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ORIGINAL RESEARCH

Association Between Subclinical Depression and the Severity of Lower Urinary Tract Symptoms/ Benign Prostatic Hyperplasia and the Mediating Effect of Sleep Quality in Elderly Chinese Men

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Background and Objective: Subclinical depression and lower urinary tract symptoms (LUTS) /benign prostatic hyperplasia (BPH) are both common diseases. Studies have shown that there is an association between them, and sleep disturbances may play an important role in this relationship, however, the underlying mechanisms remain unknown. This study aims to explore the potential association between subclinical depression and LUTS/BPH, and to investigate the role of sleep quality in this relationship.

Methods: This is a cross-sectional study based on clinical patients. Inpatients with BPH were recruited from the urology department as the research subjects; all were aged 60 years or older. The Patient Health Questionnaire-9 (PHQ-9), the Pittsburgh Sleep Quality Index (PSQI), and the International Prostate Symptom Score (IPSS) were used to assess subclinical depression, sleep quality, and the severity of LUTS/BPH. The patients were divided into mild and moderate-to-severe groups based on IPSS scores. Logistic regression analysis was used to assess the association between subclinical depression and LUTS/BPH severity. The mediating role of sleep quality was examined through a Structural Equation Model.

Results: 806 participants were included in this study, with 218 in the mild group and 588 in the moderate-to-severe group. Results showed significantly higher PHQ-9 and PSQI scores in the moderate-to-severe group compared with those in the mild group. Logistic regression analysis revealed that subclinical depression was significantly and positively correlated with increased severity of LUTS/ BPH (OR:1.90, 95% CI:1.16–3.11). Subgroup analysis indicated a stronger association between subclinical depression and LUTS/BPH severity among participants with poor sleep quality (OR: 2.95, 95% CI:1.12–7.73). Mediation analysis showed that sleep quality partially mediated this relationship (β=0.006, P<0.001).

Conclusion: The study illustrates that subclinical depression can serve as a predictor of the severity of LUTS/BPH, with sleep partially mediating this relationship. Consequently, it is crucial to incorporate mental health assessment and intervention into the treatment plan when managing patients with LUTS/BPH.

Keywords: subclinical depression, sleep quality, LUTS/BPH, mediating effect

Introduction

Benign prostatic hyperplasia (BPH) is one of the most common chronic urinary system diseases in elderly men. The prevalence rate among people over 60 years old is approximately 16.78%, and it shows an upward trend in low and lower-middle socio-demographic index (SDI) regions.[1] BPH is a primary cause of lower urinary tract symptoms (LUTS) in men, characterized by urinary obstruction, narrowing of urine flow, incomplete emptying of the bladder, increased urination, urgency, and nocturia.

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Globally, an estimated 26.2% of men are affected by this condition.[2] In terms of disease burden, BPH ranks first among the six major urinary system diseases worldwide.[3] Depression, a common mental disorder, affects approximately 3.8% of the global population, with a higher incidence among the elderly. According to World Health Organization data, depression has become the third leading cause of global disease burden.[4]

As a developing country, China has witnessed an increasingly prominent aging problem alongside the rapid acceleration of economic and urbanization processes. According to data from the National Bureau of Statistics of China, the elderly population had surpassed 250 million by 2021.[5] Existing studies have demonstrated that among Chinese elderly men, those suffering from LUTS/BPH exhibit a significantly higher risk of depression compared to those without these conditions.[6] These conditions not only severely impact the health status and quality of life of elderly men in China but also impose a substantial economic burden on families and society.

Studies have confirmed that depression can influence hormone levels and systemic inflammation in the body. Severe depression, in particular, can affect testosterone secretion in men. Furthermore, alterations in inflammation and testosterone levels may lead to prostatic hyperplasia.[7] Depression is a continuous disease spectrum. Subclinical depression, also referred to as subsyndromal depression, is characterized by the presence of depressive symptoms that do not fully meet the established diagnostic criteria for major depression. This condition is commonly recognized as the prodromal phase of depression. The prevalence of multi-morbidity coexisting with subclinical depression among elderly individuals in both community and general hospital settings is rapidly increasing. However, subclinical depression has not received sufficient attention for a considerable period of time in the past.[8,9] Existing research has demonstrated that diminished sleep duration can adversely affect hormone metabolism in elderly individuals.[10] A cohort study found that sleep is associated with LUTS/BPH, and people with LUTS/BPH are more likely to have sleep disorders.[11] Meanwhile, poor sleep quality is recognized as an independent risk factor for depression, with individuals exhibiting poor sleep quality being at a higher risk of developing depressive symptoms.[12] These pieces of evidence provide support for exploring the role of sleep quality in the progression and severity of depression and LUTS/BPH.

Previous studies have shown that the severity of LUTS is related to depressive tendencies, and that a high IPSS is highly correlated with a high Hamilton Depression Rating Scale score.[13] Moreover, patients with depression often experience sleep problems, such as difficulty falling asleep and frequent awakenings. Zheng et al found that, in middle-aged and elderly Chinese men, poor sleep quality is significantly and positively correlated with LUTS.[14] To date, few studies have investigated the impact of subclinical depression on the progression and severity of LUTS/BPH exist, and most existing studies primarily focus on the relationship between the incidence of LUTS/BPH and depression. Moreover, most of the domestic research on the correlation between LUTS/BPH and depression is based on public databases, while studies using clinical samples are scarce. On the one hand, this reflects a deficiency among urologists in identifying psychological problems and their lack of awareness regarding comprehensive intervention. On the other hand, it highlights the insufficiency of multidisciplinary cooperation in the field of urology. Among elderly men, over 50% suffer from LUTS/BPH to varying degrees. BPH has long been regarded as a surgical disease that requires surgical intervention. In fact, like chronic diseases such as hypertension, BPH requires multi-dimensional management. Actively controlling risk factors can delay the progression of the disease. Furthermore, there is a paucity of research examining the moderating effect of sleep quality on the association between subclinical depression and the severity of lower urinary tract symptoms/benign prostatic hyperplasia. Therefore, this study aims to investigate the potential link between subclinical depression and the severity of lower urinary tract symptoms/benign prostatic hyperplasia, as well as to explore the role of sleep quality in this relationship. The findings may assist clinicians in more accurately assessing the mental health status of patients with lower urinary tract symptoms/benign prostatic hyperplasia, thereby supporting the development of comprehensive intervention strategies, delaying disease progression, and improving patient outcomes. We hypothesized that (1) subclinical depression is independently associated with the severity of LUTS/BPH, and (2) sleep disturbance plays a mediating role in the relationship between subclinical depression and LUTS/BPH.

Materials and Methods

Participants

Male patients who received diagnosis and treatment in the Department of Urology of Jiangnan University Medical Center from October 2023 to April 2024 were selected as the research subjects for this study. Inclusion criteria: (1) Diagnosed with benign prostatic hyperplasia in accordance with the "Chinese urology and andrology disease diagnosis and treatment guidelines";[15] (2) Individuals aged between 60 and 90 years; (3) Received standard treatment for the first time at Jiangnan University Medical Center; (4) Capable of cooperating to complete pertinent laboratory tests, imaging studies, and scale assessments. Exclusion criteria: (1) History of previous prostate surgery; (2) History of urinary system tumors; (3) History of untreated systemic diseases; (4) History of serious mental illness or severe depressive disorder. All the patients participating in the study signed an informed consent form (Figure 1). According to the sample size estimation formula $n = (Z_{\alpha/2})^2 \times P(1 - P) / d^2$, by referring to the literature,[16] with probability P set at 0.32, allowable error $d = 0.1 \times P$, and a significance level of 0.05, the sample size $n = 1.96^2 \times 0.32 \times (1–0.32) / (0.1 \times 0.32)^2 = 1536$. Considering a 10% dropout rate, the sample size was expanded to 900 cases.

Assessment of the Severity of LUTS

The International Prostate Symptom Score (IPSS) was used to evaluate the severity of lower urinary tract symptoms in the participants.[17] The Cronbach's α coefficient of IPSS in the Chinese population was 0.815.[18] The IPSS encompasses seven dimensions: incomplete emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia. Each dimension is rated on a scale from 0 to 5 based on the frequency of symptom occurrence, yielding a total score ranging from 0 to 35. A higher score indicates more severe LUTS. In this study, participants were categorized into two groups based on their IPSS scores: a mild group (1–7 points) and a moderate-to-severe group (≥8 points).

Assessment of Sleep Quality

The Pittsburgh Sleep Quality Index Questionnaire (PSQI) was used to evaluate the sleep status of the participants over the past month. PSQI was developed by BUYSSE et al. The Cronbach's α coefficient of PSQI in the Chinese population is 0.842, and it has been widely used in the diagnosis of sleep disorders in comorbidity studies.[19–21] The Pittsburgh Sleep Quality Index (PSQI) includes seven dimensions: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction, with a total of 19 items. Each dimension is scored from 0 to 3 points, and the total score ranges from 0 to 21 points. A total PSQI score of 8 or higher indicates the presence of poor sleep quality in the subject.

Assessment of Depressive Symptoms

The 9-item Patient Health Questionnaire (PHQ-9) was used to evaluate the depressive symptoms of the participants. PHQ-9 is the simplified part of the self-rating depression scale in the Primary Care Evaluation of Mental Disorders (PRIME-MD), with high sensitivity and specificity, and its Cronbach's α coefficient is 0.86.[22–24] The PHQ-9 comprises nine items, each rated on a 4-point Likert scale (0 to 3 points), yielding a total score ranging from 0 to 27. Higher scores correspond to a greater severity of clinical depression. Scores of 10 or above suggests the presence of subclinical depressive symptoms, while a score exceeding 15 indicates severe depressive symptoms.

Assessment of Other Variables

The socio-demographic and relevant clinical data of the participants were collected by clinical physicians with corresponding qualifications. (1) Socio-demographic data: age, marital status, educational level, smoking status, drinking habits, diet, and physical activity, etc. (2) Clinical data: disease course, past medical history, personal history, height, weight, waist circumference, serum laboratory tests, imaging examinations and pathological reports of prostate biopsy (if any), etc. Based on the aforementioned data, the behavioral factors assessed for the participants encompass BMI, smoking status, alcohol consumption, dietary patterns, and exercise habits. Additionally, the presence of chronic conditions such as diabetes, hypertension, hyperlipidemia, cardiovascular diseases, and cerebrovascular diseases was confirmed.

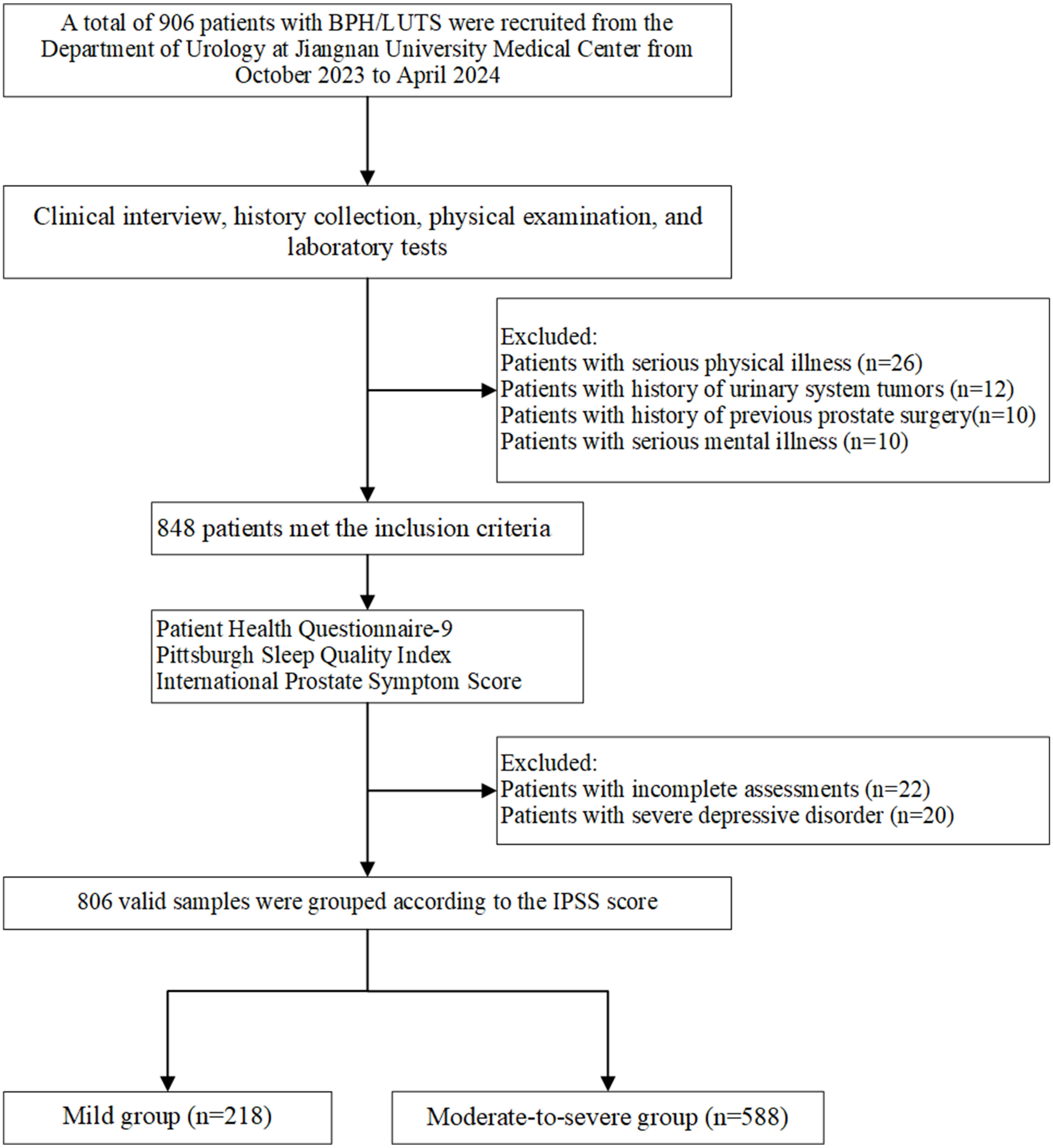

Figure 1 Flowchart of the participant selection process.
Abbreviations: BPH, benign prostatic hyperplasia; LUTS, lower urinary tract symptoms.

Quality Control

Before the project implementation, all researchers received standardized training and successfully passed the consistency assessment, achieving a Kappa value greater than 0.85. Clinical interviews, physical examinations, and scale assessments were conducted by certified clinicians. The quality of research materials was regularly reviewed by quality control personnel. Any materials that did not meet the prescribed standards — such as those with issues related to completeness, logic, or consistency — were deemed unqualified and excluded. In cases where assessment results were inconsistent, the relevant materials were submitted to the research team for further review, and the team made the final decision.

Statistical Analysis

The normally distributed continuous data were characterized by mean ± standard deviation, with intergroup comparisons conducted using the *t*-test. For non-normally distributed continuous data, medians (interquartile range, Q1 to Q3) were reported, and the Mann–Whitney *U*-test was utilized for intergroup comparisons. Categorical variables were summarized as frequencies (n) and percentages (%), with intergroup comparisons performed using the chi-squared (χ^2) test. Logistic regression analysis was employed to examine the association between the severity of LUTS/BPH and subclinical depression. Potential confounding factors were adjusted for (Crude model: adjust for none; Model I adjust for: age, BMI, waist circumference; Model II adjust for: Model I + smoking, diet, physical exercise; Model III adjust for: Model II + hypertension, cardiovascular disease, dyslipidemia, diabetes, cerebrovascular disease; Model IV adjust for: Model III + sleep quality), and smooth curves were generated to illustrate the relationships. Subgroup analysis was conducted on the adjusted model and the interaction between the independent variable and the covariate was examined. The mediating effect of sleep quality on the relationship between subclinical depression and the severity of LUTS/BPH was investigated using Structural Equation Modeling (SEM). All statistical analyses were conducted using SPSS 24.0 statistical software (IBM Corporation, Armonk, New York, USA) and R Studio (version 4.4.3). All statistical tests were two-sided, Bonferroni correction was applied, and the significance level was set at $P < 0.05$.

Result

Characteristics of Study Subjects

A total of 906 participants completed clinical interviews, scale assessments, and relevant examinations for this study. After excluding the participants who did not meet the requirements of this study according to the exclusion criteria, a total of 806 valid samples were obtained (Figure 1). In this study, the average age of the patients was 71.00 [66.00; 76.00] years old, and the baseline characteristics of the individuals are shown in Table 1. Overall, the mean PHQ-9 score was 7.20 (SD = 2.48). Participants with moderate-to-severe LUTS/BPH exhibited significantly higher PHQ-9 scores compared to those in the mild group (7.42 ± 2.56 vs 6.60 ± 2.16), and participants with moderate-to-severe LUTS were

Table 1 Baseline Characteristics

	Total Participants	LUTS/BPH		χ2 / t / Z	P-overall	Bonferroni-Adjusted p-value
		Mild	Moderate-to-Severe			
Number, n	806	218	588			
Age, years	71.00 [66.00;76.00]	69.00 [64.00;72.00]	72.00 [67.00;77.00]	7.597	<0.001	<0.001
BMI, kg/m^2	24.22 [22.34;26.20]	23.76 [21.48;25.71]	24.22 [22.49;26.36]	3.269	0.001	<0.001
Waist circumference, cm	91.00 [88.00;94.00]	90.00 [86.00;92.00]	91.00 [88.75;95.00]	5.176	<0.001	<0.001
PHQ-9, score	7.20±2.48	6.60±2.16	7.42±2.56	4.550	<0.001	<0.001
PSQI, score	6.98±2.57	6.08±1.74	7.32±2.74	7.611	<0.001	<0.001
Subjective sleep quality, score	1.26±0.51	1.32±0.55	1.24±0.500	1.888	0.060	0.420
Sleep latency, score	1.08±0.71	1.00±0.68	1.11±0.72	1.956	0.051	0.357
Sleep duration, score	1.06±0.89	0.85±0.78	1.14±0.91	4.425	<0.001	<0.001
Sleep efficiency, score	1.53±1.03	1.11±0.98	1.69±1.00	7.325	<0.001	<0.001
Sleep disturbance, score	1.11±0.39	1.02±0.33	1.14±0.40	4.345	<0.001	<0.001
Use of sleep medication, score	0.25±0.70	0.15±0.55	0.29±0.74	2.891	0.004	0.028
Daytime dysfunction, score	0.69±0.78	0.63±0.87	0.72±0.74	1.324	0.187	1.309
Age range				30.621	<0.001	<0.001
< 75y	599 (74.32%)	193 (88.53%)	406 (69.05%)			
≥ 75y	207 (25.68%)	25 (11.47%)	182 (30.95%)			
Marital status				0.015	0.903	2.709
Married or living with a partner	618 (76.67%)	166 (76.15%)	452 (76.87%)			
Living alone	188 (23.33%)	52 (23.85%)	136 (23.13%)			
Educational attainment				1.619	0.655	1.965
Primary school	46 (5.71%)	14 (6.42%)	32 (5.44%)			
Junior high school	350 (43.42%)	101 (46.33%)	249 (42.35%)			

(Continued)

Table 1 (Continued).

	Total Participants	LUTS/BPH		χ2 / t / Z	P-overall	Bonferroni-Adjusted p-value
		Mild	Moderate-to-Severe			
High school or equivalent	354 (43.92%)	89 (40.83%)	265 (45.07%)			
College or above	56 (6.95%)	14 (6.42%)	42 (7.14%)			
BMI range				4.024	0.045	0.270
< 24kg/m^2	373 (46.28%)	114 (52.29%)	259 (44.05%)			
≥ 24kg/m^2	433 (53.72%)	104 (47.71%)	329 (55.95%)			
Waist circumference range				8.230	0.004	0.024
< 90cm	296 (36.72%)	98 (44.95%)	198 (33.67%)			
≥ 90cm	510 (63.28%)	120 (55.05%)	390 (66.33%)			
Smoking				11.348	0.001	0.006
Never/former	570 (70.72%)	174 (79.82%)	396 (67.35%)			
Now	236 (29.28%)	44 (20.18%)	192 (32.65%)			
Alcohol intake				0.580	0.446	2.676
Not current /mild	733 (90.94%)	195 (89.45%)	538 (91.50%)			
Moderate-to-Heavy	73 (9.06%)	23 (10.55%)	50 (8.50%)			
Diet				10.419	0.001	0.006
Healthy	475 (58.93%)	149 (68.35%)	326 (55.44%)			
Unhealthy	331 (41.07%)	69 (31.65%)	262 (44.56%)			
Physical exercise frequency				15.246	<0.001	<0.001
Frequently	207 (25.68%)	78 (35.78%)	129 (21.94%)			
Occasionally/hardly	599 (74.32%)	140 (64.22%)	459 (78.06%)			
Hypertension				4.953	0.026	0.130
No	357 (44.29%)	111 (50.92%)	246 (41.84%)			
Yes	449 (55.71%)	107 (49.08%)	342 (58.16%)			
Cardiovascular disease				5.582	0.018	0.090
No	577 (71.59%)	170 (77.98%)	407 (69.22%)			
Yes	229 (28.41%)	48 (22.02%)	181 (30.78%)			
Dyslipidemia				8.283	0.004	0.020
No	618 (76.67%)	183 (83.94%)	435 (73.98%)			
Yes	188 (23.33%)	35 (16.06%)	153 (26.02%)			
Diabetes				9.724	0.002	0.010
No	621 (77.05%)	185 (84.86%)	436 (74.15%)			
Yes	185 (22.95%)	33 (15.14%)	152 (25.85%)			
Cerebrovascular disease				2.765	0.096	0.480
No	717 (88.96%)	201 (92.20%)	516 (87.76%)			
Yes	89 (11.04%)	17 (7.80%)	72 (12.24%)			
Subclinical depression				12.810	<0.001	<0.001
No (PHQ-9 ≤ 10)	645 (80.02%)	193 (88.53%)	452 (76.87%)			
Yes (PHQ-9 > 10)	161 (19.98%)	25 (11.47%)	136 (23.13%)			
Sleep quality				10.499	<0.001	<0.001
Good (PSQI<8)	526 (65.26%)	164 (75.23%)	362 (61.56%)			
Poor (PSQI≥8)	280 (34.74%)	54 (24.77%)	226 (38.44%)			

Notes: normally distributed data are shown as the mean ± SD; other continuous variables are shown as the median (interquartile range, Q1 to Q3).
Abbreviations: BMI, body mass index; PHQ-9, Patient Health Questionnaire-9; PSQI, Pittsburgh Sleep Quality Index.

more likely to have subclinical depression (23.13% vs 11.47%). Additionally, the PSQI scores were notably higher in the moderate-to-severe group compared to those in the mild group (7.32 ± 2.74 vs 6.08 ± 1.74), reflecting a higher prevalence of poor sleep quality in the moderate-to-severe patients (38.44% vs 24.77%). Among the seven components of sleep quality, sleep duration, sleep efficiency, sleep disturbance, and the use of sleep medication showed significant differences among patients with varying degrees of LUTS. Furthermore, statistically significant differences were observed between the moderate-to-severe and mild LUTS groups in terms of waist circumference, smoking habits, dietary patterns, exercise frequency, hypertension, diabetes, dyslipidemia, and cardiovascular diseases ($p < 0.05$).

Association Between the Severity of LUTS/BPH and Subclinical Depression

The variables that showed significant differences after Bonferroni correction in the univariate analysis were included in the logistic regression model to explore the associations between subclinical depression, sleep quality, and other possible confounding factors and the risk of LUTS/BPH progression (Table 2). No significant collinearity was detected among the independent variables in each model. In the crude model, individuals with subclinical depression had an increased risk of LUTS/BPH exacerbation (OR: 2.32, 95% CI: 1.47–3.67, p<0.001). After progressively adjusting for confounding factors across four models, subclinical depression maintained a positive correlation with the severity of LUTS/BPH (Model I: OR: 2.23, 95% CI: 1.40–3.53, p<0.001; Model II: OR: 1.94, 95% CI: 1.21–3.10, p= 0.006; Model III: OR: 1.85, 95% CI: 1.14–3.00, p= 0.012; Model IV: OR: 1.90, 95% CI: 1.16–3.11, p= 0.010), confirming that subclinical depression is an independent risk factor for LUTS/BPH progression. In Model IV, poor sleep quality was also identified as a significant risk factor (OR: 1.86, 95% CI:1.27–2.71, p=0.001) for LUTS/BPH exacerbation. All models passed the Hosmer-Lemeshow goodness-of-fit test.

Additionally, the trend of the relationship between PHQ-9 and the severity of LUTS/BPH was displayed by using a smooth curve. Higher depression scores were associated with a higher risk of moderate-to-severe LUTS/BPH (Figure 2).

Table 2 OR_S and 95% CI_S for the Severity of LUTS/BPH

Exposure	Crude Model		Model I		Model II		Model III		Model IV	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Subclinical depression										
No	1.00		1.00		1.00		1.00		1.00	
Yes	2.32 (1.47,3.67)	<0.001	2.23 (1.40,3.53)	< 0.001	1.94 (1.21,3.10)	0.006	1.85 (1.14,3.00)	0.012	1.90 (1.16,3.11)	0.010
Sleep quality										
Good			1.00		1.00		1.00		1.00	
Poor			1.73 (1.22,2.46)	0.002	1.82 (1.27,2.61)	0.001	1.78 (1.23,2.58)	0.002	1.86 (1.27,2.71)	0.001
Age range										
< 75y					1.00		1.00		1.00	
≥ 75y					3.34 (2.11,5.29)	<0.001	3.37 (2.11,5.37)	< 0.001	3.67 (2.28,5.93)	< 0.001
BMI range										
< 24kg/m²					1.00		1.00		1.00	
≥ 24kg/m²					1.12 (0.79,1.60)	0.521	1.14 (0.79,1.63)	0.485	1.00 (0.68,1.45))	0.983
Waist circumference range										
< 90cm					1.00		1.00		1.00	
≥ 90cm					1.41 (0.98,2.02)	0.061	1.28 (0.89,1.86)	0.186	1.23 (0.84,1.79)	0.292
Smoking										
Never/Former							1.00		1.00	
Now							1.93 (1.30,2.86)	0.001	1.92 (1.28,2.88)	0.002
Diet										
Healthy							1.00		1.00	
Unhealthy							1.53 (1.08,2.17)	0.017	1.56 (1.09,2.23)	0.015
Physical exercise										
Frequently							1.00		1.00	
Occasionally/hardly							1.89 (1.32,2.71)	< 0.001	1.79 (1.23,2.61)	0.002
Hypertension										
No									1.00	
Yes									1.2 (0.85,1.69)	0.303
Cardiovascular disease										
No									1.00	
Yes									2.11 (1.40,3.18)	< 0.001
Dyslipidemia										
No									1.00	
Yes									1.9 (1.22,2.96)	0.005

(*Continued*)

Table 2 (Continued).

Exposure	Crude Model		Model I		Model II		Model III		Model IV	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Diabetes										
No									1.00	
Yes									2.22 (1.40,3.51)	< 0.001
Cerebrovascular disease										
No									1.00	
Yes									1.58 (0.86,2.91)	0.137

Notes: Crude model: Adjusted for none; Model I: Adjusted for sleep quality; age, BMI, and waist circumference; Model II: Adjusted for Model I + age, BMI, and waist circumference; smoking, diet, and physical exercise; Model III: Adjusted for Model II + smoking, diet, and physical exercise; Model IV: Adjusted for Model III + hypertension, cardiovascular disease, dyslipidemia, diabetes, and cerebrovascular disease.
Abbreviations: BMI, body mass index; OR, odds ratio; CI, confidence interval.

Subgroup Analyses

Subgroup analyses were conducted using fully adjusted Model 4 to evaluate the potential association between subclinical depression and the severity of LUTS/BPH (Figure 3). The results indicated that, while OR for subclinical depression and LUTS/BPH severity were consistent across all groups, no statistically significant differences ($P > 0.05$) were observed in the following subgroups: age ≥ 75 years, BMI < 24 kg/m², waist circumference ≥ 90 cm, current smoking, unhealthy diet, frequent physical exercise, presence or absence of hypertension, cardiovascular disease, dyslipidemia, diabetes, and good sleep quality. Notably, in the subgroup of participants with poor sleep quality, the association between subclinical depression and LUTS/BPH severity was more pronounced (OR: 2.95, 95% CI: 1.12–7.73, p=0.028). Further analysis of

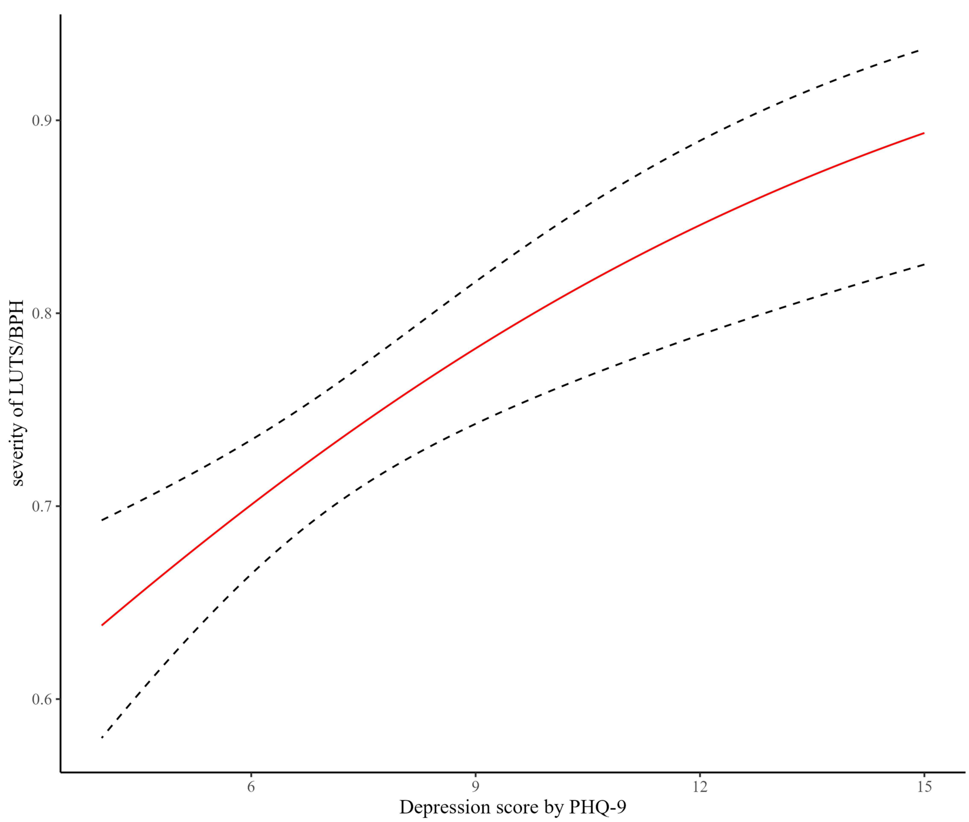

Figure 2 Smooth curve depicting the trend of the association between the severity of LUTS/BPH and depression scores measured by PHQ-9.
Abbreviations: LUTS, lower urinary tract symptoms; BPH, benign prostatic hyperplasia; PHQ-9, Patient Health Questionnaire - 9 Item Version.

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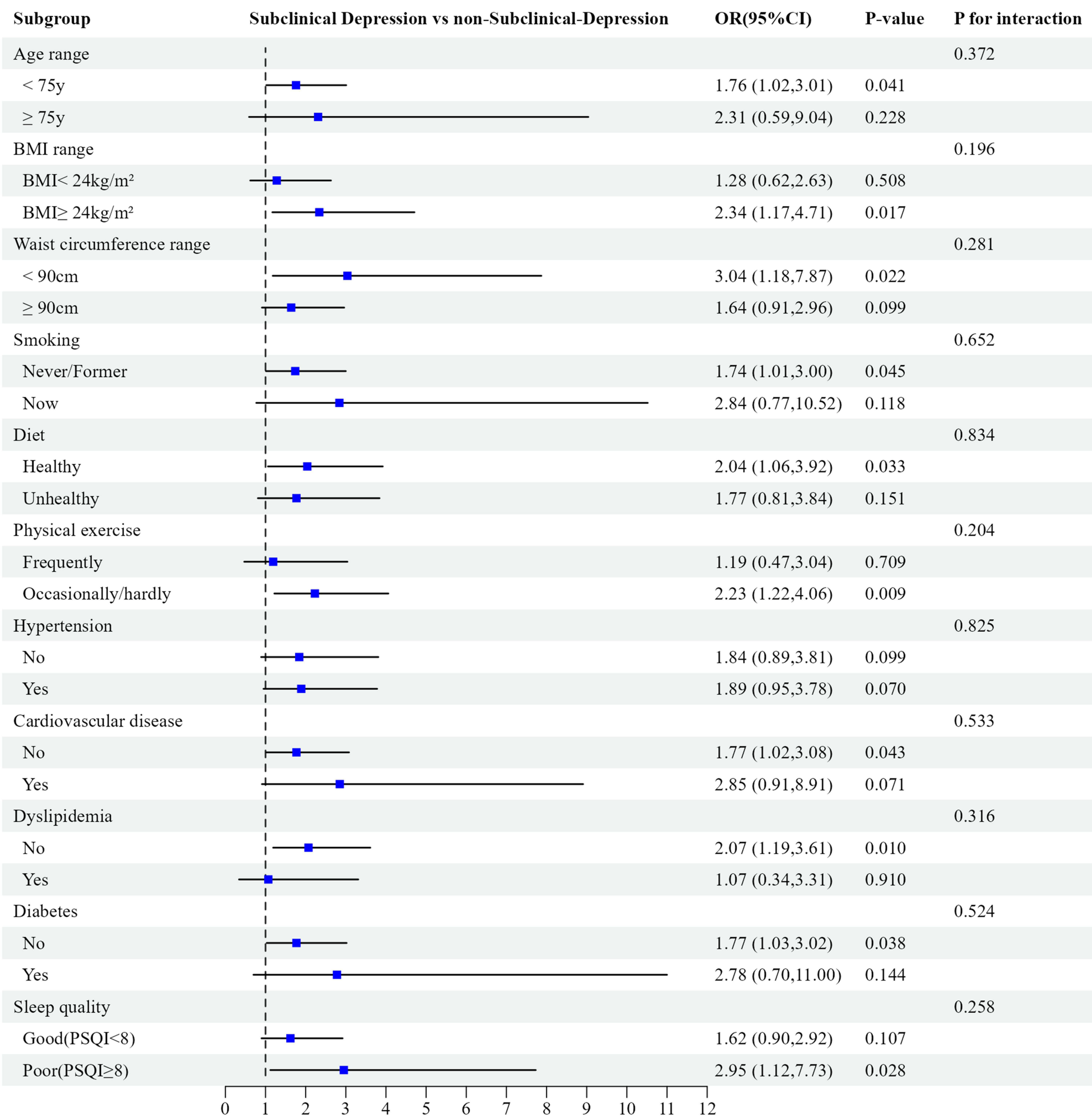

Figure 3 Subgroup analysis of the association between subclinical depression and the severity of LUTS/BPH.
Abbreviations: BMI, body mass index; PSQI, Pittsburgh Sleep Quality Index; OR, odds ratio; CI, confidence interval.

the interaction between each covariate and subclinical depressive symptoms revealed that all p-values were greater than 0.05, indicating no significant interaction effects.

Mediation Analysis

Using R (lavaan package, the Structural Equation Model), while controlling for age, BMI, waist circumference, smoking, diet, physical exercise, hypertension, diabetes, dyslipidemia, cardiovascular diseases, and cerebrovascular diseases, the mediating effect of sleep between subclinical depression and the severity of LUTS/BPH was examined (Table 3). The results showed that subclinical depression exerted a significant direct effect on the severity of LUTS/BPH (β=0.016, P=0.003) and an indirect influence on the severity of LUTS/BPH mediated through poor sleep quality (β=0.006,

Table 3 The Mediation Analysis of Sleep Quality on the Association Between Severity of LUTS/BPH and Depressive Symptoms

	Effect Size	95% CI-Lower	95% CI-Upper	P-value	Proportion (%)
Indirect effect	0.006	0.003	0.009	<0.001	27.3
Direct effect	0.016	0.005	0.027	0.003	72.7
Total effect	0.022	0.011	0.033	<0.001	

Notes: Adjusted for age, body mass index, waist circumference, smoking, diet, physical exercise, hypertension, cardiovascular disease, dyslipidemia, diabetes, and cerebrovascular disease. The effect size is reported using unstandardized regression coefficients.
Abbreviation: CI, confidence interval.

p<0.001). The total effect of subclinical depression on the severity of LUTS/BPH was 0.022 (p<0.001), with the mediating effect accounting for 27.3%. Figure 4 presents the standardized coefficients for each effect. In the analysis of the impact of subclinical depression on the severity of LUTS/BPH, two prominent pathways can be identified: (1) the direct effect of subclinical depression on LUTS/BPH severity; (2) the indirect effect mediated through poor sleep quality.

Sensitivity Analysis

We subtracted 1 point from the PHQ-9 scores of all participants while keeping the PSQI scores unchanged. In light of this adjustment, we recalculated the association between subclinical depression and the severity of LUTS/BPH and re-evaluated the mediating effect of sleep quality. The results showed that the significance of the regression results remained unchanged, as did the size and significance of the mediating effect. Subsequently, we subtracted 1 point from the PSQI scores of all participants while keeping the PHQ-9 scores unchanged. By reassessing these relationships, we found that the main results remained unchanged. This indicates that our research results are robust and do not change significantly due to these minor variations in key variables.

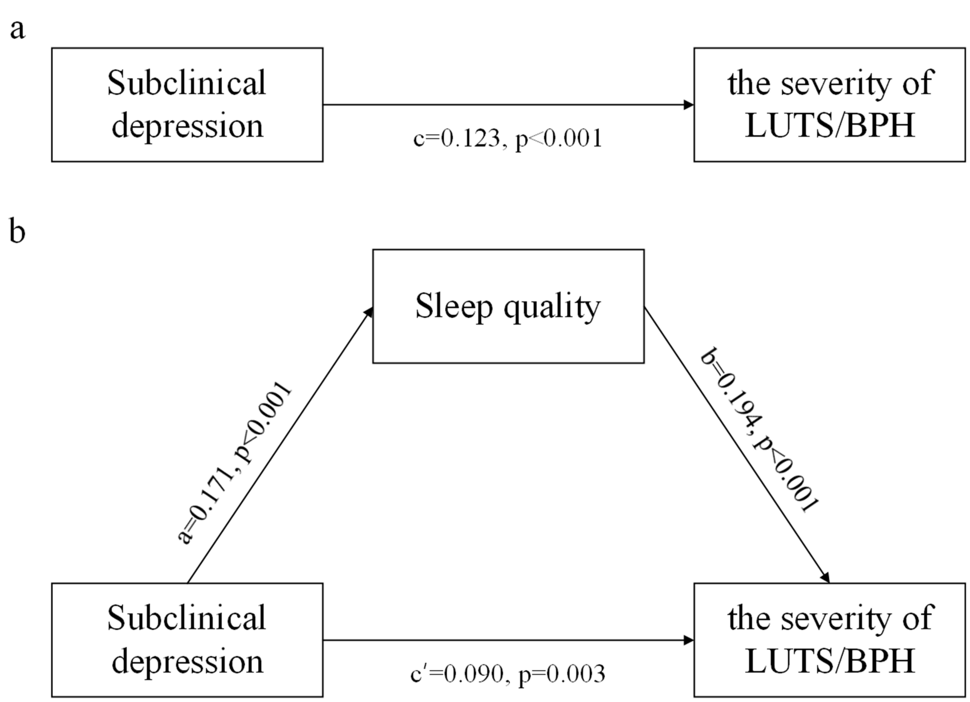

Figure 4 The mediating effect of sleep quality between LUTS/BPH and subclinical depressive symptoms; (**a**) the total effect on subclinical depression; (**b**) the direct and indirect effects of subclinical depression on the severity of LUTS/BPH decline through sleep quality; The standardized coefficients are used for a, b, c, and c′.

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Discussion

With the intensification of global population aging, the prevalence of LUTS/BPH is increasing.[25] As a country with one of the largest elderly populations globally, China confronts significant challenges from LUTS/BPH. This condition not only imposes health and economic burdens on families but also strains the allocation of medical resources.[1,3] According to statistical data, the incidence rate among Chinese men aged 60–69 is approximately 44.7%, rising to 69.2% for men aged 80 and above.[26] Existing research has shown that the onset and progression of LUTS/BPH are influenced by various comorbid conditions.[27] The results of a cross-sectional study conducted by Liu et al using LASI Wave 1 revealed the positive correlation between depression and LUTS/BPH.[28] Similar results were also observed in the study by Zhang et al, which utilized CHARLS and further identified that shorter sleep duration and multimorbidity are significant risk factors for depression among LUTS/BPH patients.[29] Current research has established that subclinical depression serves as a substantial risk factor for clinical depression and is frequently overlooked by non-psychiatric doctors.[30,31] Consequently, this study aims to further investigate the relationship between subclinical depression and the severity of lower urinary tract symptoms associated with LUTS/BPH, while also examining the role of sleep quality. The objective is to enhance the ability of physicians in relevant specialties to integrate mental health factors into personalized diagnosis and treatment plans for patients with LUTS/BPH, thereby effectively alleviating the healthcare burden on elderly men.

After adjusting for potential confounding factors, we found that individuals with subclinical depression were significantly more likely to develop moderate to severe LUTS/BPH than those without subclinical depression. Although this study found a significant positive correlation between subclinical depression and the aggravation of LUTS/BPH, the specific pathological mechanism remains undetermined. This association may be influenced by hormone metabolism.[32] According to He et al's research, subclinical depression can affect the hypothalamic-pituitary-adrenal axis (HPA).[33] In conjunction with Gold's research, the stress response induced by depression activates the cerebral cortex, thalamus, and sympathetic-adrenal-medulla (SAM) system, leading to dysregulation of the CRH/HPA axis.[34] This dysregulation disrupts the normal regulation mechanisms of CRH. Corticotropin-releasing hormone (CRH) and its receptors CRHR1 and CRHR2 play a crucial role in modulating the micturition reflex.[35] The activation of this system and the subsequent hormone release increase sympathetic nerve excitability in tissues associated with urination, such as the external urethral sphincter and urethral smooth muscle, leading to irregular contractions of the bladder detrusor muscle. Consequently, this exacerbates lower urinary tract symptoms related to benign prostatic hyperplasia.[36] Emerging evidence suggests that depression may play a significant role in promoting systemic inflammation. Depression can elevate the plasma levels of inflammatory mediators such as IL-1β, IL-6, TNF-α, and C-reactive protein. Additionally, the mRNA expression levels of these inflammatory mediators tend to increase as depressive symptoms worsen.[37–39] This association is anticipated to emerge even when depressive symptoms are present at a subclinical level.[40] In the systemic inflammatory response, the proliferation of prostate stromal cells and epithelial cells can be stimulated by increased levels of inflammatory mediators. When prostate hypertrophy leads to urodynamic bladder outlet obstruction (BOO), the symptoms of LUTS/BPH will be further aggravated, specifically manifested as voiding symptoms.[7,41,42] Our analysis also revealed that physical exercise, cardiovascular diseases, diabetes, hypertension, and dyslipidemia significantly influence both subclinical depression and the severity of LUTS/BPH, which is consistent with several prior studies.[6,43]

Existing clinical studies have confirmed that subclinical depression can affect sleep quality, and most patients with depression will develop sleep disorders as the symptoms worsen.[44] Therefore, we adjusted for sleep quality in Model 4. The results of the logistic regression indicate that subclinical depression continued to exhibit a positive correlation with the severity of LUTS/BPH after incorporating sleep quality. In the subgroup analysis, the fully adjusted model results showed that the significant association between subclinical depression and the severity of LUTS/BPH was mainly observed in participants with poor sleep quality. Meanwhile, based on Model 4, we conducted a mediation analysis. Although the cross-sectional data used in this study could not precisely determine the causal relationship, the results to some extent indicated that sleep quality played a partial mediating role in the relationship between subclinical depression and the severity of LUTS/BPH, which was consistent with the findings from the logistic regression and subgroup analysis. Several inferences can be made regarding sleep's role in the correlation between subclinical depression and the severity of LUTS/BPH. There is a perspective that poor sleep quality can trigger the immune cascade reaction. Clinical studies have confirmed that in patients with insomnia, the levels of inflammatory mediators such as IL-6, IL-10, IL-1β, TNF-α, and CRP will increase and may lead to the aggravation of

LUTS/BPH, which is similar to some effects of subclinical depression.[45] Another hypothesis posits that sleep can affect the endocrine system, such as the secretion of male sex hormones. Increased frequency of nocturnal awakenings can disrupt circadian rhythms and a reduction in total sleep time.[46] According to relevant animal experiments, it was found that a reduction in sleep quantity can alter hormone metabolism in mammals.[47] In humans, the testosterone level in elderly men is influenced by the circadian rhythm. With the reduction of nighttime sleep duration, the testosterone level in the body decreases, which can slow down the proliferation of prostate stromal cells and epithelial cells. This can result in less severe androgen-dependent LUTS/BPH.[48,49] There was also a theory that pointed out the change in sleep quality would affect the function of the human body's autonomic nervous system. In the case of poor sleep quality, sympathetic nerve activity will be enhanced, leading to an increase in catecholamine levels. The active state of the autonomic nervous system may exacerbate LUTS/BPH symptoms.[50,51] Multiple studies have shown that improving mood and sleep quality through multimodal interventions—such as cognitive behavioral therapy, mindfulness meditation, and acupuncture—has a significant impact on alleviating lower urinary tract symptoms.[52,53]

In this study, we corrected for multiple potential confounding factors, systematically explored the association between subclinical depression and the severity of LUTS/BPH, and deeply analyzed the mediating role of sleep quality in this association, providing an important supplement to understanding the impact of subclinical depression on other diseases. However, it must be pointed out that this study has certain limitations. Due to the cross-sectional design adopted in this study, the causal relationships among subclinical depression, sleep quality, and the severity of LUTS/BPH cannot be clarified. This issue needs to be addressed through further prospective and interventional studies. Therefore, we plan to conduct a longitudinal follow-up study in the future to verify the validity of the current conclusions.

Conclusion

Our findings indicated that subclinical depression is associated with the severity of LUTS/BPH, and sleep quality may mediate this association. Subclinical depression may influence lower urinary tract symptoms and benign prostatic hyperplasia symptoms through sleep quality. Our research provides preliminary data support for delaying the progression of LUTS/BPH through psychological intervention and improving sleep in the future. We suggest that clinicians should take mental health status into consideration when treating patients with LUTS/BPH and formulate individualized comprehensive treatment strategies.

Data Sharing Statement

The datasets used and analyzed in the current study will be available from the corresponding author, Ninghan Feng, upon reasonable request.

Ethics Approval and Informed Consent

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Jiangnan University Medical Center (No:2021-Y-3). All the patients participating in the study signed the informed consent form.

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Author Contributions

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

The authors declare no conflicts of interest in this work.

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