

(論文題目)

Sleep Disturbance Has a Higher Impact on General and Mental Quality of Life Reduction than Nocturia: Results from the Community Health Survey in Japan
(睡眠障害は夜間頻尿よりも一般的 Q O L および精神的 Q O L に強く影響を及ぼす)

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Background: Nocturia has been reported to be associated with sleep disturbance.

However, whether nocturia or sleep disturbance has a more negative influence on the quality of life (QOL) of individuals remains unclear.

Objective: To compare the impact of nocturia and sleep disturbance on QOL.

Design, setting, and participants: This was a cross-sectional study including 3992 adults who participated in the Iwaki Health Promotion Project between 2011 and 2015 in Hirosaki, Japan.

Outcome measurements and statistical analysis: Sleep disturbance and nocturia were assessed in all participants using the Pittsburgh Sleep Quality Index (PSQI), international prostate symptom score for men, and overactive bladder symptom score for women. Sleep disturbance was defined as a PSQI score of ≥ 6 . QOL was measured using the Short Form-36 questionnaire. Impacts of nocturia and sleep disturbance on QOL reduction (>30%) were investigated using logistic regression analyses.

Results and limitation: Of the 3992 participants, sleep disturbance was observed in 632(16%). The frequency of nocturia was significantly associated with PSQI scores. Of QOL domains, both sleep disturbance and nocturia were significantly associated with decreases in the physical component summary score (physical QOL).

However, nocturia was not associated with general health (general QOL) and mental component summary (mental QOL) scores. Multivariate logistic regression analysis showed that nocturia was not associated with a >30% reduction in general and mental QOL, whereas sleep disturbance was significantly associated with general, physical, and mental QOL reduction. As this was a cross-sectional study, the causality of nocturia and sleep disturbance could not be assessed.

Conclusions: Nocturia and sleep disturbance affect QOL domains differently. Sleep disturbance has a higher impact on general and mental QOL reduction than nocturia.

Patient summary: We compared the impact of nocturia and sleep disturbance on quality of life (QOL). Nocturia was not associated with general and mental QOL reduction, whereas sleep disturbance was associated with general, physical, and mental QOL reduction.

1. Introduction:

Nocturia (nighttime voiding) is an age-dependent and bothersome urological symptom associated with poor morbidity and quality of life (QOL) [\[1–3\]](#).

Nocturia is increased to approximately 40% in men and women aged ≥ 60 yr [\[2\]](#).

As nocturia is the leading cause of sleep fragmentation, it can also significantly influence sleep disruption and QOL. Several studies have suggested that sleep disturbances affect mental and physical QOL, and depressive status [\[4–6\]](#). Although there is a close relationship between nocturia, sleep disturbance, and decreased QOL, not many studies have evaluated the influence of nocturia and sleep disturbance on comprehensive QOL [\[3,7–10\]](#).

In addition, it remains unclear whether nocturia or sleep disturbance has a worse influence on QOL [\[7\]](#). In this study, we investigated the impact of nocturia and sleep disturbance on QOL in a community-dwelling population using the Short Form-36 (SF-36) questionnaire, Pittsburgh Sleep Quality Index (PSQI), international prostate symptom score (IPSS) in men, and overactive bladder symptom score (OABSS) in women.

2. Patients and methods

2.1. Design and ethics statement

This study was conducted in accordance with the ethical standards of the Declaration of Helsinki. The cross-sectional data collection from the Iwaki Health Promotion Project was approved by the Ethics Committee of Hirosaki University School of Medicine (authorization number, 2014–015). All participants provided written informed consent before participating in the study.

2.2. Data collection and comparison

The 3992 community-dwelling adults were selected from the Iwaki Health Promotion Project, which was a comprehensive study for the clarification of the etiology of lifestyle-related diseases such as hypertension, cardiovascular diseases (CVDs), atherosclerosis, chronic renal failure, type 2 diabetes mellitus (DM), obesity, metabolic syndrome, dementia, and Alzheimer's disease. It was planned to prevent lifestyle-related diseases and promote health to extend the life span of residents of the Hirosaki city (Iwaki district), in the northern part of Japan, in collaboration with the Hirosaki University, Hirosaki City, and Aomori Prefecture general screening center. This project conducted a comprehensive screening of the general health status, including biological and physical examinations [11–15].

The primary endpoint of the present study is to investigate the impact of nocturia and sleep disturbance on QOL by comparing the association between nocturia and QOL reduction, and between PSQI and QOL reduction. The secondary endpoints included the prevalence of nocturia, sleep disturbance, and the association between nocturia and PSQI and between IPSS/OABSS and QOL reduction.

2.3. Lower urinary tract symptoms and sleep quality evaluation

All adults were assessed for lower urinary tract symptoms using IPSS for men and OABSS for women. OABSS (developed by Homma et al [16]) was used to evaluate overactive bladder. OABSS questionnaire can be used to grade day- and nighttime frequency, urgency, and urgency incontinence (Supplementary Table 1). A frequency of nocturia was obtained from IPSS #7 and OABSS #2 questions. The prevalence of lower urinary symptoms was assessed by the severity points for the IPSS (none, 0; mild, 1–7; moderate or severe, 8–35), and the OABSS points (none, 0; mild, 1–5; moderate or severe, 6–15). Sleep quality was assessed using the global and component scores of the Japanese version of PSQI [17]. The PSQI is the most common measure of sleep quality. PSQI contains 19 self-rated questions that assess sleep quality and disturbances in the past 1 mo. The 19 items are combined to form seven “component” scores, each of which has a range of 0–3 points. In all cases, a

score of “0” indicates no difficulty, while a score of “3” indicates severe difficulty. The seven component scores are summed to produce a global score (range 0–21). Higher scores indicate worse sleep quality. Sleep disturbance was defined as a PSQI score of ≥ 6 .

2.4. QOL measurement

QOL was measured using the SF-36 questionnaire, which includes general health, physical, and mental component summary scores (general, physical, and mental QOL, respectively). These scores are standardized to have a mean (standard deviation [SD]) of 50 (10) in the general Japanese population (higher scores indicate better QOL) and to approximate a normal distribution. Based on the first quartile of QOL in SF-36 score, we defined the SF-36 reduction of $>30\%$ as a clinically significant value in the present study.

2.5. Evaluation of variables

Variables analyzed were age, gender, body mass index (BMI), smoking, hypertension, DM, CVD, and the presence of metabolic syndrome. Metabolic syndrome was assessed using the Japanese criteria [18], which included a high waist circumference (≥ 85 and ≥ 90 cm in men and women, respectively) and any two of the following: (1) high blood pressure, (2) impaired glucose, or (3) dyslipidemia.

2.6. Statistical analysis

Statistical analyses of the clinical data were performed using SPSS version 24.0 (SPSS, Inc., Chicago, IL, USA), GraphPad Prism 5.03 (GraphPad Software, San Diego, CA, USA), and R 3.3.2 (The R Foundation for Statistical Computing, Vienna, Austria). Categorical variables were compared using the Fisher's exact or chi-square test. Quantitative variables were expressed as mean SD or median with interquartile range (IQR). Differences between groups were statistically compared using the Student test for a normal distribution and the Mann-Whitney U test for a non-normal distribution. The correlation between two indices was analyzed using Spearman's correlation coefficient. All p values <0.05 were considered statistically significant. The impact of nocturia and sleep disturbance on QOL reduction of >30% was analyzed using univariate logistic regression analyses. Odds ratio (OR) with 95% confidence intervals was calculated. The inverse probability of treatment weighting (IPTW)-adjusted logistic regression analysis was also performed for QOL reductions of >30%. IPTW method reweights both exposed and unexposed groups to emulate a propensity score-matched population [19–27]. Variables included in IPTW models for QOL decline of >30% were age, sex, BMI, smoking, DM, CVD, metabolic syndrome, and PSQI, and those for sleep disturbance were age, sex, BMI, smoking,

DM, CVD, metabolic syndrome, and frequency of nocturia.

3. Results

3.1 Baseline characteristics

Participants' backgrounds are presented in Table 1. Of the 3992 participants, 1529 were men and 2463 were women (mean age, 55 yr). The frequency of nocturia (two or more voids per night) was 27% in men and 22% in women. Severe nocturia (three or more voids per night) was 8.8% in men and 7.0% in women. Median IPSS in men was 5 (IQR: 1–10), and 30% and 7.0% of the patients had moderate and severe symptoms, respectively. Median OABSS in women was 1 (IQR: 0–3), and 7.4% and 0.7% of the patients had moderate and severe symptoms, respectively. Median PSQI score was 3 (IQR, 2–5). Sleep disturbance was observed in 632 (16%) patients.

3.2. Nocturia and sleep disturbance

A higher frequency of nocturia (two or more voids) was observed in individuals aged ≥ 70 yr. The rates of individuals with single nighttime voiding were similar (36–46%) in those aged < 80 yr (Fig. 1A). The prevalence of individuals with PSQI scores of ≥ 6 (15–20%) was not associated with age (Fig. 1B). The rates of individuals with PSQI scores of ≥ 6 were increased according to the increased number of nocturia voids (Fig. 1C). PSQI scores were not significantly different between individuals with zero

to one episode of nocturia and those with two or more episodes ($p = 0.608$), whereas these were significantly higher in individuals with three or more episodes per night than in those with zero to two episodes per night ($p = 0.011$; Fig. 1D).

3.3. Association of nocturia and sleep disturbance with QOL

The prevalence of norm-based scoring in physical, mental, and general QOL is shown in Figure 2A. Physical and general QOL scores in men and women were slightly higher and lower, respectively, than those in the general Japanese population (score 50; Fig. 2A). In men, IPSS had a significant association with general ($p < 0.001$), physical ($p < 0.001$), and mental ($p < 0.001$) QOL (Fig. 2B). In women, OABSS was significantly associated with general ($p < 0.001$) and physical ($p < 0.001$) QOL, but the association was not significant with mental QOL ($p = 0.666$; Fig. 2C). PSQI scores were significantly associated with general ($p < 0.001$), physical ($p < 0.001$), and mental ($p < 0.001$) QOL (Fig. 2D). Frequencies of nocturia were significantly associated with general ($p < 0.001$) and physical ($p < 0.001$) QOL, but the association was not significant with mental QOL ($p = 0.081$; Fig. 2E).

3.4. Uni- and multivariate logistic regression analyses

Univariate analyses for >30% QOL reduction showed that PSQI scores of 16 and two or more episodes of nocturia were significantly associated with general and physical

QOL reduction, but nocturia was not associated with mental QOL reduction (Table 2).

In IPTW-adjusted multivariate analysis, a PSQI score of 16 was significantly associated with general, physical, and mental QOL reduction. Two or more nocturia episodes were not associated with general and mental QOL reduction, but were significantly associated with physical QOL reduction (Table 2 and Fig. 2F).

4. Discussion

Although a negative association between nocturia and QOL has been reported, only few studies have evaluated the impact of nocturia and sleep disturbance on comprehensive QOL using SF-36 [3,7–10]. This is the largest study evaluating the association of nocturia and sleep disturbance with QOL. Our results demonstrated a significant association of nocturia and sleep disturbance with QOL reduction in both men and women. Nocturia was not associated with a >30% reduction in general and mental QOL, whereas sleep disturbance was significantly associated with general, physical, and mental QOL reduction. Previous studies have reported similar results. A cross-sectional survey investigated the impact of nocturia on sleep quality and health-related QOL (SF-36) in 1200 elderly men (age, ≥60yr) in Egypt [7]. Their results suggested that nocturia is an independent risk factor of poor sleep

quality (OR, 5.08). In addition, poor sleep is an independent risk factor of the poor physical and mental component of QOL. However, there was no significant association between nocturia and the mental component of QOL.

Another study investigated the impact of nocturia on sleep quality and health-related QOL (SF-8) in 184 patients with nocturia in Kurume, Japan (mean age, 70.9yr). The study reported that nocturia is an independent risk factor for the poor physical component of QOL, but no association was observed with the mental component of QOL. Therefore, as our results suggest, the impact of nocturia and sleep disturbance on the physical component of QOL was significant, but this was not the case with the mental component of QOL. However, the impact of nocturia on QOL was controversial. A previous population-based epidemiological survey using SF-12 questionnaire in the Boston area (n = 5503; mean ages, 47.6 and 49.2 yr in men and women, respectively) has reported that nocturia is associated with decreased QOL scores for both physical and mental components, particularly in a younger cohort [2]. A Swedish (n = 1948; ages, 20–64 yr) study has also reported that nocturia may lead to sleep insufficiency and consequently to a decrease in mental and physical health [28]. These discrepancies may be related to the age of cohorts because nocturia and/or sleep disturbance may be more bothersome to a younger population than to

an older population. In this study, mean (SD) and median (IQR) ages of participants were 55 (15) and 58 (44–67)yr, respectively. To address this issue, we additionally investigated the impact of sleep disturbance and nocturia on QOL stratified by age between <65 (n = 2765, 69%) and ≥65 (n = 1227, 31%) yr. In the relationship between PSQI score and QOL, magnitudes of slope in general and mental QOL were higher than those of physical QOL in individuals aged <65 yr (Fig. 3A), whereas three components of QOL showed parallel reduction in individuals aged ≥65 yr (Fig. 3B). In the relationship between nocturia and QOL, three components of QOL showed parallel reduction in individuals aged <65yr (Fig. 3C), whereas the magnitude of slope in physical QOL were higher than that of general and mental QOL in those aged ≥ 65 yr (Fig. 3D). The relationship between nocturia and mental QOL in individuals aged ≥65 yr was not significant (p = 0.098). From these results, the impacts of nocturia and sleep disturbance on QOL domains may differ among age groups.

Although a potential impact of nocturia on sleep disturbance and QOL has been suggested, identifying an independent relationship among nocturia, sleep disturbance, and QOL was challenging. We conducted a comparative analysis using IPTW-adjusted logistic regression analyses and found that sleep disturbance (PSQI

score of 16) had a higher impact on general health (OR, 3.74), physical (OR, 2.41), and mental (OR, 5.81) component summary scores of QOL, but no significant impact of nocturia was observed on the general health and mental component scores of QOL (Table 2 and Fig. 2F). These results suggest a higher impact of sleep disturbance than that of nocturia on QOL. However, it is difficult to conclude whether nocturia or sleep disturbance has a more detrimental effect on QOL reduction because of a complex triangular relationship between nocturia, sleep disturbance, and QOL. There is no doubt that nocturia has been proved to have a negative impact on the QOL and sleep quality, as several studies emphasize that nocturia is a major factor in sleep disruption [1,2,28]. From the point of view of sleep disturbance, two different perspectives need to emerge when discussing nocturia [29]. The first is that an individual awakens because of a urinary urgency. The second is that an individual awakens during the night due to sleep disturbance (unrelated to urinary urgency) and then has a desire to urinate. The population-based FINNO study [30], which included a systemic evaluation of factors associated with nocturia, suggested that approximately 75% of nocturia could be attributed to urinary urgency and found that >50% of nocturia could be attributed to a specific sleep disorder. This observation suggests that two components of nocturia (urinary urgency and sleep inability) need

to be analyzed to distinguish between cause and effect. However, we could not address the reason for nocturia in the present study. Further study is necessary to investigate the relationship between nocturia, sleep disturbance, and QOL.

Several limitations need to be acknowledged, including the limited sample in the local area in Japan and the cross-sectional study design. We were unable to control selection bias and other nonmeasurable confounders. Disease duration and treatment history of comorbidities were not considered in this analysis, which may affect the observed associations. Differences in culture and economy strongly influence QOL. Further study is necessary to determine whether our finding can be translated to other similar populations or not. Regardless of these limitations, the strength of this study is inclusion of a large number of community-based individuals with a broad age range. Our results support the importance of the association of nocturia and sleep quality with QOL.

5. Conclusions

This study demonstrated that sleep disturbance may have a greater influence on the general health and mental component summary scores of QOL than nocturia, and both nocturia and sleep quality have a significant impact on the physical component

summary score of QOL.

References:

1. Nakagawa H, Niu K, Hozawa A, et al. Impact of nocturia on bone fracture and mortality in older individuals: a Japanese longitudinal cohort study. *J Urol* 2010;184:1413–8.
2. Kupelian V, Wei JT, O’Leary MP, Norgaard JP, Rosen RC, McKinlay JB. Nocturia and quality of life: results from the Boston area community health survey. *Eur Urol* 2012;61:78–84.
3. Bliwise DL, Rosen RC, Baum N. Impact of nocturia on sleep and quality of life: a brief, selected review for the International Consultation on Incontinence Research Society (ICI-RS) nocturia think tank. *Neurourol Urodyn* 2014;33(Suppl 1):S15–8.
4. Sasai T, Inoue Y, Komada Y, Nomura T, Matsuura M, Matsushima E. Effects of insomnia and sleep medication on health-related quality of life. *Sleep Med* 2010;11:452–7.
5. Aritake S, Asaoka S, Kagimura T, et al. Internet-based survey of factors associated with subjective feeling of insomnia, depression, and low health-related quality of life among Japanese adults with sleep difficulty. *Int J Behav Med* 2015;22:233–8.
6. Marques DR, Meia-Via AMS, da Silva CF, Gomes AA. Associations between sleep quality and domains of quality of life in a non-clinical sample: results from higher

education students. *Sleep Health* 2017;3:348–56.

7. Abdel-Rahman TT, Gaafary EMM. Nocturia among elderly men living in a rural area in Egypt, and its impact on sleep quality and health-related quality of life. *Geriatr Gerontol Int* 2014;14:613–9.

8. Martin SA, Appleton SL, Adams RJ, et al. Nocturia, other lower urinary tract symptoms and sleep dysfunction in a community-dwelling cohort of men. *Urology* 2016;97:219–26.

9. Shao IH, Wu CC, Hsu HS, et al. The effect of nocturia on sleep quality and daytime function in patients with lower urinary tract symptoms: a cross-sectional study. *Clin Interv Aging* 2016;11:879–85.

10. Suekane S, Ueda K, Suyama S, et al. Comprehensive health-related quality of life is influenced by nocturia and sleep disturbance: investigation based on the SF-8. *Kurume Med J* 2016;62:9–16.

11. Oikawa M, Hatakeyama S, Yoneyama T, et al. Significance of serum N-glycan profiling as a diagnostic biomarker in urothelial carcinoma. *Eur Urol Focus* 2016. <http://dx.doi.org/10.1016/j.euf.2016.11.004>, pii: S2405-4569(16)30162-6.

12. Narita T, Hatakeyama S, Yoneyama T, et al. Clinical implications of serum N-glycan profiling as a diagnostic and prognostic biomarker in germ-cell tumors.

Cancer Med 2017;6:739–48.

13. Tanaka T, Hatakeyama S, Yamamoto H, et al. Clinical relevance of aortic calcification in urolithiasis patients. BMC Urol 2017;17:25.

14. Tanaka Y, Hatakeyama S, Tanaka T, et al. The influence of serum uric acid on renal function in patients with calcium or uric acid stone: a population-based analysis. PLoS One 2017;12:e0182136.

15. Soma O, Hatakeyama S, Okamoto T, et al. Clinical implication of a quantitative frailty assessment tool for prognosis in patients with urological cancers. Oncotarget 2018;9:17396–405.

16. Homma Y, Yoshida M, Seki N, et al. Symptom assessment tool for overactive bladder syndrome—overactive bladder symptom score. Urology 2006;68:318–23.

17. Doi Y, Minowa M, Uchiyama M, et al. Psychometric assessment of subjective sleep quality using the Japanese version of the Pittsburgh Sleep Quality Index (PSQI-J) in psychiatric disordered and control subjects. Psychiatry Res 2000;97:165–72.

18. Matsuzawa Y. Metabolic syndrome—definition and diagnostic criteria in Japan. J Atheroscler Thromb 2005;12:301.

19. Austin PC, Stuart EA. Moving towards best practice when using inverse

probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. *Stat Med* 2015;34:3661–79.

20. Hamano I, Hatakeyama S, Iwamura H, et al. Preoperative chronic kidney disease predicts poor oncological outcomes after radical cystectomy in patients with muscle-invasive bladder cancer. *Onco-target* 2017;8:61404–14.

21. Hosogoe S, Hatakeyama S, Kusaka A, et al. Platinum-based neoadjuvant chemotherapy improves oncological outcomes in patients with locally advanced upper tract urothelial carcinoma. *Eur Urol Focus* 2017;231–40.

22. Kubota Y, Hatakeyama S, Tanaka T, et al. Oncological outcomes of neoadjuvant chemotherapy in patients with locally advanced upper tract urothelial carcinoma: a multicenter study. *Oncotarget* 2017;8:101500–0.

23. Kusaka A, Hatakeyama S, Hosogoe S, et al. Detecting asymptomatic recurrence after radical cystectomy contributes to better prognosis in patients with muscle-invasive bladder cancer. *Med Oncol* 2017;34:90.

24. Horiguchi H, Hatakeyama S, Anan G, et al. Detecting asymptomatic recurrence after radical nephroureterectomy contributes to better prognosis in patients with upper urinary tract urothelial carcinoma. *Oncotarget* 2018;9:8746–55.

25. Horiguchi H, Yoneyama T, Hatakeyama S, et al. Impact of bacillus Calmette-

Guerin therapy of upper urinary tract carcinoma in situ: comparison of oncological outcomes with radical nephroureterectomy. *Med Oncol* 2018;35:41.

26. Kido K, Hatakeyama S, Fujita N, et al. Oncologic outcomes for open and laparoscopic radical nephroureterectomy in patients with upper tract urothelial carcinoma. *Int J Clin Oncol* 2018. <http://dx.doi.org/10.1007/s10147-018-1248-9>.

27. Momota M, Hatakeyama S, Tokui N, et al. The impact of preoperative severe renal insufficiency on poor postsurgical oncological prognosis in patients with urothelial carcinoma. *Eur Urol Focus* 2018. <http://dx.doi.org/10.1016/j.euf.2018.03.003>, pii: S2405-4569(18)30081-6.

28. Asplund R, Marnetoft SU, Selander J, Akerstrom B. Nocturia in relation to somatic health, mental health and pain in adult men and women. *BJU Int* 2005;95:816–9.

29. Bliwise DL, Foley DJ, Vitiello MV, Ansari FP, Ancoli-Israel S, Walsh JK. Nocturia and disturbed sleep in the elderly. *Sleep Med* 2009;10:540–8.

30. Tikkinen KA, Auvinen A, Johnson 2nd TM, et al. A systematic evaluation of factors associated with nocturia—the population-based FINNO study. *Am J Epidemiol* 2009;170:361–8.

Table 1 – Background of participants.

Number of participants	3992
Age (yr)	55 ± 15
Sex (male)	1529 (38%)
Body mass index (kg/m ²)	23 ± 3.4
Smoking	1385 (35%)
Comorbidities	
Hypertension	1633 (41%)
Diabetes mellitus	361 (9.0%)
Cardiovascular disease	282 (7.1%)
Metabolic syndrome	500 (13%)
Lower urinary tract symptoms	
Male	
IPSS, median (IQR)	5 (1–10)
Mild symptom (0–7 points)	937 (63%)
Moderate symptom (8–19 points)	441 (30%)
Severe symptom (20–35 points)	103 (7.0%)
Frequency of nocturia, median (IQR)	1 (0–2)
Nocturia (≥2 voids)	407 (27%)
Severe nocturia (≥3 voids)	134 (8.8%)
Female	
OABSS, median (IQR)	1 (0–3)
Patients who had OAB	323 (13%)
Mild symptom (0–5 points)	2211 (92%)
Moderate symptom (6–11 points)	179 (7.4%)
Severe symptom (12–15 points)	16 (0.7%)
Frequency of nocturia, median (IQR)	1 (0–1)
Nocturia (≥2 voids)	544 (22%)
Severe nocturia (≥3 voids)	280 (7.0%)
Sleep disturbance	
PSQI, median (IQR)	3 (2–5)
PSQI (≥6)	632 (16%)

OAB = overactive bladder; OABSS = overactive bladder symptom score; IPSS = international prostate symptom score; IQR = interquartile range; PSQI = Pittsburgh Sleep Quality Index.

Table 1. Of the 3992 participants, 1529 were men and 2463 were women (mean age, 55 yr). The frequency of nocturia (two or more voids per night) was 27% in men and 22% in women. Severe nocturia (three or more voids per night) was 8.8% in men and 7.0% in women. Median IPSS in men was 5 (IQR: 1–10), and 30% and 7.0% of the patients had moderate and severe symptoms, respectively. Median OABSS in women as 1 (IQR: 0–3), and 7.4% and 0.7% of the patients had moderate and severe symptoms, respectively. Median PSQI score was 3 (IQR, 2–5). Sleep disturbance was observed in 632 (16%) patients.

Table 2 – Univariate and IPTW-adjusted multivariate logistic regression analyses for QOL decline >30%.

	Variable	p value	OR	95% CI
Univariate				
Mental QOL	Nocturia (≥ 2)	0.409	0.87	0.63–1.21
	PSQI (≥ 6)	<0.001	6.20	4.68–8.21
Physical QOL	Nocturia (≥ 2)	<0.001	3.65	2.94–4.52
	PSQI (≥ 6)	<0.001	2.43	1.91–3.08
General QOL	Nocturia (≥ 2)	<0.001	1.73	1.33–2.26
	PSQI (≥ 6)	<0.001	3.68	2.82–4.80
IPTW model				
Mental QOL	Nocturia (≥ 2)	0.120	1.42	0.91–2.22
	PSQI (≥ 6)	<0.001	5.81	4.36–7.75
Physical QOL	Nocturia (≥ 2)	0.012	1.37	1.07–1.75
	PSQI (≥ 6)	<0.001	2.41	1.88–3.08
General QOL	Nocturia (≥ 2)	0.116	1.33	0.93–1.89
	PSQI (≥ 6)	<0.001	3.74	2.84–4.91

BMI = body mass index; CI = confidence interval; CVD = cardiovascular disease; DM = diabetes mellitus; general QOL = general health score; IPTW = inverse probability of treatment weighting; mental QOL = mental component summary score; OR = odds ratio; physical QOL = physical component summary score; PSQI = Pittsburgh Sleep Quality Index QOL = quality of life.

Variables included in IPTW models for QOL decline of >30% were age, sex, BMI, smoking, DM, CVD, metabolic syndrome, and PSQI, and those for sleep disturbance were age, sex, BMI, smoking, DM, CVD, metabolic syndrome, and the frequency of nocturia.

Table 2 .Univariate analyses for >30% QOL reduction showed that PSQI scores of !6 and two or more episodes of nocturia were significantly associated with general and physical QOL reduction, but nocturia was not associated with mental QOL reduction (Table 2). In IPTW-adjusted multivariate analysis, a PSQI score of !6 was significantly associated with general, physical, and mental QOL reduction. Two or more nocturia episodes were not associated with general and mental QOL reduction, but were significantly associated with physical QOL reduction.

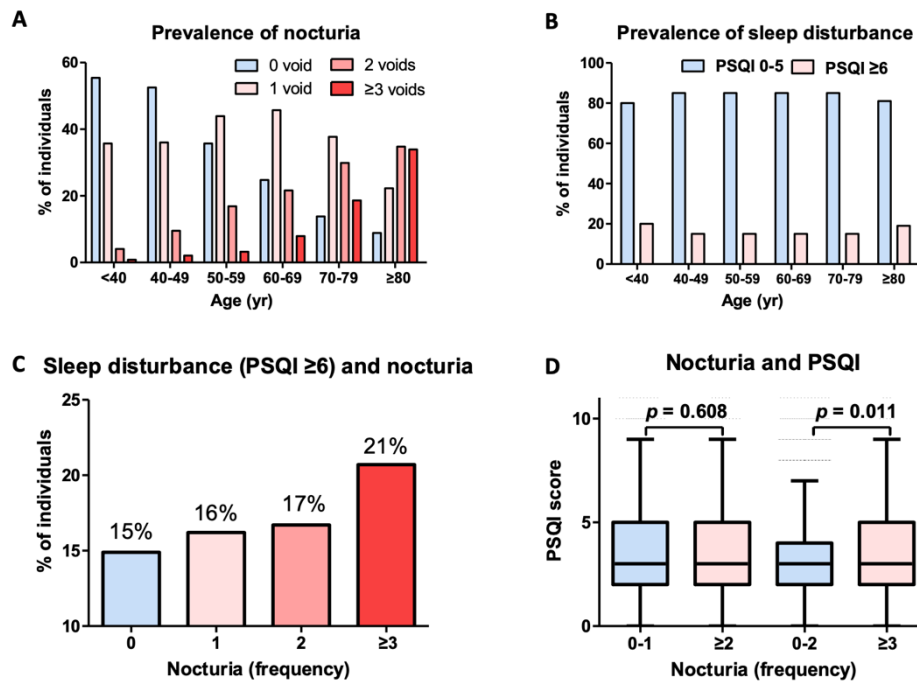


Fig. 1 – Frequency of nocturia and sleep disturbance. Numbers of participants aged <40, 40–49, 50–59, 60–69, 70–79, and ≥80 yr were 765 (19%), 581 (15%), 879 (22%), 1090 (27%), 623 (16%), and 124 (3.1%), respectively. A higher frequency of nocturia (two or more voids) was observed in individuals aged ≥70 yr. (A) The rates of single nighttime voiding were similar (36–46%) among individuals aged <80 yr. (B) The prevalence of individuals with a Pittsburgh Sleep Quality Index (PSQI) score of ≥6 was not associated with age (15–20%). (C) The rates of individuals with sleep disturbance (PSQI ≥ 6) were increased according to the increased number of episodes of nocturia. (D) PSQI scores were not significantly different between individuals with zero to one episode of nocturia and those with two or more episodes ($p = 0.608$), whereas these were significantly higher in individuals with three or more voids than in those with zero to two voids ($p = 0.011$).

Fig. 1 – Frequency of nocturia and sleep disturbance. Numbers of participants aged <40, 40–49, 50–59, 60–69, 70–79, and ≥80 yr were 765 (19%), 581 (15%), 879 (22%), 1090 (27%), 623 (16%), and 124 (3.1%), respectively. A higher frequency of nocturia (two or more voids) was observed in individuals aged ≥70 yr. (A) The rates of single nighttime voiding were similar (36–46%) among individuals aged <80 yr. (B) The prevalence of individuals with a Pittsburgh Sleep Quality Index (PSQI) score of ≥6 was not associated with age (15–20%). (C) The rates of individuals with sleep disturbance (PSQI ≥ 6) were increased according to the increased number of episodes of nocturia. (D) PSQI scores were not significantly different between individuals with zero to one episode of nocturia and those with two or more episodes ($p = 0.608$), whereas these were significantly higher in individuals with three or more voids than in those with zero to two voids ($p = 0.011$).

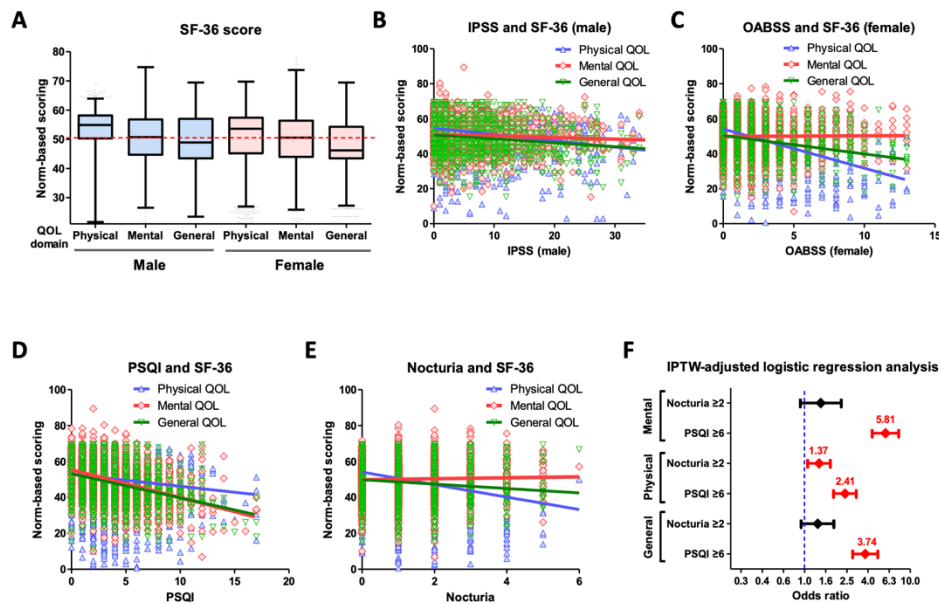


Fig. 2 – Association of nocturia, sleep disturbance, and quality of life (QOL). (A) The prevalence of norm-based scoring in physical, mental, and general QOL in the present study. (B) The international prostate symptom score (IPSS) was significantly associated with general ($p < 0.001$), physical ($p < 0.001$), and mental ($p < 0.001$) QOL in men. (C) In women, overactive bladder symptom score (OABSS) was significantly associated with general ($p < 0.001$) and physical ($p < 0.001$) QOL, but the association was not significant with mental QOL ($p = 0.666$). (D) PSQI scores were significantly associated with general ($p < 0.001$), physical ($p < 0.001$), and mental QOL ($p < 0.001$), but the association was not significant with mental QOL ($p = 0.081$). (E) Frequencies of nocturia were significantly associated with general ($p < 0.001$) and physical QOL ($p < 0.001$), but the association was not significant with mental QOL ($p = 0.081$). (F) In inverse probability of treatment weighting (IPTW)–adjusted multivariate analysis, PSQI scores of ≥ 6 were significantly associated with general, physical, and mental QOL reduction. Two or more episodes of nocturia was not associated with general and mental QOL reduction but were significantly associated with physical QOL reduction. PSQI = Pittsburgh Sleep Quality Index; SF-36 = Short Form-36.

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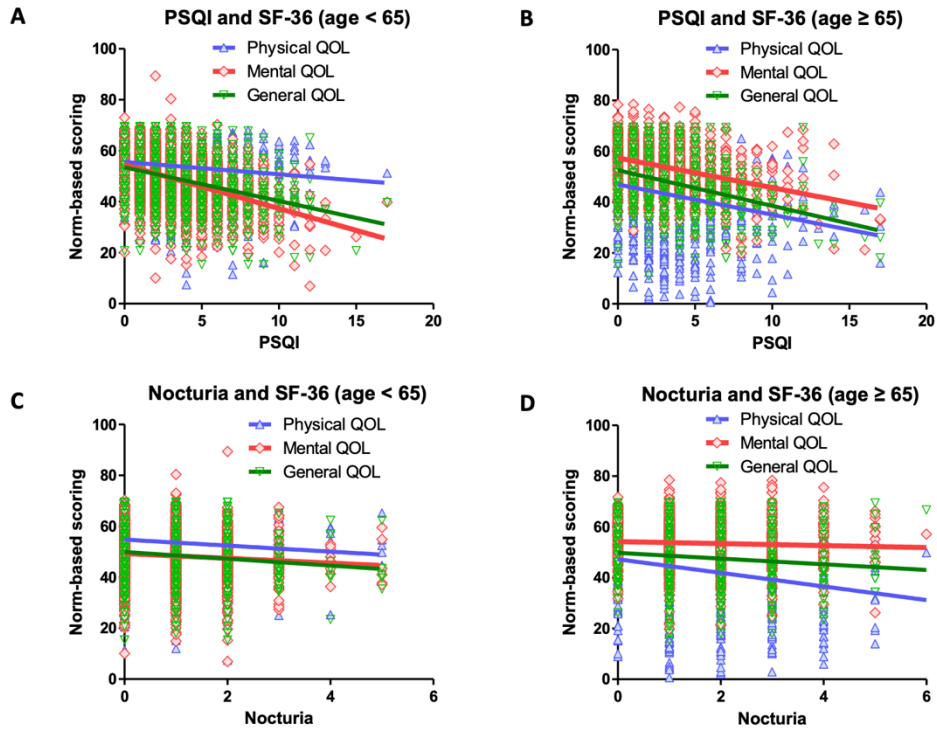


Fig. 3 – Association of nocturia, sleep disturbance, and quality of life (QOL) stratified by age group. The impact of sleep disturbance and nocturia on QOL stratified by age between <65 ($n = 2765$, 69%) and ≥ 65 ($n = 1227$, 31%) yr were investigated. (A) In the relationship between PSQI score and QOL, magnitudes of slopes in general (-1.32 , $p < 0.001$) and mental (-1.72 , $p < 0.001$) QOL were higher than that of physical QOL (-0.48 , $p < 0.001$) in individuals aged <65 yr. (B) Magnitude of slopes in general (-1.40 , $p < 0.001$), mental (-1.17 , $p < 0.001$), and physical (-1.19 , $p < 0.001$) QOL showed parallel decline for PSQI score in individuals aged ≥ 65 yr. (C) Magnitude of slopes in general (-1.34 , $p < 0.001$), mental (-0.94 , $p < 0.001$), and physical (-1.18 , $p < 0.001$) QOL showed parallel decline for nocturia in individuals aged <65 yr, whereas (D) the magnitude of slope in physical QOL reduction (-2.68 , $p < 0.001$) was higher than that of general (-1.12 , $p < 0.001$) and mental (-0.39 , $p = 0.098$) QOL in individuals aged ≥ 65 yr. PSQI = Pittsburgh Sleep Quality Index; SF-36 = Short Form-36.

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