# **Evaluation of Factors Influencing the Natural History of Nocturia in Elderly Subjects: Results of the Fujiwara-kyo Study**

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## Abbreviations and Acronyms

BMI = body mass index Ccr = creatinine clearance I-PSS = International Prostate Symptom Score LUTS = lower urinary tract symptoms OAB = overactive bladder OABSS = OAB Symptom Score

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**Purpose**: We evaluated the natural history of nocturia and determined factors influencing the incidence or remission of nocturia.

**Materials and Methods:** Study subjects were 4,427 volunteers 65 years old or older who participated in the Fujiwara-kyo Study. The nocturia prevalence was assessed at baseline and 1 year later. Nocturia incidence and remission rates were calculated and factors influencing these results were evaluated based on characteristics, including gender, age, body mass index, HbA1c, creatinine clearance, life style, comorbidities, depressive status, metabolic syndrome and voiding symptoms. Independent factors were determined by multivariate analysis.

**Results:** Of the 4,427 subjects 3,685 provided complete replies to self-administered questionnaires at baseline and 1 year later. The prevalence of nocturia at baseline and 1 year later was 47.0% and 50.3%, and nocturia incidence and remission rates were 20.0% and 15.4%, respectively. Male gender, high body mass index, voiding symptom deterioration and new onset overactive bladder were independent factors associated with the nocturia incidence. Male gender, sum of the voiding symptoms, age and new onset overactive bladder were independent negative factors associated with nocturia remission.

**Conclusions:** The prevalence of nocturia worsened with time, although nocturia in older subjects progressed dynamically. Male gender, age, body mass index, sum of voiding symptoms, voiding symptom deterioration and new onset overactive bladder influence the natural history of nocturia.

Key Words: urinary bladder, nocturia, aged, quality of life, questionnaires

NOCTURIA, defined by the International Continence Society as awakening at night to void 1 or more times, is the most prevalent lower urinary tract symptom.<sup>1</sup> The sleep fragmentation and chronic sleep loss attributable to nocturia have a negative impact on quality of life and are associated with increased morbidity and mortality.<sup>2</sup> Fewer than 2 voids each night may cause no major problem, while 2 or more give rise to impaired quality of life due to sleep disturbance.<sup>3</sup> Many case-control studies have evaluated the prevalence of nocturia, and the association of LUTS,<sup>4</sup> obesity,<sup>5</sup> life style<sup>6</sup> and clinical factors<sup>6,7</sup> with nocturia. These cross-sectional studies show differences in the background of subjects with and without nocturia. However, examining the persistence and potential reversibility of nocturia, and factors influencing incidence and remission requires longitudinal studies. Therefore, we evaluated the natural history of nocturia

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and determined factors influencing incidence and remission using data from the longitudinal Fujiwara-kyo community based study.

#### SUBJECTS AND METHODS

#### Subjects

This study was performed as part of the Fujiwara-kyo Study, a community based, longitudinal evaluation that has been done in Nara Prefecture in Japan since 2007. Subjects were 4,427 men and women 65 years old or older who lived at home and could walk independently. All subjects volunteered to participate in the study.

#### **Study Outline**

Baseline data were obtained on all subjects in 2007 to 2008, including physical examination results (weight, height, body fat percent, abdominal circumference and blood pressure), comorbidities, blood tests (blood count, blood chemistry tests and glycohemoglobin) and self-administered questionnaires, including the I-PSS, OABSS, International Physical Activity Questionnaire and Geriatric Depression Scale. One year later a self-administered questionnaire was sent to all subjects, including the I-PSS and OABSS.

#### Nocturia Incidence and Remission

Information on nocturia was collected using I-PSS question 7. Nocturia was defined as 2 or more episodes of nocturnal voiding per night. Nocturia onset was defined as no nocturia at baseline but nocturia 1 year later. Nocturia remission was defined as nocturia at baseline but no nocturia 1 year later. Prevalence at baseline and 1 year was calculated as the number of subjects with nocturia/total number. Incidence was calculated as the number of subjects with new onset nocturia after 1 year/number without nocturia at baseline. The remission rate was calculated as the number of subjects with remission in 1 year/number with nocturia at baseline.

#### **OAB Evaluation**

OAB was diagnosed using the OABSS, which was validated by Homma et al.<sup>8</sup> The change in OAB with time was also evaluated using the OABSS.

#### Voiding Symptoms

Voiding symptoms were evaluated using the I-PSS. I-PSS intermittence, weak stream and straining scores were summed to obtain the final score with a higher score indicating more severe voiding symptoms (score range 0 to 15). Changes in voiding symptoms with time were evaluated using the difference in the sums of voiding symptoms in 2008 and 2009, including a negative value—deterioration, 0—no change and a positive value—improvement.

#### Other Recorded Variables

Depression was evaluated using the Geriatric Depression Scale (score range 0 to 5 with a cutoff of 5/6).<sup>9</sup> Physical activity was evaluated using the International Physical Activity Questionnaire.<sup>10</sup> Metabolic syndrome was assessed using the metabolic syndrome criteria defined by the Japan Society for the Study of Obesity.<sup>11</sup> Subjects were asked about comorbidities (cancer, cerebrovascular disease, myocardial infarction, diabetes mellitus and hypertension), alcohol consumption (never, occasional drinker, 1 or 2 drinks per week, 3 or 4 drinks per week or daily) and smoking status (never, previous or current) on a self-administered questionnaire. Ccr was calculated using the Cockcroft-Gault formula.<sup>12</sup>

### Factors Associated with

#### Nocturia Incidence or Remission

Factors projected to contribute to the incidence or remission of nocturia included gender, voiding symptoms, age, HbA1c, Ccr, BMI, physical activity, alcohol consumption, smoking status, comorbidities (cancer, cerebrovascular disease, myocardial infarction, diabetes mellitus and hypertension), depression and metabolic syndrome at baseline. Changes in voiding symptoms and OAB with time were used as additional factors.

#### **Statistical Analysis**

We examined the difference in characteristics between subjects with or without nocturia onset or remission during 1 year using the Mann-Whitney U and chi-square tests. Logistic regression was used to analyze factors associated with nocturia onset or remission. Variables with p < 0.05 on intergroup comparisons were evaluated in multivariate models. All statistical analyses were performed using SPSS®, version 17.0.

#### RESULTS

#### Subjects

The figure shows the study stages. Of the 4,427 subjects 3,915 (88%) completed the self-administered questionnaire at baseline. Of these subjects 3,685 completed the self-administered questionnaire 1 year later. Average  $\pm$  SD age of the 3,685 subjects was 72.3  $\pm$  5.2 years (range 65 to 93). The male-to-female ratio was 1,869:1,816.





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