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The Association of Nocturia with Incident Falls in an Elderly Community-Dwelling Cohort

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Summary

Objective—To examine the association of nocturia with incident falls in a population-based sample of community-dwelling elderly persons.

Methods—The University of Alabama at Birmingham Study of Aging is a prospective cohort study of 1000 community-dwelling older adults in the USA designed to examine factors associated with impaired mobility. Subjects were recruited from a stratified, random sample of Medicare beneficiaries to include equal numbers of black women, black men, white women and white men. Nocturia was assessed at baseline and falls were assessed at baseline and every six months for a total of 36 months of follow-up.

Results—692 individuals (mean age 74.5±6.2, 48% female, 52% black) did not fall in the 12 months prior to baseline. Of these 692, 214 (30.9%) reported falling at least once during the subsequent three years. In unadjusted analysis, three or more nightly episodes of nocturia was associated with an incident fall (RR=1.27, 95% CI (1.01-1.60)). After multivariable logistic regression, three or more episodes of nocturia was associated with an increased risk of falling (RR=1.28, (1.02-1.59)).

Discussion—In a racially diverse, community-based sample of older men and women who had not fallen in the previous year, nocturia three or more times a night was associated in multivariable analysis with a 28% increased risk of an incident fall within three years. While this study has several advantages over previous reports (longitudinal follow-up, performance-based measures of function, population-based sampling), causality cannot be ascertained. Further research is needed to ascertain the impact of treatments to reduce nocturia as part of a multi-component program to reduce fall risk.

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Author Contributions

All authors contributed to the concept/design, data interpretation, drafting and critical revision of the article, and approval of the final version. Dr. Allman secured funding for the Study of Aging. Dr. Vaughan performed data analysis.

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Keywords

Nocturia; Falls; Aged

Introduction

Falls occur in one-third of persons 65 years of age or older each year [1-2]. Approximately one in ten accidental falls result in an injury such as hip fracture, serious soft tissue injury, or subdural hematoma [3-4]. As a geriatric syndrome, multiple, modifiable risk factors for falls have been identified including gait abnormality, orthostatic hypotension, polypharmacy, impaired vision, cognitive decline, and impaired proprioception. In addition, urgency urinary incontinence has been identified in some studies as a risk factor for falling [1, 5-9]. In one study the authors postulated that nocturia (*waking from sleep at night to void* [10]) could be an important component of the association between urgency urinary incontinence and incident falls [9].

Population-based cross-sectional studies suggest that the prevalence of nocturia at least two times per night increases with age. A study from Finland suggested that the increase in prevalence with age occurs more dramatically in men, while a study from the United States did not find significant gender difference in the increase of nocturia prevalence associated with age [11-12]. These studies have shown that the population-based prevalence of nocturia at least twice per night is between 12% and 14%. With increasing age, the prevalence of nocturia rises: among individuals older than 60, the prevalence of at least two episodes of nocturia is between 25% and 45%.

Nocturia has previously been associated with falls in a retrospective, cross-sectional study of older adults living in a retirement community in Florida [13]. A second retrospective analysis assessed the association of frequent nocturia with hip fractures that occurred in the previous 5-year period among community-dwelling elderly in Sweden [14]. A recent prospective study in men suggested that nocturia could increase the one-year risk of an incident fall [15]. No prospective, population-based cohort studies of community-dwelling elderly have evaluated the association of nocturia with incident falls in a racially diverse group of men and women. This current study examined the association between nocturia and incident falls through a prospective, cohort study design.

Methods

Subjects

The University of Alabama at Birmingham (UAB) Study of Aging includes 1000 individuals 65 years of age and older from five counties in west central Alabama, USA, including three rural counties and two urban counties. The participants were randomly selected from Medicare beneficiary lists stratified by race and gender so that the cohort includes equal numbers of men and women, black and white, and urban and rural residence. Persons unable to understand the recruiter, those residing in nursing homes, or those who were unable to independently coordinate an appointment for the baseline, in-home interview were excluded. Written informed consent was obtained prior to beginning study procedures. All study procedures were approved by the Institutional Review Board at UAB.

The primary purpose of the UAB Study of Aging is to identify risk factors for impaired mobility in aging persons. The study enrolled subjects between 1999 and 2001 and is currently ongoing. A two-hour, in-home assessment was performed at baseline that included a medical history, cognitive screening test, screening for depression, assessment of activities

of daily living, and questions regarding multiple facets of functional status, as well as a basic physical examination and three standardized measures of physical performance (gait speed, standing balance, and the ability to rise from a chair).

Measurements

Falls—Participants were asked to report if they had fallen in the year prior to the baseline assessment using the question, “In the past year, have you fallen?” Incident falls were assessed at each six-month follow-up telephone encounter through the question, “Have you fallen in the last six months?” These questions correspond with assessment recommendations from the American Geriatrics Society guidelines for fall prevention in the elderly [16]. Participants were also queried regarding injuries or medical care that resulted from a fall. Once a fall was recorded during any period, a person was identified as a ‘faller’ in the outcome analysis. Thus, the number of ‘fallers’ reflects the number of individuals who fell at least once during the 36 months of follow-up and not a cumulative number of falls that occurred. Other events surrounding the fall including the timing of the fall were not queried in this data collection period, but have been included in subsequent studies.

Nocturia—Nocturia was assessed using the following question: “How many times do you usually get up at night to urinate?” The wording of the question shows strong agreement with the International Continence Society (ICS) definition of nocturia [10] although the development of the question used in the UAB Study of Aging preceded the ICS standardization of the term. Participants were asked to record an integer value. Nocturia was assessed at the baseline interview only which allowed an evaluation of the relationship between nocturia and falls such that the exposure to nocturia occurred prior to an incident fall.

Covariates—Covariates were selected based on their potential to impact the relationship between nocturia and falls, either as confounders or as significant risk factors for either condition [1, 5, 17-22]. Demographic variables included age, gender, and race. Medical conditions included hypertension, diabetes, a history of heart failure, a history of cerebrovascular disease, obesity, and the presence of orthostatic hypotension. Medical conditions were verified in one of three ways: confirmation of a medication prescribed to treat the condition, a primary care provider note verifying the diagnosis, or hospital discharge records confirming the diagnosis. Height and weight measurements were used to determine body mass index (BMI). A BMI of greater than 30 kg/m² was considered obese [23]. Orthostatic blood pressure measurements were taken at the baseline assessment in a sitting position and after standing for three minutes. Subjects were deemed to have orthostatic hypotension if the systolic blood pressure decreased by at least 20 mmHg or the diastolic blood pressure dropped by at least 10 mmHg after changing position from sitting to standing [24]. Medications included in the analysis were benzodiazepines [25] and diuretics. Diuretic medications included potassium-sparing, loop, and thiazide diuretics [26].

While several measurements of mobility were assessed, the measure utilized in this analysis was timed gait speed which has been closely correlated with increased risk of falling [21]. Participants were asked to walk at their normal pace for 2.7 meters or nine feet. Subjects were timed during two walks, and the faster of the two walks was recorded for analysis. Based on norms from a previous study [27], a gait speed of walking 2.7 meters in more than 3.5 seconds was considered abnormal.

Statistical Analysis

The first 36 months of data collected for each participant were included in this analysis. Because a previous history of falling strongly predicts future falls [28] and many potential

confounding factors could be present within individuals with a previous history of falling that might further impact the relationship of nocturia and falls, a conservative analysis was conducted, in which, only the data from those individuals reporting no falls in the 12 months prior to the baseline assessment would be included.

Initial descriptive analyses included examining the frequencies of the selected predictor variables among both fallers and non-fallers. These included: age, gender, race, nocturia, hypertension, diabetes, history of heart failure, history of cerebrovascular accident, orthostatic hypotension, benzodiazepine use, obesity, diuretic use, and gait speed. Chi square tests were used to test differences in the proportion of fallers and non-fallers with each of the characteristics. In univariable analysis, nocturia was examined as a dichotomous and a continuous variable. However, because examining nocturia as a continuous variable significantly subdivided the selected population, the nocturia variable was dichotomized in multivariable analysis. Three or more episodes of nocturia was chosen because this cut point has been associated previously with moderate or major bother among a population-based cohort [29] and previous studies of the association of nocturia and falls have used a similar frequency of nightly nocturia as a reference point [13-15].

Logistic regression was utilized to test the association of nocturia more than three times per night with the outcome of an incident fall during the 36-months of follow-up. The first model was adjusted for race, gender, age, and length of follow-up. Subsequent modeling utilized backward and forward selection with a significance level of 0.05 to assess possible confounding variables. Possible confounders were also considered significant if the addition of the variable in multivariable analysis led to a greater than ten percent change in the relative risk association between nocturia and falls. In addition, confounders of the causal pathway implicating nocturia as a risk factor leading to an incident fall were considered. Gait speed and diabetes were the only additional variables included in the final analysis. Analyses were performed using SAS 9.1 (SAS Institute, Cary, NC).

Results

Of the 1000 individuals in the UAB Study of Aging cohort, 692 reported no falls in the 12 months prior to the baseline assessment and comprised the population for analysis. Of these individuals, 332 (48%) were female and 358 (52%) reported their race as black. Specifically, the selected cohort included 163 (23.6%) white women, 169 (24.4%) black women, 171 (24.7%) white men, and 189 (27.3%) black men, similar to the entire Study of Aging cohort. The annual fall rate varied between 13.5% and 16.6% during the 36 months of follow-up. In total, two hundred and fourteen (30.9%) individuals fell during the 36 months of follow-up and were considered 'fallers.' Missing data on falls was uncommon at the first 6-month follow-up assessment (5%) and highest at the 36-month follow-up assessment (18%). Response to the nocturia question was present for all but 12 individuals at baseline (92.8%). The mean length of follow-up among the entire cohort was 30 months, with a median of 36 months.

Table 1 presents the baseline characteristics of the fallers and non-fallers: age, divided into four age categories (65-74, 75-79, 80-84, and 85+), gender, race, comorbid medical conditions (hypertension, diabetes mellitus, congestive heart failure, history of cerebrovascular disease, orthostatic hypotension), use of benzodiazepines, diuretic use, obesity, and gait speed. Fallers were more likely than non-fallers to be 85 years or older, female, have a diagnosis of diabetes, to use diuretics, and have an abnormally slow gait speed at the baseline assessment. While benzodiazepines were more likely to be used by fallers, the percentage of persons using benzodiazepines in this cohort was small (53/692, 7.7%). In order to assess for an association between the risk of falling and an increasing

frequency of nocturia compared to those with no nocturia, figure 1 shows the relative risk of falling with nocturia as a continuous variable.

Nocturia that was reported to occur on average three or more times a night was associated with a 1.27, 95% CI (1.01 – 1.60) increase in the risk of an incident fall in univariable analysis (Table 2). After analysis using logistic regression modeling, with adjustment for age, gender, race, and length of follow-up, the effect of nocturia remained essentially unchanged at 1.31, 95% CI (1.05 – 1.64) (Table 2). Diuretic use was not a significant factor in multivariable analysis by forward and backward selection procedures and did not change the relative risk or confidence interval for the association of nocturia and falls. Multivariable analysis including benzodiazepine use led to a less than ten percent change in the relative risk of a fall related to three or more episodes of nocturia (RR 1.23), and widened the 95% confidence interval to include the null value (95% CI 0.98 – 1.54). Adjustment for an abnormally slow gait speed and diabetes, as shown in Model 2 (Table 2) revealed a relative risk of an incident fall associated with three or more episodes of nocturia of 1.28, 95% CI (1.02 – 1.59).

Discussion

In this prospective study of a community-dwelling elderly cohort, nocturia at least three times a night was associated with an approximately 28% increased risk of falling. With adjustment for age, race, gender, diabetes, length of follow-up, and a marker of impaired mobility (abnormally slow gait speed), the effect size did not change significantly. After selecting those without a fall in the year prior to the baseline assessment, the fallers and non-fallers were relatively similar in comorbid disease history, and differed only slightly in the prevalence of diabetes mellitus which may indicate the importance of controlling for a prior history of falls to accurately assess other important risk factors.

The prevalence of nocturia at least two times a night was higher than previous reports [11-12]. This may reflect the advanced age of the cohort. While there was a trend toward an increased risk of falls with increasing frequency of nightly nocturia, the small number of participants in each group likely did not provide adequate sample size to fully assess a 'dose-response' effect.

Stewart et al. first published on the association between nocturia and falls [13]. As a cross-sectional study in a single retirement community, these results may not be generalizable to a more diverse population. In addition, the study was unable to control for measures of function and relied upon recalled falls in the year prior to the assessment. Therefore, it was possible for the outcome variable – *a fall* – to precede the predictor event – *nocturia*. Another retrospective study queried baseline voiding patterns and reported falls from the previous five years in an elderly, community-dwelling cohort in Finland [14]. While the study found an increased odds of hip fracture with both increased nocturnal voided volumes and nocturia at least three times a night, this long of a recall period could introduce significant imprecision.

A recent study by Parsons et al. provides longitudinal data from a large cohort of elderly men associating lower urinary tract symptoms as measured by the American Urologic Association Symptom Inventory [30] with the risk of one-year incident falls in a multivariable-adjusted analysis [15]. When the subscale for frequent nocturia (occurring four or more times per night) was evaluated in adjusted analysis, the risk of an incident fall (1.23 (1.08 – 1.41)) was similar in effect size to the results from the UAB Study of Aging cohort.

The current analysis has several advantages over previous studies. The UAB Study of Aging represents a racially diverse, community-based sample of elderly men and women that have been followed longitudinally. Detection of a significant association between frequent nocturia and incident falls is further strengthened by the relatively conservative statistical analysis plan. By limiting the analysis to those individuals who did not report a fall in the 12 months prior to baseline, which is a major risk factor for falls, the error introduced by this significant confounding variable is greatly reduced. All subjects underwent performance-based measures of function at baseline allowing for control in the adjusted analysis of an assessment of mobility previously associated with increased fall risk. Comorbid medical diagnoses, which were considered as possible confounding variables, were verified through review of medical records or contact with the individual's primary care provider. Follow-up was fairly complete as evidenced by minimal missing data throughout the 36 months of reporting.

This study could be strengthened by including a reassessment of the nocturia variable at another time point as there may have been some variability in the occurrence of nocturia. Those with persistently frequent nocturia might have different risk than those with variable nocturia. The impact of recall bias in reporting the presence of nocturia and other covariates was lessened because of the exclusion of persons reporting falls at baseline, when the exposure status to covariates was obtained, and longitudinal follow-up of all subjects to document incident falls. Limiting the cohort to those without a history of a previous fall, while providing a more robust analysis when considering potential unmeasured confounders, did limit the sample size. The assessment of self-reported falls every six months may be less reliable than other methods of fall assessment, such as fall diaries or more frequent encounters with subjects. One study demonstrated an 84% agreement between 6-month retrospective fall recall and monthly calendars with a sensitivity of 56% and specificity of 95%. However, the authors acknowledged a bias toward under-reporting of falls [31]. In other studies of community-dwelling older adults, approximately 30% fall each year [1-2]. This includes those with a history of falls. In the UAB Study of Aging cohort, 30.8% of the subjects reported a fall in the year prior to the baseline assessment. After elimination of those with a history of falling, 13.5% – 16.6% of the participants reported falling each year. Falls may have been under-reported in this cohort. Despite this limitation, a significant association between frequent nocturia and incident falls was still found.

The variables included in multivariable analysis reflect the possible causal pathway of nocturia leading to an incident fall as well as the most likely known confounders of the association. Diuretic use could lead to more frequent nocturia and has been linked to a slight increased risk of falling based on pooled results (1.08 95% CI 1.02-1.16) [20, 26]. However, this association was not seen in the UAB Study of Aging cohort. Benzodiazepine use has been associated with an increased risk of falling, but has not previously been associated with frequent nocturia [22, 32]. While this analysis sought to assess the association of nocturia and incident falls, no causal relationship can be directly inferred, because information regarding the timing of falls (i.e. night vs. day) or events surrounding the falls was not obtained during this data collection period. Future studies have been planned which will collect more detailed data surrounding fall events.

Previous research on interventions to reduce the risk of falls in older individuals has highlighted the importance of using a multi-component approach, in which several potential contributors can be addressed [33]. The results of our study support the notion that repeatedly arising from bed, perhaps in a sleepy state, to walk to the bathroom in a dark or dimly lit room may be amongst the contributors that should be included in such a multi-component program. Further, it is possible that nocturia could result in daytime falls due to the sleep deprivation that can occur from multiple nighttime awakenings. Frequent nocturia

may be improved with appropriate assessment and treatment [34–36]. Thus, further research is warranted to elucidate the causal mechanisms between nocturia and falls and to test whether interventions to reduce nocturia have potential to reduce fall risk.

Conclusion

Nocturia is independently associated with incident falls in older, community-dwelling men and women without a recent history of falling. Given that nocturia is a potentially modifiable risk factor, it is important to consider interventions to reduce nocturia when designing multi-component programs for fall prevention in older adults.

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What's known: Nocturia has been associated with falls in cross-sectional studies among older persons and in one longitudinal study of elderly men.

What's new: This study shows that nocturia is associated in multivariable analysis with incident falls in a longitudinal study of a racially diverse cohort of elderly men and women using a conservative analysis plan that excluded subjects with a fall reported in the 12 months prior to baseline.

Frequency of Nightly Nocturia (N= participants with this level of frequency, Total N = 680)	Relative Risk	95% Confidence Interval
No nocturia (N=98)	1.00	Reference Group
One episode (N=197)	0.77	(0.58 – 1.00)
Two episodes (N=190)	0.89	(0.69 – 1.16)
Three episodes (N=111)	1.14	(0.85 – 1.53)
Four episodes (N=49)	1.28	(0.88 – 1.86)
Five or more episodes (N=35)	1.21	(0.77 – 1.90)

Figure 1.
Nocturia variable – Relative risk for falling associated with increasing frequency of nocturia compared to those with no nocturia

Table 1

Baseline characteristics of fallers and non-fallers

	Fallers (N=214)		Non-Fallers (N=478)		P-value
	Number	Percent	Number	Percent	
Nocturia 3 times or more	71	33.8	124	26.4	0.048
Age 65-74	99	46.3	284	59.4	0.003
Age 75-79	57	26.6	106	22.1	
Age 80-84	29	13.6	54	11.3	
Age 85+	29	13.6	34	7.1	
Race – Black	103	48.1	255	53.3	0.2
White	111	51.9	223	46.7	
Gender – Female	124	57.9	208	43.5	<0.001
Male	90	42.1	270	56.5	
Hypertension	157	73.3	327	68.4	0.19
Diabetes	58	27.1	97	20.3	0.047
Heart failure	29	13.6	79	16.5	0.24
Stroke	23	10.7	44	9.2	0.53
Orthostatic Hypotension	9	4.2	24	5.0	0.64
Benzodiazepine use	27	12.6	26	5.4	0.001
Obesity	73	34.1	136	28.5	0.13
Diuretic use	96	44.9	175	36.6	0.04
Gait Speed (abnormal)	188	87.9	367	76.8	0.001

Table 2
Association of nocturia three or more times nightly with an incident fall in 36 months of follow-up among community-dwelling elderly with no history of falls at baseline

	Unadjusted		Multivariable Adjusted Model 1 *		Multivariable Adjusted Model 2 †	
	RR	95% CI	RR	95% CI	RR	95% CI
Nocturia ≥ 3 times nightly	1.27	(1.01 – 1.60)	1.31	(1.05 – 1.64)	1.28	(1.02 – 1.59)

* Adjusted for age (continuous variable), gender, race, and length of follow-up

† Adjusted for all previous factors, gait speed (abnormally slow vs. normal), and diabetes