



Nocturia and its clinical implications in older women

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ABSTRACT

The aim of this study is to demonstrate the relationship between nocturia and geriatric syndromes, and comprehensive geriatric assessment parameters (CGA) in older women. 858 older outpatient women were included in this cross-sectional study. For the nocturia variable, the question, “Generally, during the past 30 days, how many times did you usually urinate after you have gone to sleep at night until the time you got up in the morning?” was used. The relationships between nocturia status and common geriatric syndromes, and CGA parameters were determined. The mean age of patients was 74.1 ± 8.0 years. The prevalence of patients who reported average of 0, ≥ 1 , ≥ 2 , ≥ 3 , and ≥ 4 nocturnal episodes was 14.7%, 85.3%, 66.3%, 42.13%, and 24.1%, respectively. When all the covariates including age, education, Charlson Comorbidities Index score, glomerular filtration rate, antimuscarinic drugs and alpha-blockers use, diabetes mellitus, chronic obstructive pulmonary disease, and incontinence were adjusted, there were higher rates of insomnia, recurrent falls and higher scores of Timed Up-Go test in older women with ≥ 2 nocturia episodes ($p < 0.05$). There was a significant correlation between ≥ 3 nocturia episodes and lower Instrumental Activities of Daily Living scores and a significant correlation between ≥ 4 nocturnal episodes and frailty and polypharmacy ($p < 0.05$). Nocturia is quite common and associated with insomnia, frailty, polypharmacy, incontinence, falls, lower gait speed, and functionality in older women. Therefore, nocturia is very important for geriatric practice and ≥ 2 nocturia episodes can be a marker of poor health status in older women.

1. Introduction

Nocturia has been identified as the most bothersome and prevalent lower urinary tract complication (Goessaert, Krott, Walle, & Everaert, 2015). It is defined by the International Continence Society (ICS) as the complaint that the individual awakens one or more times to void per night (van Kerrebroeck et al., 2007). However, more recently nocturia has been defined as the complaint of interruption of sleep one or more times because of the need to micturate (An International Urogynecological Association/ICS terminology of female pelvic floor dysfunction), to differentiate from poor sleep induced micturition at night (Bernard T. Haylen et al., 2010; Rogers et al., 2018). Despite this definition, in many studies, nocturia is defined as two or more wakings (Goessaert et al., 2015). Because of the differences in definition, mean

age, gender, and comorbidities of the individuals participating in the studies, reported nocturia prevalence varies widely (Nakagawa et al., 2010). Overall, all studies have shown that few young adults ($< 5\%$) report nocturia, while about half of elderly over 60 years of age report nocturia and about 80% of those older than 80 years are affected (Duffy, Scheuermaier, & Loughlin, 2016). Therefore, advancing age is a primary risk factor for the development of nocturia (Varilla, Samala, Galindo, & Ciocon, 2011). Age-related changes in the urinary system include reduced bladder and functional capacity, reduced maximum urinary flow rate, decreased ability to postpone urination and renal ability to concentrate urine, and increased postvoid residual volume (Varilla et al., 2011). Age-related changes in detrusor muscle activity also lead to overactive bladder; which results in nocturia (Varilla et al., 2011). On the other hand, nocturnal polyuria is another important

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cause of nocturia and may occur due to low levels of antidiuretic hormone at night, which can be attributed to changes in the circadian rhythm in older adults, and to mobilization of fluids in patients with oedema, and autonomic dysfunction (van Doorn & Bosch, 2012). Other biochemical changes, including a decrease in melatonin levels and an increase in plasma natriuretic peptide levels at night, may contribute to nocturia. Another cause of nocturia may be deterioration of brain and spinal cord on micturition in the elderly (Ranson & Saffrey, 2015). Given these age-related changes and the high prevalence of nocturia among older adults, nocturia is often accepted as a natural part of aging.

Although some risk factors for nocturia such as lifestyle, obstructive sleep apnea, hypertension, and medications are common to both sexes, gender differences have also been observed (Varilla et al., 2011). Even though nocturia is traditionally thought to be a male condition that presents as a sign of benign prostatic hyperplasia, prostate cancer, testosterone deficiency or prostatectomy, nocturia in women may develop due to parity, postmenopausal hormonal changes and hysterectomy, and is as frequent as in men (Mobley & Baum, 2014). Moreover, in studies comparing both genders, it was shown that nocturnal risk factors and their relationship with comorbid conditions were different in men and women. For example, nocturia was associated with overactive bladder, diabetes mellitus, and coronary artery disease in women, but not in men (Tikkinen et al., 2009). Because hormonal differences between men and women are important contributors to the development of nocturia; the present study was conducted among only older women (Varilla et al., 2011).

Furthermore, there are many negative outcomes related to nocturia such as sleep disorders, falls, hip fractures, decreased quality of life, depression, death, (Varilla et al., 2011). Nevertheless, to the best of our knowledge, there are no studies on the relationship between geriatric syndromes/comprehensive geriatric assessment parameters and nocturia/nocturia frequency. Thus, the aim of this study is to determine clinical importance of nocturia in geriatric practice.

2. Methods

2.1. Patients

A total of 858 elder outpatient women, who were admitted to a geriatric center between December 2016 and April 2018, were included in this study. The investigation conformed to the Declaration of Helsinki and was approved by the local ethics committee. Informed consent was provided by each participant or a legal guardian before participating in the study.

Patients who have severe illness that may impair general health status, such as acute cerebrovascular event, sepsis, acute renal failure, acute coronary syndrome, and acute respiratory failure; patients under 65 years of age and male; patients who did not agree to undergo the CGA; patients who had active malignancy and a history of urinary tract cancers such as renal, pelvis, and bladder cancer even if they were in complete remission; and patients who had urinary catheters; patients who had lower urinary tract infections symptoms such as fever, lower abdomen discomfort, frequent and painful urination or who had uropathologic condition such as urinary stones were excluded. Patients with moderate and severe dementia were also ruled out because self-reports based on their memory may be unreliable for nocturia questions.

2.2. Patients' characteristics

Patients' age, gender, and education level were recorded. Those with hypertension, ischemic heart disease, congestive heart failure, diabetes mellitus, peripheral arterial disease, chronic obstructive pulmonary disease (COPD), osteoporosis, cerebrovascular disease, or constipation were identified by their or caregivers' self-reports. In

addition, comorbidity status of the patients was evaluated using the Charlson Comorbidity Index (CCI).

2.3. Comprehensive geriatric assessment

All the participants underwent the CGA including Mini-Mental State Examination, Geriatric Depression Scale-15 for neurocognitive evaluation, Basic and Instrumental Activities of Daily Living (BADL and IADL) for functional evaluation, Tinetti Performance-Oriented Assessment of Mobility, and Timed Up and Go Test (TUG) for mobility evaluation, and MNA for nutritional evaluation. If the total MNA score was < 17, it was accepted that there was malnutrition (Vellas et al., 1999).

The drugs, drug groups, and number of drugs that the patients used were recorded. Using five or more drugs was considered polypharmacy (Unutmaz, Soysal, Tuven, & Isik, 2018). Dementia and depression were diagnosed according to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, criteria. Urinary incontinence was defined as involuntary urinary leakage at the last 3 months except for urinary tract infection (Ates Bulut, Soysal, & Isik, 2018; Gajewski et al., 2018). Recurrent falls was considered positive if the patient had fallen at least two times in the previous year except for tripping on a rug and slipping on wet floor (Ku et al., 2013). Pain was evaluated by the individual's response to the questions 'Do you hurt anywhere?' or 'What is stopping you from doing what you want to do?' (Schofield, 2018).

Handgrip test of the dominant hand (mean of 3 measurements) was measured by a Jamar hand dynamometer. Dynapenia was defined as handgrip strength < 20 kg and the diagnosis of sarcopenia was defined according to the criteria of the European Working Group on Sarcopenia in Older People (Ates Bulut et al., 2018). Frailty status was defined based on 5 dimensions of frailty phenotype, including shrinking, exhaustion, low levels of physical activity, weakness, and slowness. People with 0 criteria were considered robust, 1–2 prefrail, and ≥ 3 frail (Fried et al., 2001). All patients were administered the Insomnia Severity Index (ISI), and insomnia was accepted if ISI scores were ≥ 8 (Wong et al., 2017).

2.4. Assessment of nocturia

For the nocturia variable, the question, "Generally, during the past 30 days, how many times do you usually urinate after you have gone to sleep at night until the time you got up in the morning?" was used. The wording of the question shows strong agreement with the (ICS) definition of nocturia (van Kerrebroeck et al., 2007). Response options included choices ranging from 0 to 3, or 4 or more per night.

2.5. Laboratory findings

Laboratory tests performed to assess biochemical, metabolic, and nutritional status of the patients included measurements of complete blood count, kidney and liver functions, cholesterol levels, thyroid stimulating hormone, HbA1c, and levels of vitamin B12, folic acid, and vitamin D. The Glomerular Filtration Rate (GFR) was calculated using Modification of Diet in Renal Disease. All these biochemical tests were performed using the Diagnostic Modular Systems auto analyser (Roche E170 and P-800). Although urinalysis and urine cultures should not be performed for asymptomatic residents, we have also taken urinalysis to investigate the relationship between urinalysis findings and nocturia (Ali & Snape, 2004).

2.6. Statistical analyses

Data were analysed using SPSS, version 22. Descriptive statistics are shown as mean $\pm$ standard deviation for variables with normal distribution, median (minimum to maximum) for non-normal distributions, and number of cases and percentage for nominal variables. When the group number was 2, the significance of differences between the

groups in terms of averages was investigated by t test, and for median values using the Mann-Whitney test. When the number of groups was more than 2, the significance was investigated by analysis of variance and the Kruskal-Wallis test for averages and medians, respectively. Nominal variables were assessed by the Pearson chi-square or Fisher exact test. Variances in more than 2 groups were assessed by post hoc Tukey tests. For the analysis, nocturia was categorized as 1, 2, 3, or 4 or more times per night. Potential correlates included sociodemographic variables (age, education level), comorbidities (CCI, GFR, diabetes mellitus, COPD, and drugs as well as urge incontinence. Logistic regression was used to assess the association between nocturia groups with regard to the number of urinate and CGA parameters. All variables were entered into a comprehensive multivariable model, and odds ratios (OR) and 95% confidence intervals (95% CI) were calculated. For $p < 0.05$, results were considered statistically significant. The sample size needed was calculated to be at least 322 patients with an acceptable error of 5% and a 95% confidence level.

3. Results

The mean age of patients was 74.1 ± 8.2 ($n = 858$). At first, nocturia was categorized as 1, 2, 3, or 4 or more times per night. The prevalence of patients without nocturia was 14.7%. The prevalence of patients who report average of 1, 2, 3, or 4 or more times nocturia episodes was 19.0%, 24.2%, 18.4%, and 24.1%, respectively. The patients' characteristics, comorbidities, and geriatric syndromes, and drug groups are summarized in Table 1. There was a significant difference between groups in terms of age, education, CCI, presence of insomnia, recurrent falls, polypharmacy, frailty, diabetes mellitus, COPD, and urge type incontinence ($p < 0.05$). Only antimuscarinic drugs used for overactive bladder and alpha blockers (eg, doxazosin) were significantly higher in patients with four or more nocturia episodes ($p < 0.05$) (certain drugs that are probably associated with nocturia are shown in Table 1). There was no difference between the groups in terms of urinary and blood laboratory findings with the exception of GFR ($p > 0.05$).

The 5 groups were compared with respect to CGA parameters, and lower scores of MMSE, Tinetti balance and gait test, BADL and IADL scores and hand grip strength; and higher scores of TUG, ISI and Fried frailty scores were detected in patients with 2, 3 and 4 or more nocturia episodes compared to the patients with 0 or 1 nocturia ($p < 0.05$). When groups were adjusted for age, education level, CCI, GFR, diabetes mellitus, COPD, and antimuscarinic drugs and alpha blockers as well as urge incontinence, the significant differences between frailty, insomnia, recurrent falls, polypharmacy, TUG, ISI, Fried frailty scores, IADL scores and nocturia persisted ($p < 0.05$).

Nocturia was also dichotomized into ≥ 1 , ≥ 2 , ≥ 3 , and ≥ 4 nocturia and compared with no nocturia, ≤ 1 , ≤ 2 , and ≤ 3 , respectively. The prevalence of patients with ≥ 1 , ≥ 2 , ≥ 3 and ≥ 4 nocturia was 85.3%, 66.3%, 42.13%, and 24.1%, respectively. The relations between the CGA parameters and nocturia groups were investigated using logistic regression analysis adjusting for all the covariates. Results showed that there was statistically significant relationships between the risk for geriatric syndromes, including recurrent falls, frailty, polypharmacy, incontinence and CGA parameters, including higher number of drugs, Fried frailty and ISI scores, lower TUG, and IADL and dichotomized nocturia groups ($p < 0.05$).

There were significant relationships between ≥ 1 void/night and the presence of insomnia (OR = 2.0, 95% CI: 1.2–3.4, $p = 0.006$), and urinary incontinence (OR = 2.7, 95% CI: 1.7–4.2, $p < 0.001$). There were significant associations between ≥ 2 void/night and recurrent falls (OR = 1.6, 95% CI: 1.0–2.7), insomnia (OR = 2.3, 95% CI: 1.6–3.4), urinary incontinence (OR = 3.1, 95% CI: 2.2–4.4) and significant correlation between ≥ 2 void/night and number of drugs, (OR = 1.1, 95% CI: 1.0–1.2), ISI index scores (OR = 1.6, 95% CI: 1.3–1.8) and TUG (OR = 1.9, 95% CI: 1.1–3.3) ($p < 0.05$). In addition to these

parameters, it was also found that the relationship between ≥ 3 void/night and IADL scores was significant (OR = 0.9, 95% CI: 0.9–1.0, $p = 0.006$). The presence of polypharmacy, frailty and Fried Frailty Score was significantly associated with ≥ 4 void/night (OR = 1.6, 95% CI: 1.0–2.2, $p = 0.048$; OR = 1.4, 95% CI: 1.1–1.7, $p = 0.006$, and OR = 2.1, 95% CI: 1.2–3.7, $p = 0.013$, respectively) (Table 2).

4. Discussion

In this study, it was found that nocturia was common in older women and there was a correlation between some geriatric syndromes and CGA parameters depending on the frequency of nocturia. In older women, ≥ 2 nocturia episodes per night was associated with recurrent falls, polypharmacy, insomnia, decreased TUG score, while ≥ 3 nocturia was found to be associated with decreased Instrumental Activities of Daily Living and ≥ 4 nocturia was related to frailty. Urinary incontinence was the most strongly associated parameter /condition with nocturia.

A recent review of the literature on lower urinary tract symptoms suggests that although nocturia has been described as the most common and bothersome symptom, it has neither been adequately studied, nor considered as important as urinary incontinence (Bosch & Weiss, 2013). In this study, it was shown that more than 85% of older women over 65 years old woke up to void at least once during the night and about 70% at least twice. These results support findings from previous literature, in a review published by Bosh et al., the rate of 1 and more voiding episodes was 68.9%–93%, while 2 and more was 29%–59.3% in older men, whereas in elderly women these rates were 74.1%–77.1% and 28.3%–61.5%, respectively (Bosch & Weiss, 2013). In the majority of studies, nocturia is observed to be very common in the elderly and it is more common in women than men (Wang et al., 2015). However, despite this high prevalence, the importance of nocturia in geriatric practice is not fully known. Therefore, in this study, for the first time, the relationship of nocturia with comorbid diseases, drugs and geriatric syndromes in elderly people was examined in detail.

Nocturia is a multifactorial syndrome. There is a linear relationship between comorbid diseases and nocturia. The prevalence of patients with COPD (likely owing to hypoxia, coughing, and frequent use of anticholinergic drugs) and diabetes mellitus (since high blood glucose has been attempted to be removed from the body through more urine) increases with incidence of nocturia (Ayik, Bal, & Akhan, 2014). In addition, a decrease in the ability of the kidneys to concentrate urine due to age leads to the development of nocturia and in the present study, with decrease in GFR, the frequency of nocturia increased (Varilla et al., 2011). In addition, diminished functional bladder capacity, increased postvoid residual volume, detrusor overactivity and weak pelvic floor are responsible for the development of both nocturia and urge type incontinence in women (Varilla et al., 2011). Therefore, the strong correlation between nocturia and incontinence is not surprising. In women with nocturia, urinary incontinence may be 2.5–3.0 times more frequent. Therefore, these two lower urinary tract symptoms should be evaluated together and both conditions should be considered when evaluating the response to treatment (Cipullo et al., 2014). It should be noted that, in most studies performed on nocturia, urinary incontinence is not evaluated simultaneously, it is thus not clear whether findings are caused by nocturia or urinary incontinence (Lee et al., 2012; Lightner et al., 2012). Therefore, unlike studies carried out to date, the results of the present study were adjusted according to incontinence, thus clinical significance of nocturia in geriatric patients can be observed.

The relationship between nocturia and insomnia is well known. For example, in a study of 1485 people aged 50–93 years, nocturia (67.5%) was found to be the most common cause of deterioration of sleep continuity (Middelkoop, Smilde-van den Doel, Neven, Kamphuisen, & Springer, 1996). However, it is difficult to say whether the nocturia is the cause or the result of the insomnia. In a few studies, the use of

Table 1
Patients Characteristics.

	NOCTURIA GROUP (N = 858)					p value
	0 (126)	1 (163)	2 (208)	3 (154)	≥ 4 (207)	
Age (years)	73.34 ± 8.70	72.48 ± 7.30	74.15 ± 8.14	75.0 ± 8.63	75.50 ± 8.07	0.001
Education (years)	3.5 ± 3.9	4.1 ± 4.2	3.1 ± 3.5	3.1 ± 3.9	2.3 ± 3.2	0.001
CCI	1.24 ± 7.37	0.86 ± 1.45	0.94 ± 1.39	1.38 ± 6.40	1.34 ± 5.18	0.001
COMORBIDITIES (%)						
Cerebrovascular Events	2.	4.3	6.3	2.0	3.0	0.188
Diabetes Mellitus	21.8	33.1	39.5	39.7	40.0	0.005
Ischemic Heart Disease	6.5	8.6	11.2	8.6	12.7	0.360
Congestive heart failure	4.0	6.7	3.4	5.3	5.4	0.653
Hypertension	71.8	68.7	67.3	76.8	70.7	0.374
COPD	3.3	9.5	13.8	23.3	20.0	0.000
Osteoarthritis	19.4	17.2	16.6	19.7	23.6	0.418
Parkinson's disease	0.8	1.2	1.9	1.3	3.9	0.228
Constipation	32.5	43.2	41	43.9	46.1	0.076
DRUG CLASS (%)						
NSAIDs	20.5	20.1	21.1	31.6	27.5	0.075
Antimuscarinics	3.4	3.8	6.3	7.0	12.6	0.001
Thiazide	44.4	51.9	42.7	57.8	48.2	0.055
Amlodipine	13.8	11.3	15.0	16.3	13.1	0.751
Alpha blockers	0.0	0.6	0.0	0.0	1.6	0.03
Furosemide	1.7	5.0	2.0	3.4	4.2	0.362
URINE LABORATORY						
Glycosuria	5.4	6.9	10	6.7	10.2	0.276
Pyuria	31.3	32.2	31	32.4	35.7	0.810
Hematuria	12.9	14.4	13.7	14.3	15.3	0.972
*Urine culture positive (%)	17.2	20.7	10.9	14.3	21.1	0.673
BLOOD LABORATORY VALUES						
GFR	79.85 ± 20.54	79.74 ± 19.44	78.10 ± 19.49	79.52 ± 18.27	76.16 ± 19.39	0.032
GERIATRIC SYNDROMES (%)						
Dementia	2.4	4.9	4.4	3.3	5.9	0.601
Insomnia	57.6	58.1	72.0	84.4	87.3	0.000
Recurrent falls	20.6	23.3	34.6	25.5	38.2	0.001
Depression	40	47.1	41.8	46.2	52.5	0.094
Polypharmacy	28.9	41.4	41.7	44.9	48.9	0.002
Pain	70.6	65.7	70.3	66.5	73.9	0.279
Frailty	30.5	26.3	26.8	37.7	48.6	0.000
Dynapenia	39.6	36.1	41.6	43.3	55.6	0.006
Malnutritionbod	7.1	3.6	2.8	6.2	8.5	0.247
Sarcopenia	18.3	20.2	26.9	29.9	31.9	0.038
Orthostatic Hypotension	24.8	33.8	29.1	36.5	34.6	0.240
Urinary Incontinence						
None	66.5	64.3	48	47.7	29.4	0.000
Urge	21.9	25.4	38.1	33.8	52.8	
Stress	7.1	3.3	5.3	5.9	2.5	
COMPREHENSIVE GERIATRIC ASSESSMENT						
Tinetti Gait	14.02 ± 3.66	14.7 ± 2.42	14.19 ± 3.26	13.95 ± 3.37	13.56 ± 3.59	0.002
Tinetti Balance	10.65 ± 2.88	11.03 ± 2.12	10.76 ± 2.58	10.58 ± 2.81	10.10 ± 3.03	0.001
Tinetti Total	24.53 ± 6.40	25.56 ± 4.34	24.85 ± 5.32	24.49 ± 5.79	23.63 ± 6.19	0.000
TUG	13.78 ± 10.99	12.13 ± 6.64	13.61 ± 8.48	13.52 ± 7.50	15.51 ± 8.62	0.000
Hand Grip strength	21.87 ± 7.87	23.58 ± 7.99	23.22 ± 8.57	23.32 ± 8.57	21.02 ± 8.28	0.003
Basic ADL	89.84 ± 17.2	91.07 ± 15.84	90.42 ± 14.19	93.42 ± 65.33	85.24 ± 14.79	0.000
Instrumental ADL	17.91 ± 6.08	19.30 ± 9.50	18.59 ± 7.74	16.66 ± 6.25	15.95 ± 6.26	0.000
GDS	4.47 ± 4.47	4.97 ± 4.62	4.23 ± 3.78	4.63 ± 4.14	5.32 ± 4.22	0.068
MMSE	24.72 ± 4.86	25.05 ± 4.16	24.95 ± 3.70	24.19 ± 4.41	23.90 ± 4.96	0.028
MNA	23.71 ± 4.39	24.17 ± 3.77	24.29 ± 3.53	24.03 ± 3.95	23.23 ± 4.13	0.059
Fried Score	1.50 ± 1.60	1.43 ± 1.46	1.47 ± 1.47	1.61 ± 1.45	2.15 ± 1.54	0.000
Insomnia Severity Index	10.4 ± 8.01	11.79 ± 8.46	13.57 ± 7.68	14.88 ± 6.99	16.99 ± 7.02	0.000

BADL: Barthel Index of Activities of Daily Living; CCI: Charlson Comorbidity Index; COPD: Chronic Obstructive Pulmonary Disease; GDS: Geriatric Depression Scale; GFR: Glomerular filtration rate; IADL: The Lawton Instrumental Activities of Daily Living Scale; MMSE: Mini-Mental State Examination. MNA: The Mini Nutritional Assessment; NSAIDs: Non-steroidal anti-inflammatory drugs; TSH: Thyroid stimulating hormone; TUG: Timed Up And Go Test. * Definition of a positive culture: Bacteriuria is $\geq 10^5$ colony forming units (CFU)/mL.

antimuscarinic drugs and desmopressin improved sleep time and quality, reducing the nocturia episodes; in other words, the nocturia was shown to be the cause of insomnia (van Kerrebroeck et al., 2007). More nocturnal voids may lead to further sleep disturbance. Similar to present findings, Asplund found that patients with three or more nocturnal episodes (vs. 2 nocturnal) had a greater frequency of sleep

disturbances (Asplund, 2002).

In addition to nocturia-related insomnia, daytime sleepiness, an impaired attention and balance function, and the episode of getting out of bed in the dark in the night and going to the bathroom are potential risk factors for falls in the elderly (Varilla et al., 2011). Therefore, nocturia causes falls in the night and also during the day (Nakagawa

Table 2
Associations Between Comprehensive Geriatric Assessment Parameters and Nocturia Groups.

	≥ 1 void/night		≥ 2 void/night		≥ 3 void/night		≥ 4 void/night	
	OR (%95 CI)	p	OR (%95 CI)	p	OR (%95 CI)	p	OR (%95 CI)	p
Women								
Recurrent falls	—	—	1.6 (1.0-2.7)	0.031	1.6 (1.2-2.3)	0.005	1.5 (1.1-2.1)	0.021
Polypharmacy	—	—	—	—	—	—	1.6 (1.0- 2.2)	0.048
Insomnia	2.0 (1.2-3.4)	0.006	2.3 (1.6- 3.4)	0.000	2.7 (1.8 - 4.1)	0.000	2.5 (1.5 - 4.2)	0.000
Frailty	—	—	—	—	—	—	1.4 (1.1 - 1.7)	0.006
Urinary Incontinence*	2.7 (1.7-4.2)	< 0.001	3.1 (2.2-4.4)	< 0.001	2.6 (1.8-3.5)	< 0.001	2.7 (1.8-4.0)	< 0.001
Number of Drugs	1.2 (1.1-1.4)	0.002	1.1 (1.0-1.2)	0.021	1.1 (1.0-1.2)	0.007	1.1 (1.0-1.2)	0.039
ISI Index Scores	1.5 (1.2-1.7)	< 0.001	1.6 (1.3-1.8)	< 0.001	—	—	—	—
TUG	—	—	1.9 (1.1-3.3)	0.017	2.0 (1.6-2.5)	< 0.001	1.9 (1.5-2.5)	< 0.001
IADL scores	—	—	—	—	0.9 (0.9-1.0)	0.006	—	—
Fried Frailty Score	—	—	—	—	—	—	2.1 (1.2-3.7)	0.013

IADL: The Lawton Instrumental Activities of Daily Living Scale; OR: Odd Ratio; ISI: Insomnia Severity Index; TUG: Timed Up And Go Test.*Adjusted for age, education level, CCI, GFR, diabetes mellitus, COPD, antimuscarinic drugs and alpha blockers. While evaluating ORs of other parameters, it was adjusted for same covariates plus urge incontinence.

et al., 2010). Stewart et al showed that patients who described two or more nocturnal episodes were at increased risk of falling, this risk further increased as the number of nocturnal episodes increased (Stewart, Moore, May, Marks, & Hale, 1992). Asplund found that a nocturnal frequency ≥ 3 was associated with increased risk of hip fracture (Asplund, 2006). In the present study, it was found that in older women and those who reported $\geq 2-4$ nocturia episodes, the risk of falling was higher, which indicates that nocturia may be a risk factor for falling, independent of incontinence.

To date, there is no study showing the relationship between polypharmacy and. In the present study, a 1.6 fold increased risk of ≥ 4 nocturia episodes was observed when polypharmacy was present. This may be owing to increased drug interactions and adverse drug reactions as the number of drugs taken increases (Unutmaz et al., 2018). It may be another reason why some drugs such as antidepressants, antipsychotics, and bronchodilators cause detrusor overactivation as a result of anticholinergic burden (Unutmaz et al., 2018). Therefore, before starting treatment, clinicians assessing nocturia should be cautious when prescribing drugs such as diuretics, calcium channel blockers, as well as polypharmacy per se. On the other hand, since diuretics were taken in the morning or at noon in the present study, no relationship may have been found between nocturia and these specific drugs.

For the first time the present study found a significant correlation between nocturia and frailty, independent of incontinence. It was found that frailty is more common in older women who have four or more voiding episodes a night. Importantly, the relationship between low gait speed and decreases in daily living activities suggests that nocturia can be considered as an indicator of physical frailty and poor health. In frailty, many urinary system changes due to aging may be more severe. For example, in a study that evaluated frailty with the TUG, it was found that overactive bladder syndrome was found to be higher in frail patients, regardless of age (Pratt & Suskind, 2018). In fact, 27% of frail patients fall in the night and more than half of these falls are associated with getting up to void (Pratt & Suskind, 2018). On the other hand, frailty has been shown to cause autonomic nervous system insufficiency through its cardiac effects (Parvaneh et al., 2015). The autonomic nervous system is also responsible for the regulation of bladder relaxation and contraction; therefore, there may be a connection between frailty and nocturia, but further studies are needed to explain this. Numerous nocturnal episodes and increased insomnia may cause patients to participate in fewer daily activities, which decreases their physical function over time. This may be reflected in the geriatric assessment as a decrease in gait speed and deterioration in activities of day living.

Findings from the present study must be interpreted in light of its

limitations. First, this is a cross-sectional study thus the direction of the observed association cannot be established. Second, patients were not asked to complete the three-day frequency volume (FV) charts and nocturnal polyuria, and low nocturnal bladder capacity was not evaluated. Third, night time fluid intake and coffee or alcohol intake were not assessed. Finally, any validation scale, such as overactive bladder symptom score by Blaivas or bladder diary was not used for nocturia evaluation (Blaivas, Panagopoulos, Weiss, & Somaroo, 2007). The present study also has several strengths. First, because the study was performed only in older women, gender-related hormonal and structural factors can be eliminated. Second, urinary incontinence is also evaluated simultaneously and the effect on the parameters is also eliminated.

5. Conclusions

Nocturia is common and associated with insomnia, frailty, polypharmacy, incontinence, falls, lower gait speed, and functionality in older women. Therefore, clinicians should be alerted to older women with 2 and more nocturnal episodes, because, if the number of episodes of nocturia can be reduced or treated (e.g. by avoiding polypharmacy), the risk of falls and insomnia can be reduced. Additionally, ≥ 2 nocturia episodes can be a clinical marker of poor health status, because these patients are more likely to have frailty, polypharmacy, incontinence, and lower functional capacity, which are high risk indicators for a large number of adverse clinical events. As a result, these findings have shown that nocturia assessment is very important for geriatric practice; evaluation of nocturia and nocturia frequency should be a part of comprehensive geriatric assessment.

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