their interaction with the sinoatrial node sustains normal cardiac variability, measurable via HRV. HRV encompasses a set of parameters that quantify variations in R-R intervals using various algorithms. Statello et al[33] found that SDNN and RMSSD were independently associated with sleep-disordered breathing. The negative association between PSQI scores and HRV index reflects that the PD patients suffering from poor sleep quality had the impaired

autonomic nerve regulatory capacity. Furthermore, compromised sleep quality exacerbates the disarray within the body's autonomic nervous system.

Recently, the innovative technique of SKNA recording has emerged as a valuable complement to traditional HRV analysis, opening up new avenues for exploration. SKNA signals can be captured noninvasively using standard ECG patch electrodes and exhibit a linear correlation with direct recordings of stellate ganglion nerve activity (SGNA). This method allows for an authentic representation of the real-time physiological state of cardiac sympathetic nerve activity. Night shift work can disrupt the circadian rhythms of individuals, leading to a decline in sleep quality.[34] In our study, impaired SKNA was associated with poor sleep quality of PD patients. However, it remains to be further investigated which of cardiac autonomic nerve function and sleep quality is the cause and which is the effect; it is possible that they are part of a positive feedback loop.

There are several advantages in our study. First, there are few study indicating the association between autonomic nervous activity and sleep quality among PD patients. Second, we evaluated autonomic nervous activity with HRV and SKNA, which are advanced and non-invasive detection methods. Moreover, we identified several risk factors for poor sleep quality of PD patients.

However, this study had some limitations. Firstly, there is a possibility of inaccuracies while using the PSQI questionnaire due to recollection bias and subjective assessment. Secondly, the current investigation was cross-sectional, and the sample size was relatively inadequate. Thirdly, additional possible risk variables that might influence sleep quality were not assessed, including nutritional status, the existence of depression, anxiety, and physical activity level. Fourthly, this study did not exclude the participants diagnosed with insomnia or other sleep disorders, such as sleep apnoea and restless legs syndrome, which may introduce confounding variables. Furthermore, the health status and cardiac autonomic nerve function of an individual is an influencing factor for sleep problems that may adversely impact an individual's health and cardiac autonomic nerve function, and the relationship may be bidirectional and complex.

Conclusion

In summary, this investigation demonstrated that poor sleep quality may be significantly determined by cardiac autonomic nerve function disorder in PD patients. Improving autonomic nervous function have the potential to be beneficial in the treatment of poor sleep quality in PD patients.

Data Sharing Statement

The data used during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The studies involving human participants were reviewed and approved by The Bioethics Committee of the First Affiliated Hospital of Nanjing Medical University (2019-SR-368). The patients provided their written informed consent to participate in this study. This study complies with the Declaration of Helsinki.

Ethical Considerations

Participants are free to choose whether or not to participate in this study at any time. Participants are aware of the purpose, benefits, and risks of the study before agreeing or refusing to participate in. The researcher explained to the participants that refusing to participate would not result in any negative consequences or impacts. The participants' data is confidential and anonymous. Researchers need to consider the potential harm that may be caused to participants.

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Author Contributions

Baodi Huang and Yujun Qian have contributed equally to this work and share first authorship. Haibin Ren and Jing Wang contributed equally to this study. Baodi Huang - Conceptualization and writing original draft. Yujun Qian - Data curation, writing original draft, and funding acquisition. Ying Gao - Formal analysis. Zhenye Chen – Investigation and methodology. Li Zhang - Project Administration and resources. Huijuan Mao - Supervision and resources. Changying Xing - Validation and supervision. Haibin Ren - Project Administration and writing review & editing. Jing Wang – Investigation, funding acquisition, and writing review & editing. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All other authors declare no competing interests.

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