

# Linkage of Lower Urinary Tract Symptoms to Sleep Quality in Elderly Men with Nocturia: A Community Based Study Using Home Measured Electroencephalogram Data



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## Abbreviations and Acronyms

BPH = benign prostatic hyperplasia  
EEG = electroencephalography  
HUS = hours of undisturbed sleep  
I-PSS = International Prostate Symptom Score  
LUTS = lower urinary tract symptoms  
NREM = nonrapid eye movement  
NUV = nocturnal urinary volume  
PSG = polysomnography  
PSQI = Pittsburgh Sleep Quality Index  
 $Q_{max}$  = maximum flow rate  
QOL = quality of life  
SWS = slow wave sleep

**Purpose:** We objectively investigated the relationship between sleep quality/efficiency and factors associated with micturition using at-home electroencephalogram assessment.

**Materials and Methods:** Participants were recruited from among those enrolled in the Fujiwara-kyo Study, a community based longitudinal evaluation that began in Nara Prefecture, Japan, in 2007. Included participants were men at least 65 years old who woke up in the middle of the night/early morning at least 3 times per week with the urge to void. We evaluated lower urinary tract symptoms using the I-PSS and subjective sleep quality using the Pittsburgh Sleep Quality Index. Uroflowmetry and 3-day frequency volume charting measurements were also obtained. Electroencephalogram recordings were obtained during sleep to evaluate objective sleep quality.

**Results:** Final analysis included data from 47 participants. I-PSS-quality of life score and slow wave sleep time were independent predictors of good subjective sleep quality as determined by Pittsburgh Sleep Quality Index scores. Nocturnal urinary volume was an independent predictor of greater sleep efficiency. Maximum flow rate was an independent predictor of longer slow wave sleep time.

**Conclusions:** In elderly men with nocturia, sleep quality is associated with lower urinary tract function. Higher subjective sleep quality is associated with longer slow wave sleep time and less severe lower urinary tract symptoms. Higher objective sleep quality is further associated with a higher urinary flow rate and lower nocturnal urinary volume.

**Key Words:** sleep, nocturia, lower urinary tract symptoms

NOCTURIA is defined by the International Continence Society as the complaint that the individual has to wake at night 1 or more times to void.<sup>1</sup> Nocturia is one of the most bothersome lower urinary tract symptoms,<sup>2</sup> affecting subjective and objective sleep quality.<sup>3</sup> Sleep disruption due to nocturia reduces HUS, the time between falling asleep

and first awakening to void, leading to a deteriorating quality of life.<sup>4</sup> As restorative slow wave sleep occurs during the first third of the night after an individual falls asleep, at least 3 to 4 HUS are recommended.<sup>4</sup> Disruption of SWS, even without a reduction in total sleep time or sleep efficiency, is associated with increased discomfort and fatigue.<sup>5</sup>

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Objective assessments are preferable in the evaluation of SWS, which greatly influences sleep quality. Although PSG is the method of choice for such objective assessment, it is not easy to perform due to the large number of monitoring lines and the restricted laboratory environment required for assessment. Therefore, previous studies have instead used actigraphy to obtain objective measurements of sleep related parameters.<sup>3,6</sup> Actigraphy, which measures movements to evaluate states associated with sleep and wakefulness, can support large scale, population level sleep studies beyond the capabilities of PSG. Although research has indicated that actigraphy is useful for evaluating total sleep and wake time after the initial onset of sleep,<sup>7</sup> some reports suggest that the method may overestimate sleep time while underestimating the time spent awake.<sup>8</sup> The recent development of single-channel portable EEG has further simplified the objective assessment of sleep quality. In this study we investigated the relationship between sleep quality and factors associated with micturition using this new EEG approach.

## PARTICIPANTS AND METHODS

Participants were recruited from among those enrolled in the Fujiwara-kyo Study, a community based longitudinal evaluation that began in Nara Prefecture, Japan in 2007. Included participants were men at least 65 years old who lived at home, could walk independently and had reported waking up in the middle of the night/early morning at least 3 times per week. Men experiencing other factors that may influence sleep quality, such as frequent use of sleeping pills, snoring related to sleep apnea, history of stroke and depression were excluded from the study. Participants were enrolled between June 2011 and March 2013.

Lower urinary tract symptoms were evaluated using the I-PSS while subjective sleep quality was evaluated using the Pittsburgh Sleep Quality Index. Additional data were collected using uroflowmetry and 3-day frequency volume charting. EEG recordings were obtained during sleep to objectively evaluate sleep quality.

### International Prostate Symptom Score

We examined total I-PSS, voiding symptom scores (feeling of incomplete bladder emptying, intermittency, weak stream and straining) and storage symptom scores (frequency, urgency and nocturia). We adequately explained the I-PSS to the participants to avoid the discrepancy between I-PSS question 7 (nocturia) and the actual diary derived nocturnal frequency. We asked the participants to answer I-PSS question 7 according to the frequency volume chart that they had recorded themselves.

### Pittsburgh Sleep Quality Index

The PSQI is a standardized questionnaire designed to assess sleep quality in clinical populations based on an

individual's responses to 19 items across the 7 domains of subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleeping medication and daytime dysfunction.<sup>9</sup> Responses to individual items are rated from 0 to 3, with lower scores indicative of better sleep quality. In this study a global PSQI score of 5 or less was used to distinguish good sleep quality from poor sleep quality in accordance with the original PSQI report, in which the authors concluded that a global PSQI score greater than 5 yielded a diagnostic sensitivity of 89.6% and specificity of 86.5% in distinguishing good and poor sleepers.<sup>9</sup>

### EEG and Assessment of Sleep Stage

EEG recordings were obtained during sleep using a single-channel portable EEG device (Brainwave Sensor ZA<sup>®</sup>), which collected data at a sampling rate of 128 Hz. Participants were instructed to obtain EEG measurements at home for 3 consecutive nights. EEG data were analyzed using specialized software (SleepSign<sup>®</sup>) and visually examined by a clinical laboratory technologist. Brainwave Sensor ZA operates in a manner similar to that of another portable EEG device (Sleepscope<sup>®</sup>), using disposable Ag/AgCl surface electrodes placed on the participant's forehead as well as behind the ears.<sup>10,11</sup> Visual analysis of EEG data was performed to determine sleep stage during each 30-second period. EEG data were classified into the 4 sleep stages of 1) awake, 2) rapid eye movement sleep, 3) light (stage 1 and 2) NREM sleep, and 4) deep (stage 3 and 4) NREM sleep.

### Statistical Methods

All statistical analyses were performed using PASW<sup>®</sup> Statistics 17.0. All p values less than 0.05 were considered statistically significant. Comparisons between the 2 groups were made using the Mann-Whitney U test. Binary logistic regression analysis was used for univariate and multivariate analyses. The institutional review board approved this prospective study and informed consent was obtained from all patients following a full explanation of the study aims and methods.

## RESULTS

A total of 65 participants were enrolled in the study. For 8 participants EEG data were not recorded properly because the surface electrodes had detached from the scalp or sweat had disturbed the electrode connection. For 5 participants uroflowmetry data were not recorded properly due to incorrect operation. Five participants had improperly completed the questionnaires. Therefore, final analysis included data from 47 participants.

Participant characteristics are presented in table 1. Participants with global PSQI scores of 5 or lower were classified as good sleepers while participants with scores higher than 5 were classified as poor sleepers. Age and prostate volume were not significantly different between the groups. I-PSS and QOL scores were significantly higher in the poor sleep group than in the good sleep group. Furthermore,

**Table 1.** Participant characteristics

	Total	PSQI Global Score 5 or Less	PSQI global Score Greater than 5	p Value
No. participants	47	29	18	
Median age (range)	75 (63–88)	75 (68–88)	72 (63–80)	0.1502
Median kg/m <sup>2</sup> body mass index (range)	22.3 (18.0–33.5)	22.4 (18.0–27.7)	22.2 (18.4–33.5)	0.9417
No. hypertension (%)	23 (48.9)	13 (72.2)	10 (55.6)	0.5556
No. diabetes (%)	3 (6.4)	1 (3.4)	2 (11.1)	0.5493
No. snoring (%)	17 (36.2)	8 (27.6)	9 (50.0)	0.2111
Median ml prostate vol (range)	21.3 (9.8–75)	20 (9.8–75.0)	30 (10.0–56.0)	0.3543
Median I-PSS (range):				
Total score	7 (1–24)	5 (1–18)	11 (5–24)	<0.0001
Voiding symptoms	3 (0–17)	1 (0–13)	7 (2–17)	0.0003
Storage symptoms	4 (1–14)	3 (1–14)	6 (3–12)	0.0008
QOL	3 (0–6)	2 (0–4)	4 (1–6)	0.0002
Median Q <sub>max</sub> (range)	14.5 (2–35)	15.0 (2.0–35.0)	9.4 (4.8–26.6)	0.0444
Median ml post-void residual urine (range)	0 (0–45)	0 (0–45)	0 (0–40)	0.1991
Median ml NUV (range)	438 (74–1,080)	428 (74–975)	550 (150–1,190)	0.1196
Median EEG variables (range):*				
Time in bed (mins)	452.5 (235.5–647)	486.0 (235.5–647.5)	423.0 (356.5–584.0)	0.0297
Sleep period time (mins)	420.5 (196–612)	431.0 (196.0–612.0)	403.0 (294.0–483.0)	0.0543
Total sleep time (mins)	340.5 (168–473)	361.0 (168.0–473.0)	312.0 (203.0–406.5)	0.0475
Wake time after sleep onset (mins)	78.4 (7–254)	74.5 (7.0–254.0)	81.0 (8.0–173.0)	0.7019
Sleep efficiency (%)	81.8 (25.5–97)	84.5 (25.5–96.5)	80.0 (55.5–97.0)	0.5546
SWS time (mins)	44 (0–116)	48.5 (10.5–116.0)	34.5 (0.0–78.5)	0.0147

\* Sleep period time (SPT)—time from inset of sleep to final arousal. Wake time after sleep onset (WASO)—sum of arousal time during SPT. Total sleep time (TST)—SPT—WASO. Sleep efficiency—TST/SPT\*100.

Q<sub>max</sub> was significantly lower in the poor sleep group than in the good sleep group, suggesting that lower urinary tract function is subjectively and objectively worse in individuals with poor sleep. EEG data indicated that total sleep time and SWS time were significantly shorter in the poor sleep group than in the good sleep group.

### Predictive Variables of Good Subjective Sleep Quality

We conducted univariate and multivariate analyses of the prediction of good subjective sleep quality for I-PSS and EEG variables. The multivariate analysis demonstrated that the I-PSS-QOL score and slow wave sleep time were independent variables in the prediction of good subjective sleep quality, indicating that good sleep is associated with higher QOL in terms of LUTS and longer slow wave sleep (table 2).

### EEG Variables and Subjective/Objective Variables Associated with LUTS

We conducted univariate and multivariate analyses to determine variables associated with sleep efficiency higher than 81.8% and slow wave sleep time longer than 44 minutes (median values), as well as those associated with Q<sub>max</sub> and nocturnal urinary volume for the 8-hour range from 22:00 to 6:00. The multivariate analysis demonstrated that nocturnal urinary volume was an independent variable predictive of higher sleep efficiency (table 3), while Q<sub>max</sub> was an independent variable predictive of longer SWS time (table 4).

## DISCUSSION

This study is the first to our knowledge to demonstrate that subjective sleep quality is associated with LUTS related QOL and slow wave sleep time using a single-channel portable EEG device at home. Previous studies have demonstrated the relationship between subjective sleep quality and objective sleep quality using actigraphy to measure objective parameters of sleep quality.<sup>3,6</sup> While such studies analyzed the length of sleep or wakefulness periods after the initial onset of sleep, they did not report data associated with specific stages of sleep, including SWS. Although actigraphy overestimates sleep time while underestimating wake time,<sup>8</sup> the sensitivity for sleep is high (greater than 0.95) while

**Table 2.** Univariate and multivariate analyses of factors associated with good sleep quality

	Univariate			Multivariate		
	OR	95% CI	p Value	OR	95% CI	p Value
I-PSS:						
Total score	0.825	0.732–0.930	0.0016			
Voiding symptoms	0.793	0.677–0.929	0.0040			
Storage symptoms	0.720	0.560–0.926	0.0105			
QOL	0.414	0.242–0.706	0.0237	0.416	0.223–0.775	0.0058
EEG variables:						
Time in bed	1.01	0.998–1.01	0.168			
Sleep period time	1.01	0.998–1.01	0.186			
Total sleep time	1.01	0.999–1.02	0.0852			
Wake time after sleep onset	0.999	0.988–1.01	0.901			
Sleep efficiency	1.00	0.960–1.05	0.882			
SWS time	1.03	1.01–1.06	0.0181	1.05	1.01–1.09	0.0178

**Table 3.** Univariate and multivariate analyses of factors associated with greater sleep efficiency

	Univariate			Multivariate		
	OR	95% CI	p Value	OR	95% CI	p Value
I-PSS:						
Total score	0.976	0.882–1.08	0.637			
Voiding symptoms	0.960	0.840–1.10	0.545			
Storage symptoms	0.998	0.790–1.26	0.987			
Nocturnal frequency	0.878	0.486–1.59	0.666			
QOL	0.945	0.626–1.43	0.788			
Qmax	0.970	0.889–1.06	0.500			
NUV	0.995	0.992–0.998	0.0034	0.995	0.992–0.998	0.0034

the specificity is low (about 0.3) compared with PSG.<sup>7</sup> Differences in wake time after the initial onset of sleep tend to be larger if the wake time is longer.<sup>7</sup> For example, older people exhibit longer wake times after sleep onset,<sup>12</sup> which should affect the objective evaluation of sleep since most urological patients are elderly. In addition, the accuracy of actigraphy is not reliable for the evaluation of sleep stages. Therefore, an alternative method is preferable.

We analyzed factors associated with good sleep quality based on participant responses to the PSQI. Univariate analyses revealed a relationship between sleep quality and LUTS based on I-PSS and QOL scores, although multivariate analyses indicated a relationship only with QOL scores. This result matches those of previous studies reporting that male LUTS and nocturia in particular are associated with poor sleep quality.<sup>13</sup> Furthermore, transurethral prostate resection improves sleep quality in patients with benign prostatic obstruction and nocturia.<sup>14</sup> With regard to the EEG variables multivariate analyses revealed a relationship between good sleep quality and longer SWS time. SWS was detected by the EEG mainly during the first third (3 to 4 hours) of the night for participants in the present study, consistent with patterns observed in previous studies.<sup>15</sup> SWS is referred to as restorative sleep due to the significant release of

**Table 4.** Univariate and multivariate analyses of factors associated with longer slowwave sleep

	Univariate			Multivariate		
	OR	95% CI	p Value	OR	95% CI	p Value
I-PSS:						
Total score	0.926	0.832–1.03	0.157			
Voiding symptoms	0.895	0.774–1.04	0.137			
Storage symptoms	0.929	0.732–1.18	0.544			
Nocturnal frequency	0.661	0.356–1.23	0.190			
QOL	1.13	0.745–1.71	0.569			
Qmax	1.16	1.03–1.31	0.0124	1.16	1.03–1.31	0.0124
NUV	0.999	0.997–1.00	0.524			

growth hormone during the beginning of NREM sleep,<sup>15</sup> and because disruption of SWS for several consecutive nights is associated with increased discomfort and fatigue.<sup>5</sup> The results of the present study support the adoption of treatment strategies in which HUS are maintained for 3 to 4 hours to improve sleep quality in patients with nocturia.

We then analyzed factors associated with greater sleep efficiency based on EEG data. Although nocturnal urinary volume was associated with sleep efficiency, no such associations were observed for LUTS or  $Q_{max}$ . Indeed, as decreased urinary production results in longer time to fill the bladder and cause urinary sensation, less sleep disruption should occur in patients with lower nocturnal urinary volumes. As the odds ratio for NUV relating to greater sleep efficiency was small, the clinical significance of the results remains suspect and further studies are required. However, this study marks the first report in which the relationship between NUV and sleep efficiency has been assessed using EEG rather than a self-reported questionnaire, and is an important component of objective planning for future studies.

In addition, we analyzed the relationship between micturition factors and SWS. Surprisingly, higher  $Q_{max}$  was associated with longer deep sleep, a result that defies explanation based on our present understanding. Clinically, some patients complain of difficulty with nocturnal voiding as well as insomnia. Yoshimura et al reported that patients who are affected by sleep disturbances due to nocturnal voiding tend to suffer from other LUTS, with the exception of urgency and incontinence.<sup>16</sup> Sympathetic hyperactivity associated with BPH or overactive bladder may result in the development of bladder outlet obstruction, leading to lower  $Q_{max}$ . Similarly, nocturnal hypertension may have also been associated with reduced sleep quality and decreased time spent in deep sleep because NREM sleep is associated with lower sympathetic nerve activity compared with rapid eye movement sleep.<sup>17</sup>

Although it is somewhat apparent that the treatment of nocturnal urinary frequency can improve sleep quality, Helfand et al demonstrated that treatment of daytime LUTS may also improve sleep quality in patients with moderate to severe symptoms (CAMUS trial).<sup>18</sup> Some research has also suggested that daytime LUTS may be associated with underlying sleep disorders. For instance, sympathetic nerve hyperactivity associated with BPH/bladder outlet obstruction may result in the development of LUTS. These underlying mechanisms may contribute directly or indirectly to sleep disorders even if patients do not exhibit symptoms of nocturia. We hypothesize that treatment for

LUTS may reduce sympathetic hyperactivity, thereby reducing nocturnal hypertension in patients with BPH/bladder outlet obstruction. Indeed, the treatment of overactive bladder with imidafenacin has been observed to reduce nocturnal hypertension, while the treatment of BPH with tamsulosin decreases nighttime urine production.<sup>19,20</sup> Failure to treat these underlying physiological disturbances may result in detriments to sleep quality that significantly impact energy levels, mood and quality of life.

This study is limited in that it is merely an exploratory investigation. Prospective studies are required to more adequately examine the relationship among SWS, sleep quality and LUTS. Furthermore, the participants may have belonged to a unique population. They were interested in participating in a community based longitudinal

study and may have been relatively healthy compared to average elderly people. Further investigation of patients affected by nocturia with/without moderate or severe insomnia and LUTS is required. In addition, comparison of patients with LUTS receiving treatment to those who have not yet begun treatment may be a promising direction for future work.

## CONCLUSIONS

In elderly men with nocturia, sleep quality is associated with lower urinary tract function. Higher subjective sleep quality is associated with longer slow wave sleep time and less severe LUTS. Higher objective sleep quality is further associated with a higher urinary flow rate and lower nocturnal urinary volume.

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## EDITORIAL COMMENT

Matsushita et al compared EEG recordings and sleep quality with the severity and bother of lower urinary tract symptoms. The authors document that

decreased sleep quality is associated with shorter deep sleep time and more severe bother from LUTS. It has been previously suggested that shorter deep

sleep may impair memory consolidation and performance on remembering tasks.<sup>1</sup> Thus, this may be another mechanism explaining the relationship among nocturia, LUTS and overall performance in the workplace.<sup>2</sup> Since it has been suggested that treatment of LUTS may improve sleep quality (reference 18 in article), this may provide a rationale for considering more aggressive treatment interventions for patients with concomitant sleep disorders and moderate to

severe LUTS. Certainly this study provides additional evidence to suggest that clinicians should be regularly assessing sleep quality in patients who present with LUTS.

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