Nocturia and Comprehensive Geriatric Assessment Parameters in Older Men

Geriatrik Erkeklerde Nokturi ve Ayrıntılı Geriatrik Değerlendirme Parametreleri

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Amaç: Bu çalışmanın amacı yaşlı erkeklerde noktüri ile geriatrik sendromlar arasındaki ilişkiyi ve ayrıntılı geriatrik değerlendirme parametreleri (AGD) göstermektir.

Gereç ve Yöntemler: Bu kesitsel çalışmaya AGD uygulanan toplam 397 daha yaşlı ayakta hasta erkek dahil edildi. Noktüri değişkeni için, "Genel olarak, son 30 gün içinde, gece uyuduktan sonra sabah kalkana kadar genellikle kaç kez idrara çıktınız?" sorusu kullanılmıştır.

Bulgular: Hastaların ortalama yaşı 75,6±8,1 idi. Noktüri sıklığı ile ilaç sayısı, Kalk ve Yürü testi, İnsomnia Şiddet Skoru arasında pozitif (p<0,05); Mini Nütrisyon Değerlendirmesi (MNA), Temel Günlük Yaşam Aktiviteleri (TGYA), Tinetti toplam skoru ve el kavrama gücü arasında negatif (p<0,05) korelasyon vardı. 0, ≥1, ≥2, ≥3 ve ≥4 noktürnal epizodlu hastaların prevalansı sırasıyla %11,6, %88,4, %70,5, %47,3 ve %25,4 idi. Noktüri ≥2 olan hastalar, noktürisi 1 olan hastalara kıyasla daha düşük MNA skorlarına ve daha yüksek düşme riski, depresyon ve dinapeni gösterdiler. 2 noktüri epizodlarına göre ≥3 nokturi atakları ile daha yüksek uykusuzluk, depresyon, kırılganlık, dinapeni, daha düşük TGYA ve beslenme durumu oranları vardı (p <0.05).

Sonuç: Nokturi yaygındır ve yaşlı erkeklerde dinapeni, uykusuzluk, kırılganlık, polifarmasi, inkontinans, artmış düşme riski ve depresyon ile ilişkilidir. Bu nedenle nokturi, geriatri pratiği için önemlidir ve ≥3 noktüri atakları, yaşlı erkeklerde kötü sağlık durumunun bir belirteci olarak kullanılabilir.

Anahtar kelimeler: Noktüri, ayrıntılı geriatrik değerlendirme, kas gücü, uykusuzluk

Aim: The aim of this study was to demonstrate the relationship between nocturia and geriatric syndromes, and comprehensive geriatric assessment parameters (CGA) in older men.

Material and Methods: A total of 397 older outpatient men who had undergone CGA 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.

Results: The mean age of patients was 75.6 ± 8.1. There was a significant positive correlation between the frequency of nocturia and number of drugs, Timed-up Go, and Insomnia severity score (p<0.05), while there was a significant negative correlation between Mini Nutritional Assessment, Basic activities of daily living (BADL) and Tinetti total score, and hand grip strength (p<0.05). The prevalence of patients with 0, ≥1, ≥2, ≥3, and ≥4 nocturnal episodes was 11.6%, 88.4%, 70.5%, 47.3% and 25.4%, respectively. Patients with nocturia ≥2 had lower MNA scores and had a higher fall risk, depression, and dynapenia compared to patients with nocturia ≤1. There were higher rates of insomnia, depression, frailty, dynapenia, lower BADL and nutritional status with ≥3 nocturia episodes compared to ≤ 2 nocturia episodes (p<0.05).

Conclusions: Nocturia is common and associated with dynapenia, insomnia, frailty, polypharmacy, incontinence, increased fall risk and depression in older men. Therefore, nocturia is important for geriatric practice and ≥3 nocturia episodes may be used as a marker of poor health status in older men.

Keywords: Nocturia, comprehensive geriatric assessment, muscle strength, insomnia

INTRODUCTION

Nocturia is one of the most common lower urinary tract symptoms in older people [1]. Studies have shown that 69 to 93% of men over 70 years of age have at least one time of urination per night and 29 to 59% have at least twice per night [2]. Although age is the most important risk factor for nocturia, the frequency of nocturia also varies between genders. While it is more common in the female gender in young adults, it is more common in the male gender in older adults [3]. The primary causes of nocturia include reduced bladder capacity, increased fluid intake, increased diuresis, comorbidities [1,2]. Factors such as decreased urinary bladder capacity, detrusor overactivity, reduced ability to delay micturition with increasing age may also explain the increase in the frequency of nocturia in older people [3,4].In men, benign prostatic hyperplasia (BPH), prostate cancer, and low testosterone levels; in women, nocturia frequency due to gender-specific causes such as multiparity, estrogen deficiency may account for some of the variability in the risk of developing nocturia between genders [4,5]. Therefore, nocturia may have different clinical results between gender, not only due to these urological differences but also anthropometric differences, changes in gait patterns, and physical activity levels [6].

However, although nocturia is a major problem affecting older people, the importance of nocturia and its frequency in geriatric practice is not yet known. A recent study that included only older women shed light on this topic and revealed that ≥2 nocturia episodes per night was associated with recurrent falls, polypharmacy, insomnia, decreased walking speed, while ≥3 nocturia was found to be associated with decreased Instrumental Activities of Daily Living and ≥ 4 nocturia was related to frailty [5]. However, there is no such study for older men.

Therefore, the aim of the present study was to evaluate the relationship between the frequency of nocturia and geriatric syndromes and comprehensive geriatric assessment (CGA) parameters, to determine the clinical implications of nocturia in older men.

MATERIAL AND METHODS

Patients

A total of 397 male patients admitted to one geriatrics outpatient clinic in Turkey were included in the study. The investigation was in accordance with the Helsinki Declaration and approved by Kayseri Erciyes University Clinical Research Ethics Committee (18.07.2018 – 2018/376). Informed consent was given by each participant or a legal guardian before participating in the study.

Patients with severe disease likely to severely impair their general health status (with an expected life time <6 months) such as acute cerebrovascular event, sepsis, acute renal failure, acute coronary syndrome and acute respiratory failure; female patients; patients under 65 years; patients who did not accept CGA; patients with active malignancy and a history of urinary tract cancer, such as kidney, pelvis and bladder cancer, even in complete remission; and patients with urinary catheters; patients who had urinary catheters; patients who had lower urinary tract infections symptoms such as fever, lower abdomen discomfort, frequent and painful urination, or uropathology such as urinary stones, were excluded. Moderate (Clinical Dementia Rating Scale 2) and severe dementia (Clinical Dementia Rating Scale 3) patients were also excluded as their self-reports based on memory will likely be unreliable for nocturia questions.

Patients' Characteristics

Age and educational level of the patients were recorded. The use of five or more drugs was regarded as polypharmacy [7,10]. The comorbidity status of the patients was also

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appraised using the Charlson Comorbidity Index.

Comprehensive Geriatric Assessment

CGA was given to all participants, including Mini-Mental Status Examination and Geriatric Depression Scale-15, Basic and Instrumental Activities of Daily Life (BADL and IADL), Mini Nutritional Assessment, and Tinetti Performance Oriented Mobility Assessment and Timed Up and Go test (TUG) for gait and balance function [9]. TUG score ≥13.5 seconds was considered to be at risk of falling [10].

Handgrip test of the dominant hand (mean of 3 measurements) was measured with Jamar hand dynamometer and dynapenia was defined as handgrip strength <27 kg whereas the diagnosis of sarcopenia was identified [11]. Frailty was specified by the size of the 5 frailty phenotypes, including shrinkage, exhaustion, low levels of physical activity, weakness and slowness. Subjects with 0 criteria were considered to be no-frail, 1-2 prefrail and ≥3 frail [9]. Insomnia Severity Index (ISI) was applied to all patients and a ISI scores ≥8 determined insomnia [12]. Urinary incontinence was defined as involuntary leakage in the last 3 months except when urinary tract infection was present [13]. The fall was considered positive if the patient had fallen at least once times in the previous year, with the exception of being attached to a carpet and sliding on the wet floor. Pain was appraised by the patient's response to the following questions: Does any part of your body hurt? 'or 'What prevents you from doing what you want to do?' [5].

Assessment of Nocturia

For the nocturia variable, we asked 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?'' The wording of the question shows strong agreement with the (ICS) definition of nocturia [14]. Response options ranged from 0 to 3 or 4 or more per night [5].

Statistical Analyses

Data were analysed using SPSS, version 22. Descriptive statistics were categorised as mean ± standard deviation. When the number of groups was 2, the significance of differences between the groups with regard to averages was inquired by Mann-Whitney test. When the number of groups was more than 2, significance was inquired by analysis of variance and Kruskal-Wallis test. Nominal variables were appraised by Pearson chi-square or Fisher's exact test. Logistic regression was used to evaluate the relationship between CGA parameters and each nocturia group (≥1, ≥2, ≥3, and ≥4) according to 0 (no nocturia), ≤1, ≤2, and ≤3, respectively. Spearman's correlation was performed to reveal if the severity of nocturia is associated with geriatric parameters or not. Post-hoc analysis was also applied. Results were considered statistically significant for P <0.05. The sample size required was calculated as at least 278 patients with an acceptable 5% and 95% confidence level error.

RESULTS

The mean age of the 397 patients was 75.6 ± 8.1 years. At first, nocturia was categorized 1, 2, 3, or 4 or more times per night. The prevalence of patients without nocturia was 11.6%. The prevalence of patients reporting one, two, three and four or more times of nocturia episodes was 17.9%, 23.2%, 21.9%, and 25.4%, respectively. The patients' characteristics, comorbidities, and geriatric syndromes, and CGA parameters are seen (Table I). There was a remarkable difference between the groups in terms of age, education, presence of hypertension, depression, insomnia and urinary incontinence (p<0.05). Only nonsteroidal anti-inflammatory drugs (NSAID) were considerably higher in patients with three or more episodes of nocturia (p<0.05). There

Table I. Patients characteristics

	NOCTURIA GROUP (n=397)					
	0	**1**	**2**	**3**	**≥ 4**	**p**
Age (years)	74.9±7.2	74.9±8.4	76.2±7.6	73.6±7.4	77.3±8.8	**0.045**
Education (years)	6.7 ±3.8	7.1±4.3	6.0±4.7	5.9 ±4.5	4.4±3.4	**<0.001**
Body Mass Index (kg/m^2)	27.8 ±4.4	28.0±3.9	28.9±4.4	29.8±7.3	29.7±8.8	0.537
CCI	0.8±0.8	1.0±2.0	0.9±1.0	1.0±1.4	1.1±1.0	0.233
Number of Drugs	3.9 ±3.4	4.3±3.5	4.5±3.4	4.2±3.4	5.0±3.2	0.153
COMORBIDITIES (%)						
Cerebrovascular Events	10.9	7.0	7.6	6.9	12.9	0.551
Diabetes Mellitus	34.8	35.2	34.8	36.8	39.6	0.957
Ischemic Heart Disease	15.2	23.9	25.0	23.0	31.7	0.288
Congestive Heart Failure	4.3	11.3	9.8	8.0	8.9	0.764
Hypertension	37.0	59.7	51.1	65.5	58.4	**0.023**
COPD	6.5	5.6	13.0	13.8	12.9	0.349
Chronic Kidney Disease	12.3	14.6	24.3	30.2	45.4	
Osteoarthritis	13.0	12.7	18.5	10.3	12.0	0.566
Parkinson's Disease	8.7	4.2	5.4	8.0	6.9	0.826
Benign Prostatic Hyperplasia	10.9	21.1	30.4	25.3	22.8	0.138
GERIATRIC SYNDROMES (%)						
Dementia	6.7	18.3	8.7	10.6	19.0	0.080
Insomnia	31.8	38.0	34.0	58.7	69.6	**<0.001**
Falls	21.7	23.9	25.3	24.1	34.0	0.410
Depression	20.9	23.0	9.8	18.7	28.2	**0.044**
Polypharmacy	37.8	42.0	45.1	40.0	54.5	0.223
Pain	70.6	65.7	70.3	66.5	73.9	0.279
Frailty	28.6	24.5	19.2	21.3	32.9	0.287
Dynapenia	34.2	38.5	37.6	41.3	47.3	0.599
Malnutrition	10.5	9.2	7.9	5.1	15.2	0.243
Sarcopenia	18.3	20.2	21.9	22.9	24.1	0.388
Orthostatic Hypotension	23.9	33.8	29.1	33.9	34.6	0.440
Urinary Incontinence	19.6	19.7	31.9	33.3	67.3	**<0.001**
COMPREHENSIVE GERIATRIC ASSESSMENT						
Tinetti Gait	13.9±4.4	14.8±2.6	14.6±2.8	14.2±3.1	13.8±4.1	0.068
Tinetti Balance	10.2±3.7	11.0±2.2	11.1±2.4	10.9±2.8	10.4±3.1	0.434
Tinetti Total	24.1±8.0	25.8±4.7	25.9±4.3	25.1±5.6	24.2±6.8	0.096
TUG	10.4±10.8	11.8±11.4	12.2±6.9	12.8±10.9	17.7±9.9	**<0.005**
Hand Grip Strength	28.3±9.6	30.3±9.2	31.7±8.7	29.8±8.7	26.6±9.4	**0.020**
Basic ADL	88.3±21.6	91.5±12.9	93.3±10.8	89.0±16.1	81.7±20.3	**<0.001**
Instrumental ADL	17.09±6.7	18.0±5.7	18.3±5.0	17.9±10.8	15.1±7.1	0.051
GDS	3.8±4.6	3.0±3.9	2.1±2.8	3.1±4.0	3.7±4.2	0.275
MMSE	25.5±4.3	25.2±3.9	25.2±4.4	24.9±4.0	23.6±6.6	0.546
MNA	24.3±4.7	24.8±4.4	25.1±4.3	25.0±3.5	23.2±5.5	0.081
Fried Score	1.5±1.7	1.2±1.4	1.1±1.3	1.2±1.3	1.6±1.7	0.415
Insomnia Severity Index	6.2±7.3	8.7±8.7	7.5±7.2	12.5±8.8	13.9±9.1	**<0.001**

BADL: Barthel Index of Activities of Daily Living; CCI: Charlson Comorbidity Index; COPD: Chronic Obstructive Pulmonary Disease; GDS: Geriatric Depression Scale; ADL: Activities of Daily Living Scale; MMSE: Mini-Mental State Examination. MNA: Mini Nutritional Assessment; TUG: Timed Up And Go Test.

*All the significant values are different between ≥4 nocturia groups and the other groups

was no difference between the groups in terms of urine and blood laboratory findings except GFR (p> 0.05). The 5 groups were compared for CGA parameters and lower BADL scores, lower hand grip strength, and higher TUG and ISI scores were observed in patients with 4 or

more nocturia episodes compared to patients with 0, 1, 2 and 3 episodes (p<0.05). Significant differences persisted when the groups were adjusted for age, educational level, GFR and urinary incontinence (p <0.05).

The prevalence of patients with ≥1, ≥2, ≥3 and ≥4 was 88.4%, 70.5%, 47.3% and 25.4%, respectively. Patients with nocturia ≥2 had a lower MNA scores (OR:1.4, 95% CI: 1.1-1.9, p<0.05) and had a higher fall risk (OR:2.3, 95% CI:1.1-5.4, p<0.05), depression (OR:5.1, 95% CI:1.1-24.6, p<0.05), and dynapenia (OR:1.1, 95% CI:3.1-8.9, p<0.05) compared to patients with nocturia ≤1, even after adjustment for age, educational level, and GFR. Those with nocturia ≥3 had a risk of depression (OR:3.2, 95% CI:1.04-9.9, p<0.05), dynapenia (OR:4.9, 95% CI:1.4-15.6, p<0.05), and frailty (OR:3.8, 95% CI:1.2-12.3), p<0.05), higher ISI scores (OR:1.2, 95% CI:1.1-1.2, p<0.05), and lower MNA scores and BADL scores (OR:1.3, 95% CI:1.0-1.7, p<0.05; OR:0.9, 95% CI:0.8-1.0, p<0.05, respectively), compared to patients with ≤2 nocturia, after adjustment for age, educational level, incontinence and GFR. There are no differences between ≤4 nocturia group and ≤3 nocturia group (p>0.05). Odd Ratios are shown (Table II).

There was a significant positive correlation between the frequency of nocturia and number of drugs, TUG scores, and ISI scores (p<0.05) while there was a significant negative correlation between MNA, BADL and Tinetti total score, and hand grip strength (p<0.05).

DISCUSSION

In this study, nocturia was found to be quite common in older men and there was a relationship between some geriatric syndromes and CGA parameters depending on the frequency of nocturia. Especially in those with nocturia episodes of 3 or more, it has been shown that dependence in basic daily living activities increases with decreased gate speed and decreased hand grip. Moreover, in older men, ≥2 nocturia episodes was associated with polypharmacy, depression, dynapenia, low MNA scores, and high fall risk. Those with ≥3 nocturia was associated with insomnia, dynapenia, frailty, depression, low nutritional status and functionality.

It is well known in both women and men that nocturia and its frequency increases with age. However, previous studies showed that the number of nocturia episodes is more important for possible adverse clinical outcomes than for the presence of nocturia [5]. Moreover, the results are also affected by gender differences. Therefore, this study was carried out only with the participation of older men and was classified according to nocturia status ≥1, ≥2, ≥3, and ≥4. Only a small proportion (11.6%) of participants did not wake up to void at night, 88% had at least one nocturia episode and 70.5% at least two. These results are akin to

Table II. Associations between comprehensive geriatric assessment parameters and nocturia groups

	≥1 void/night (n:351)		≥2 void/night (n:280)		≥3 void/night (n:188)		≥4 void/night (n:101)	
	OR (%95 CI)	p	OR (%95 CI)	p	OR (%95 CI)	p	OR (%95 CI)	p
Polypharmacy	---	---	1.5 (1.1-2.2)	0.027	---	---	---	---
MNA scores	---	---	1.4 (1.1-1.9)	0.008	1.3 (1.0-1.7)	0.026	---	---
ISI score	---	---	---	---	1.2 (1.1 – 1.3)	0.004	---	---
Frailty	---	---	---	---	3.8 (1.2-12.3)	0.025	---	---
High fall risk	---	---	2.3 (1.1-5.4)	0.049	---	---	---	---
Dynapenia	---	---	3.1 (1.1-8.9)	0.034	4.9 (1.4-15.6)	0.04	---	---
Depression	---	---	5.1 (1.1-24.6)	0.042	3.2 (1.04-9.9)	0.043	---	---
Barthel score	---	---			0.9 (0.8-1.0)	0.044	---	---

OR: Odd Ratio; ISI: Insomnia Severity Index; MNA: Mini Nutritional Assessment

*Adjusted for age, educational level, incontinence and GFR.

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previous study findings. In a review published by Bosh et al., the rate of 1 and more voiding was 68.9% -93%, while 2 and more was 29%-59.3% in older men respectively [2,15]. In the present study, the findings that almost one in two people had 3 or more episodes of nocturia and one in four people had nocturia episodes 4 or more times reveals how prevalent and thus clinically important nocturia is for older men. Although there are very few other studies examining the frequency of ≥3 and ≥4 nocturia episodes per night, Endeshaw et al. found that the prevalence of ≥3 nocturia episodes was 22.3% in older men [15]. However, despite this high prevalence, the importance of nocturia in geriatric administration is not fully understood. Therefore, the present study investigated the relationship between nocturia and geriatric syndromes in older men for the first time.

Nocturia, a multifactorial syndrome, was found to be affected by hypertension, decreased GFR level, and the use of nonsteroidal anti-inflammatory drugs only. Hypertension may be associated with nocturia owing to its effects on glomerular filtration and tubular transport [16]. The kidneys cause more urine production in hypertensive patients than those without hypertension, owing to a greater sodium production at night [17]. Although it is known that antihypertensive agents used, especially diuretics, can also cause nocturia, this was not observed in the present study [18]. This may be due to diuretics' application in the morning or midday in the clinical practice where data collection took place. When the relationship between NSAIDs and nocturia development was examined, it was observed that the results of the study are contradictory. However, two major studies in men found that these drugs exacerbate lower urinary tract symptoms, including nocturia [19,20].

Decreased bladder capacity, increased residual volume after voiding, detrusor overactivity, and BPH account for the development of both nocturia and incontinence in older men. For this reason, these two lower urinary tract symptoms should be appraised together and both conditions should be questioned when assessing the response to treatment [1,21]. Another important point here is that, since in most of the studies carried out on nocturia, urinary incontinence is not assessed simultaneously, it is not clear whether the outcomes result from nocturia or urinary incontinence [22,23]. Consequently, unlike the previous studies, the outcomes of this study were adjusted according to incontinence, and the clinical significance of nocturia in geriatric patients was clearly indicated.

Although the relationship between insomnia and nocturia is well known, it is not clear whether it causes nocturia or vice versa. In several studies, the use of antimuscarinic drugs and desmopressin decreased the number of nocturia episodes by increasing sleep time and quality; In other words, nocturia has been shown to be the cause of insomnia [24]. More nocturnal voiding can cause more sleep disturbances. The present study supports Asplund, who reported that patients with three or more nocturnal episodes (vs. 2 nocturnal) experienced more sleep disturbances [18]. Similar to insomnia, the relationship between depression and nocturia is complex, and the cause-effect relationship is difficult to resolve. On the one hand, depression causes negative effects on the perception, development and duration of lower urinary tract symptoms [25]. On the other hand it can cause depressive symptoms due to factors such as nocturia, sleep interruption and decreased work productivity [25]. However, in a 2-year follow-up study of 866 older people without depression initially, it was shown that depression developed more in patients with ≥2 nocturia, as in the present study [26].

For the first time in our study, in older men, ≥2 nocturia episodes were compared with dynapenia and increased risk of falls; ≥3 nocturia was found to be related to frailty and worsening functional capacity (low BADL scores), all of which can be considered as

indicators of physical frailty and poor health [27]. In frailty, many changes in the urinary system due to aging may be more serious. For example, a study evaluating frailty with low gate speed found that overactive bladder was higher in frail patients, regardless of age [28]. Another study found an association between high International Prostate Symptom Score and increased frailty prevalence in community-dwelling older males [29]. However, in patients with numerous nocturnal episodes, increased insomnia and depression may cause patients to participate in lesser daily activities to protect themselves, which decreases their physical function over time. This can be reflected in the geriatric evaluation as a reduction in gait speed and muscle strength. In fact, two large studies have shown that ≥3 nocturia episodes cause increased mortality in older men, proving that nocturia is an indicator of poor health status and indirectly supports our results [29,30].

To the best of our knowledge, there is no other study showing the relation between polypharmacy and nocturia in older men. However, in a similar study of geriatric female patients the risk of polypharmacy was found to be greater in patients with ≥4 nocturia, regardless of the type of medication used, likely owing to increased drug interactions and untoward drug reactions as the number of drugs used by older people increases [7]. This may be another reason why some anticholinergic drugs such as antidepressants, antipsychotics, and bronchodilators are likely to cause detrusor over activation [7]. Therefore, before starting treatment, clinicians evaluating nocturia should also question polypharmacy.

Strengths of the present study include the ability to rule out the influence of gender-related hormonal and structural factors on the observed associations, owing to a focus on older men only. Moreover, urinary incontinence was assessed simultaneously and thus controlling its influence on the investigated parameters. Findings from this study should be interpreted in light of its limitations. First, the present study is of a cross-sectional nature, and thus direction of observed associations cannot be assumed. Second, patients were not asked to complete the three-day frequency volume charts and nocturnal polyuria, and low nocturnal bladder capacity was not evaluated. Third, nighttime fluid intake and coffee or alcohol intake were not evaluated.

CONCLUSION

Nocturia, which is associated with insomnia, frailty, polypharmacy, dynapenia, incontinence, worsening functional capacity and nutritional status, high fall risk, and depression is very common and in older men. Therefore, clinicians may wish to consider these negative health parameters associated with nocturia when assessing older men, especially with those who have 2 or 3 and more nocturnal episodes per night. ≥3 nocturia episodes may be a clinical marker of poor health status, since such patients are more likely to have adverse geriatric results. As the assessment of nocturia in older men is quite significant for geriatric practice, nocturia and the frequency should be part of comprehensive geriatric assessment.

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