#### ORIGINAL RESEARCH

## The effect of nocturia on sleep quality and daytime function in patients with lower urinary tract symptoms: a cross-sectional study

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Background: Nocturia has been proven to have a negative impact on the quality of life and sleep quality in general elderly population. However, there are limited studies on the quantitative effect of nocturia on sleep quality and daytime dysfunction, specifically in patients with lower urinary tract symptoms.

Patients and methods: During March 1, 2015 to December 31, 2015, a total of 728 patients who visited our urology department due to voiding dysfunction and experienced nocturia at least once per night were enrolled. Three questionnaires were administered to them after obtaining their written consents. Pittsburgh Sleep Quality Index (PSQI) questionnaire, Epworth Sleepiness Scale (ESS) questionnaire, and International Prostate Symptom Score (IPSS) questionnaire were applied to evaluate their sleep quality, daytime dysfunction, and voiding problems, respectively. Statistical analysis of the impact of nocturia on sleep quality and daytime dysfunction was performed.

**Results:** The mean age of patients was 61 years, with a male-to-female ratio of 2.7. The mean nocturia number was 3.03. The IPSS, PSQI, and ESS scores were 17.56, 8.35, and 8.22, respectively. The nocturia number increased with age and was significantly correlated to ESS score (daytime dysfunction) and PSQI total score (sleep quality) in overall group. Among subgroups divided by age and sex, there was a significant correlation between nocturia number and daytime dysfunction in male patients or patients younger than 65 years.

Conclusion: In patients with lower urinary tract symptoms, nocturia number increased with age and was significantly correlated with poor sleep quality. Nocturia plays an important role in patients younger than 65 years in daytime dysfunction.

Keywords: nocturia, sleep quality, lower urinary tract symptoms, daytime dysfunction

## Introduction

The International Continence Society defines nocturia as the need to void one or more times during the night, with each of the voids preceded and followed by sleep. Nocturia has the following two main causes: increased nocturnal urine volume and vesical instability.<sup>1</sup> As one of the most common complaints in patients with lower urinary tract symptoms (LUTS), nocturia is reported to negatively affect the quality of life and quality of sleep.<sup>2,3</sup> Since its prevalence and severity increase with age,<sup>4</sup> the negative effect of nocturia on the elderly requires more attention. Jensen et al<sup>5</sup> reported that 25% of falls experienced by older individuals occur during the night and 25% of these occur when the individual is waking up to void.

Studies have shown a significant association between nocturia and sleep quality, but most of these investigations were among the general elderly population.<sup>6-8</sup>

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Obayashi et al used objective actigraphy and subjective questionnaires to quantitatively evaluate the association between nocturnal voiding frequency and sleep quality in the general elderly population.<sup>9,10</sup> Considerable number of patients with benign prostate hyperplasia, bladder outlet obstruction, overactive bladder, or other diseases that affect urinary function may suffer from nocturia, and there are some reports focusing on nocturia and sleep.<sup>6,11,12</sup> However, studies on the quantitative effect of nocturia on both sleep quality and daytime function, specifically in adult patients with LUTS, are sparse. In this cross-sectional study of 728 individuals with LUTS, we used three survey tools to evaluate the effect of nocturia on sleep quality and daytime sleepiness.

## **Patients and methods** Participants and study protocol

Our study is a cross-sectional and questionnaire-based survey conducted among patients with LUTS and nocturia. Inclusion criteria were as follows: patients who visited our urologic department from March 1, 2015 to December 31, 2015 due to LUTS and experienced nocturia at least once per night were enrolled in this study. Exclusion criteria were as follows: patients with a history of drug treatment for LUTS and those with concomitant urinary tract infection or urolithiasis were excluded. A total of 728 patients met the criteria and completed the questionnaires. All patients provided written informed consent to participate in this study. The Cathay General Hospital Institutional Review Board approved the study protocol.

## Data collection

We conducted our face-to-face survey based on three internationally validated, reliable, and widely used questionnaires, namely Pittsburgh Sleep Quality Index (PSQI) questionnaire,<sup>10,13</sup> Epworth Sleepiness Scale (ESS) questionnaire,<sup>14,15</sup> and International Prostate Symptom Score (IPSS) questionnaire. After obtaining their written informed consents, the patients were asked to complete the questionnaires at their first visit before medications for LUTS were prescribed, with the assistance of trained research assistants. Each interview took ~10–20 minutes.

# Measuring sleep quality and daytime dysfunction

The PSQI questionnaire was used to evaluate sleep quality and disturbance over the past month. It contains 19 items. The first four items are open questions, and 5–19 items are rated on a four-point scale. The item scores yield the following seven subscores ranging from 0 to 3: sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, sleep medication use, and daytime dysfunction due to sleepiness. The total scores ranging from 0 to 21 were obtained by summing up the seven subscores. Most studies have consistently stated that a total PSQI score of  $\leq$ 5 suggests a good sleep quality, whereas a total PSQI score of >5 suggests a poor sleep quality.<sup>10,13,16,17</sup>

The ESS questionnaire consists of eight questions that are rated on a four-point scale ranging from 0 to 3. A total score between 0 and 24 is used to evaluate our participants' general level of daytime sleepiness or the average sleep propensity over the past month. An ESS score of >8 suggests significant sleepiness.<sup>14,16,17</sup>

## Measuring LUTS

We used the IPSS questionnaire to evaluate their voiding dysfunction. It is a basic and widely used questionnaire used by urologists. It contains the seven-item American Urological Association (AUA) Symptom Index and one question on the quality of life, which is used to evaluate male LUTS, such as benign prostate hyperplasia-related voiding problem. The seven-item AUA Symptom Index, developed and psychometrically validated by an AUA Measurement Committee in 1992, reliably assesses the severity of LUTS and is responsive to changes in treatment.<sup>18</sup> The World Health Organization in 1993 adopted the eight-item IPSS, which uses the same seven questions assessing LUTS severity as the AUA Symptom Index and an eighth disease-specific quality of life question that assesses the pain associated with LUTS. It has also been proven reliable for the evaluation of female patients with lower urinary tract dysfunction.<sup>19</sup> The seven questions are divided into the following two parts: IPSS voiding scores and IPSS storage scores.<sup>20</sup> The IPSS voiding scores consist of weak stream, intermittency, straining, and feeling of incomplete bladder emptying, whereas the IPSS storage scores consist of frequency, urgency, and nocturia. Each scoring ranges from 1 to 5 for a total of maximum 35 points. The eighth question on voiding-related quality of life is assigned a score of 0-6. The higher the score is, the lower the quality is.

#### Other parameters

Nocturia number was defined as the number of voids during the time from going to bed at night to waking up next morning, excluding the last void before bedtime and the first void after waking up in the morning. Patients' basic characteristics, including age, sex, height, weight, and body mass index, were collected from their medical charts.

## Statistical analyses

The statistical analyses were performed on a personal computer using the statistical package SPSS for Windows (Version 17.0, SPSS Inc., Chicago, IL, USA). We used generalized linear model to perform multivariate analysis between several parameters versus PSQI and ESS scores. We used the independent samples t-test to compare the differences of age, nocturia number, ESS score, PSQI score, and IPSS score between subgroups dividing by sex and age (<65 and  $\geq$ 65 years). The associations between nocturia number and sleep quality (PSOI scores C1-C7 and total score) and daytime dysfunction (ESS score) were analyzed by Pearson's correlation test. The analysis was performed not only for the overall patient group but also for the patients divided into subgroups according to age (older than and younger than 65 years) and sex (male and female). Pearson's correlation test was used to compare the subgroups.

## Results

The patients' characteristics and detailed subscale scores of IPSS, ESS, and PSQI are presented in Table 1. The mean age of the patients was  $61.4\pm13.7$  years, with a male-to-female ratio of 2.7. Of the 728 patients, 101 (13.9%) patients

reported one nocturia episode, 188 (25.8%) patients reported two nocturia episodes, 170 (23.4%) patients reported three nocturia episodes, 124 (17.0%) patients reported four nocturia episodes, and 145 (19.9%) patients reported five or more nocturia episodes. The mean nocturia number was 3.03 per night. The mean IPSS total score, PSQI total score, and ESS score were 17.56 $\pm$ 8.62, 8.35 $\pm$ 3.66, 3.23 $\pm$ 2.48, and 8.22 $\pm$ 5.07, respectively. The results revealed that our participants have both poor sleep quality and daytime dysfunction compared to the normal population.<sup>10,13-16</sup>

The result of multivariate analysis using the generalized linear model is disclosed in Table 2. Taking the ESS total score as a dependent variable, we found that it is positively correlated with PSQI score with statistical significance, and the 95% confidence interval does not cover zero. While using the PSQI score as a dependent variable, we found that it is positively correlated with nocturia number and ESS score with statistical significance, and the 95% confidence interval does not cover zero. The PSQI score is higher in female patients.

By age and sex, we divided our participants into subgroups (male and female, <65 years and  $\geq 65$  years). The independent samples *t*-test was used to clarify the differences

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Characteristics	Mean	Range	Units
Age	61.4±13.7	17–87	Years
Sex, n (%)			
Male	530 (72.8%)		
Female	198 (27.2%)		
Height	163.2±7.8	150–176	cm
Weight	64.8±14.6	42–102	kg
Body mass index	24.2±4.2	17–34	kg/m <sup>2</sup>
Nocturia number	3.03±1.3	I—5	Number per night
IPSS scores			
Voiding score	9.11±5.59	0–20	
Storage score	8.46±3.79	0-15	
Total score	17.56±8.62	0–35	
Voiding-related QoL score	3.62±1.19	0–6	
PSQI scores			
C1 (subjective sleep quality)	1.36±0.68	0–3	
C2 (sleep latency)	1.36±1.03	0–3	
C3 (sleep duration)	1.76±0.89	0–3	
C4 (habitual sleep efficiency)	1.33±1.16	0–3	
C5 (sleep disturbance)	1.55±0.57	I_3	
C6 (use of sleeping medication)	0.50±1.04	0–3	
C7 (daytime dysfunction)	0.48±0.65	0–3	
Total score	8.35±3.66	I-18	
ESS score	8.22+5.07	0–24	

Note: Data presented as mean  $\pm$  standard deviation unless stated otherwise.

Abbreviations: ESS, Epworth Sleepiness Scale; IPSS, International Prostate Symptom Score; PSQI, Pittsburgh Sleep Quality Index; QoL, quality of life.

Dependent variables	Parameters	Estimate	Partial correlation	Significance	95% confidence interval of the estimate
ESS score	Age	0.015	0.041	0.296	-0.013 to 0.044
	Sex	0.461	0.040	0.307	-0.425 to 1.347
	Nocturia number	0.146	0.038	0.345	-0.157 to 0.449
	PSQI score	0.186	0.135	0.001*	0.077 to 0.295 <sup>a</sup>
PSQI score	Age	0.019	0.072	0.049	0.000 to 0.039
	Sex	-2.311	-0.275	0.000*	-2.886 to -1.737ª
	Nocturia number	0.636	0.230	0.000*	0.436 to 0.835ª
	ESS score	0.085	0.117	0.001*	0.035 to 0.135 <sup>a</sup>

Table 2 Multivariate analysis for the association of parameters with daytime dysfunction and sleep quality using GLM

Notes: For the parameter of sex, we define male as 1 and female as 0. 395% confidence interval does not cover zero. \*P-value >0.05.

Abbreviations: ESS, Epworth Sleepiness Scale; GLM, generalized linear model; PSQI, Pittsburgh Sleep Quality Index.

between them. The results are shown in Table 3. The mean age, nocturia number, IPSS storage score, and voiding-related quality of life were similar between different sex groups, whereas a higher PSQI total score, a lower IPSS voiding score, and a lower IPSS total score were found in female group with significant difference. Among subgroups of patients <65 and ≥65 years old, patients older than 65 years had significantly worse performance in all parameters, including nocturia number, PSQI total and subscores, IPSS total and subscores, and voiding-related quality of life, except for ESS score.

The effects of nocturia number on sleep quality and daytime function, which were analyzed using Pearson's correlation test, are revealed in Table 4. In the overall group, the higher nocturia number was significantly correlated with the higher ESS score and the higher PSQI scores C1–C6 and total score but not for score C7. In subgroups divided by age, nocturia number was still significantly correlated with the higher ESS score in patients younger than 65 years, but it had no significant effect on ESS score in patients older than 65 years. The severity of nocturia significantly correlated with higher PSQI total score in both subgroups. For patients

divided by sex, more nocturia number was still significantly correlated with ESS score in male patients but not in female patients. In both subgroups, the higher nocturia number was significantly correlated with higher PSQI total scores. The relationships between nocturia numbers and ESS score and PSQI score respectively are shown in Figure 1.

#### **Discussion**

Nocturia is a persistent LUTS and is often regarded as a natural consequence of aging.<sup>21</sup> However, the negative effect of nocturia has been underestimated until recently, not only for its underreported prevalence<sup>7,22,23</sup> but also for the resulting physical and psychiatric problems.<sup>2,3,24,25</sup> Increasing numbers of studies are now describing the negative effect of nocturia on sleep quality, associated diseases, and mortality in the aging population. Most of the previous studies have reported an association between nocturia that was categorized using cutoff points but have not quantified its severity.<sup>9</sup> In this study, we investigated the correlation of nocturia number with sleep quality and daytime dysfunction in patients with LUTS.

In this study, we also compared the differences of each parameter between males and females and patients older

	Overall	Sex			Age		
	(n=728)	Male (n=530)	Female (n=198)	P-value	<65 years (n=442)	≥65 years (n=286)	P-value
Age (years)	61.4	61.9	60.1	0.091	52.3	75.0	0.000*
Nocturia number	3.03	3.08	2.91	0.130	2.76	3.46	0.000*
ESS score	8.22	8.27	8.12	0.720	8.01	8.57	0.143
PSQI score	8.35	7.80	9.80	0.001*	7.90	9.04	0.000*
IPSS score							
IPSS voiding score	9.11	9.54	7.95	0.001*	8.20	10.50	0.000*
IPSS storage score	8.46	8.50	8.35	0.624	7.63	9.74	0.000*
IPSS total score	17.56	18.03	16.30	0.015*	15.83	20.24	0.000*
Voiding related quality of life	3.62	3.65	3.56	0.333	3.45	3.88	0.000*

Table 3 Comparison of parameters between subgroups dividing by sex and age

**Note:** \**P*-value <0.05.

Abbreviations: ESS, Epworth Sleepiness Scale; IPSS, International Prostate Symptom Score; PSQI, Pittsburgh Sleep Quality Index.

	Overall		Sex				Age			
	(n=728)		Male (n=530)		Female (n=19	8)	< <b>65</b> years (n=	:442)	≥65 years (n=	286)
	Pearson's correlation coefficient	P-value								
ESS score	0.093	0.012*	0.105	0.016*	0.033	0.654	0.105	0.027*	0.053	0.372
PSQI score										
CI (subjective sleep quality)	0.177	0.000**	0.188	0.000**	0.198	0.007**	0.111	0.020*	0.269	0.000**
C2 (sleep latency)	0.103	0.005**	0.093	0.034*	0.225	0.002**	0.098	0.040*	0.070	0.235
C3 (sleep duration)	0.166	0.000**	0.193	0.000**	0.169	0.021*	0.151	0.001**	0.157	0.008*
C4 (habitual sleep efficiency)	0.187	0.000**	0.193	0.000**	0.276	0.000**	0.105	0.028*	0.234	0.000**
C5 (sleep disturbance)	0.201	0.000**	0.223	0.000**	0.145	0.049*	0.150	0.002**	0.235	0.000**
C6 (use of sleep aid)	0.152	0.000**	0.124	0.005**	0.213	0.004**	0.067	0.160	0.199	0.001**
C7 (daytime dysfunction)	0.062	0.094	0.026	0.557	0.178	0.015*	0.047	0.320	0.129	0.029*
Total score	0.247	0.000**	0.250	0.000**	0.338	0.000**	0.157	0.001**	0.299	0.000**

than or younger than 65 years. Female patients had similar nocturia number and daytime dysfunction but had significant worse sleep quality than male patients. Such a correlation was revealed by multivariate analysis in our study shown in Table 2. The average of PSQI total score was 9.80 in female and 7.80 in male patients, which is shown in Table 3. This is consistent with the relatively higher frequency of prescription sleep aids use in the female population,<sup>26</sup> and in our data, the PSQI C6 scores were 0.69 and 0.43 among females and males, respectively (PSQI C6 score refers to use of sleeping medication: never =0; <1 per week =1; 1-2 per week =2; and  $\geq$ 3 per week =3).<sup>10</sup> The IPSS storage score for females was similar to that for males, but the IPSS voiding score was significantly lower for females than for males. The high prevalence of prostatic disorder-related voiding dysfunction in aging males could explain this finding.<sup>20</sup> As for age, in patients older than 65 years, all parameters were significantly worse than those in the younger group, except for similar ESS scores, which were compatible with some published study results.<sup>7-9</sup> In multivariate analysis, PSQI score was positively correlated with age, but the ESS score was not.

Nocturia has been recognized as a potential risk for sleep disturbance.<sup>27</sup> Our study also found that the severity of nocturia increased significantly with age in patients with LUTS. More severe nocturia also significantly correlated with worse sleep quality and daytime dysfunction. However, score C7 (daytime dysfunction) is not correlated with higher nocturia number (Table 4), which is not compatible with other published studies.28 This inconsistency with ESS score could be explained by the fact that the score C7 ranges from 0 to 3 while the ESS score ranges from 0 to 24. We suggested that ESS score is a more definite and detailed evaluation for daytime dysfunction. We found that the negative effect of nocturia on daytime dysfunction (ESS score) among patients older than 65 years and female patients was not statistically significant. This phenomenon could be explained by the fact that the subjective perception of daytime dysfunction is more obvious and stronger in people with jobs who need higher concentration and focus. Most patients older than 65 years were retired from active work, and the impact of nocturia on daytime function is easily overlooked. Foley et al<sup>28</sup> reported that frequent napping is common among older adults or patients without employment to compensate their sleep disruption. A similar situation exists for the female subgroup of our participants. A considerably high proportion (68%) of our female participants were housewives, for whom working hours are more flexible and who have less need to concentrate for a long time. Such result suggested



Figure I The mean ESS score (A) and PSQI score (B) referring to different nocturia numbers. Abbreviations: ESS, Epworth Sleepiness Scale; PSQI, Pittsburgh Sleep Quality Index.

that nocturia plays an important role in patients younger than 65 years in daytime dysfunction, and hence treating nocturia might improve their work performance. Clinically, this blunt perception of the effect of nocturia on daytime spirit and dysfunction among aging people might also be one of the causes of nocturia being underestimated or regarded as a natural consequence of getting older and resulting in delays in seeking treatment.

We used questionnaires to quantify the negative effect of nocturia not only on sleep quality but also on daytime function among patients with LUTS. We also evaluated the severity of nocturia, rather than using a binary yes-or-no measure, and found a significant correlation. However, the evaluations of sleep quality and daytime dysfunction were based on subjective perception only. More objective tools, such as actigraphy and polysomnography, may provide more accurate information on actual sleep quality in future studies. The male-to-female ratio was 2.7, reflecting the fact that our patients were sourced mainly from the urologic department. The relatively small size of the female population may have affected the statistical analysis. In Table 4, Pearson's correlation coefficients are not high but still with statistical difference, which might result from the large number of our participants. In order to emphasize on the effect of nocturia numbers, more prospective studies are also needed.

## Conclusion

In patients with LUTS, nocturia number increased with age and was significantly correlated with poor sleep quality. Nocturia plays an important role in patients younger than 65 years in daytime dysfunction, which should not be overlooked. With similar nocturia number, female patients reported worse sleep quality, with higher rate of sleeping pill use.

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#### Disclosure

The authors report no conflicts of interest in this work.

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