Nocturia Associated With Depressive Symptoms

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OBJECTIVES To assess the relationship between nocturia and depression, two inflammatory conditions that affect a significant number of men worldwide.

METHODS We asked 547 male patients to self-administer the American Urological Association Symptom Score (AUA-SS) and the Geriatric Depression Scale (GDS), a validated screening tool for depression. Univariate analysis identified significant differences in patient characteristics between depressed and nondepressed patients, and binary logistic regression was used to assess the potential relationship between nocturia and depression while controlling for patient demographics and quality of life.

RESULTS Of the cohort, 17.0% screened positive for depression. Depressed and nondepressed patients reported a mean (SD) of 2.7 (1.4) and 1.9 (1.4) episodes of nocturia per night, respectively ($P < .001$). After controlling for demographic variables and overall quality of life, patients with 5 or more episodes of nocturia per night experienced a 6.5-fold increased risk of depression compared with patients without nocturia (OR, 6.530; 95% CI, 2.107-20.239, $P < .001$).

CONCLUSIONS A significant correlation exists between nocturia and depression. Consequently, clinicians might use nocturia as a predictor of depression. Patients with increased frequency of nocturia may be considered for referral for further mental health evaluation. UROLOGY 77: 183–186, 2011. © 2010 Elsevier Inc.

Nocturia is perhaps the most widely reported symptom associated with benign prostatic hyperplasia (BPH).[1] Along with other lower urinary tract symptoms, nocturia significantly increases anxiety and diminishes quality of life (QoL).[1-7] In fact, some data suggest that these symptoms affect QoL more than gout, hypertension, angina, and diabetes.[6,7] However, recent data suggest a significant relationship between nocturia and depressive symptoms.[2,5] Therefore, rapid screening of depression could prove useful in the urology clinic.

Although numerous screening tools for depression exist, such as the Geriatric Depression Scale (GDS), these tools tend to require several minutes to administer, which may prolong clinical visits and lead to patient frustration associated with filling out multiple forms.[8] Currently, the most widely accepted clinical tool in the diagnosis of nocturia is the American Urological Association Symptom Index (AUA-SI).[9] Both the European Association of Urology (EAU) and the American Urological Association (AUA) consider the AUA-SI integral to the assessment of BPH.[10,11] Although it has a QoL question, it remains unknown whether the nocturia question of the AUA-SI predicts depressive symptoms. Therefore, we conducted this study to assess the ability of the AUA-SI's nocturia question to predict depression. We hypothesized that patients with higher nocturia scores will also be at greater risk for depression.

MATERIAL AND METHODS

Study Setting and Population

This cross-sectional study enrolled 547 consecutive male patients presenting to the urology clinics of Grady Memorial Hospital and Emory University Hospital. Grady Memorial Hospital is a tertiary care facility serving the needs of a primarily underprivileged urban patient population, and Emory University's Urology Department is a tertiary care clinic. Exclusion criteria consisted of age <40 years and an inability to speak English. After complete description of the study to the subjects, written informed consent was obtained. The study received Institutional Review Board approval.

Data Collection Procedures

This protocol was used from previously published protocols.[12] Participants were first asked a series of demographics questions.

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Table 1. Characteristics of the study population: Univariate analysis

Patient Characteristics	Depressed Patients (n = 93)	Nondepressed Patients (n = 454)	Univariate Analysis *P* Value
Average age, years (SD)	55.1 (12.4)	58.3 (15.6)	.067
Average years of school completed (SD)	13.0 (2.4)	13.9 (3.5)	.013
Average monthly income, US$ (SD)	1231 (2285)	3820 (6668)	.002
Race n (%)			
White	24 (25.8%)	217 (47.8%)	<.001
Black/African-American	60 (64.5%)	208 (45.8%)	.001
Other	9 (9.7%)	29 (6.4%)	.720
Hispanic n (%)	5 (5.4%)	20 (4.4%)	.684
Self-reported AUA-SS, mean total (SD)	17.5 (10.1)	10.8 (8.0)	<.001
Self-reported nocturia score, mean (SD)	2.7 (1.4)	1.9 (1.4)	<.001
Self-reported QOL, mean score (SD)	4.0 (1.9)	2.5 (1.8)	<.001

Participants were then asked to self-administer the AUA-SI, which assesses the symptoms commonly associated with BPH: incomplete emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia. Except for nocturia, the AUA-SI assesses the frequency with which patients experience symptoms associated with urinating on a scale from "Not at all" to "Almost always." For nocturia, the scale corresponds to the number of times a patient urinates per night. The answers to the 7 symptom questions are totalled to determine the severity of the patient's urinary symptoms: 0-7 = mild; 8-19 = moderate; 20-35 = severe.[13]

Participants were finally asked to complete the short version of the GDS. In response to the high prevalence and difficulty in diagnosing depression in the elderly, Yesavage et al. designed the GDS to be a rapid, reliable screening tool for geriatric depression.[8] The short version of the GDS consists of 15 "Yes/No" questions—with a score of >10 indicating depression and a score of >5 strongly suggesting depression—and has been widely validated through multiple studies among different cohorts of patients, including younger patients.[14-16]

Statistical Analysis

Patients were initially grouped into 3 categories based on GDS score: score ≤5, score >5, and score >10. However, subsequent analysis revealed no significant difference in the latter 2 groups of patients, so these patient groups were combined, resulting in 2 final groups of patients: nondepressed patients (GDS ≤5) and depressed patients (GDS >5). Descriptive analyses and frequencies were conducted to assess patient demographics. Univariate analyses were performed to identify variables significantly associated with one year of depression. Chi-square analysis was used for categorical variables and one-way analysis of variance for continuous variables. Variables in univariate analysis with $P \leq .100$ were included in multivariate analysis. Finally, binary logistic regression analysis with forward stepwise regression was conducted to assess the relationship between depression and nocturia symptom severity while controlling for patient age (as a continuous variable), education level, race, ethnicity, homeless status, native language, employment status, QoL score, and overall AUA-SI score. Statistical significance in this study was set at $P < .05$. Models were examined for interaction and co-linearity. All analyses were conducted using SPSS version 15.0 (SPSS, Inc., Chicago, IL).

RESULTS

Patient Characteristics

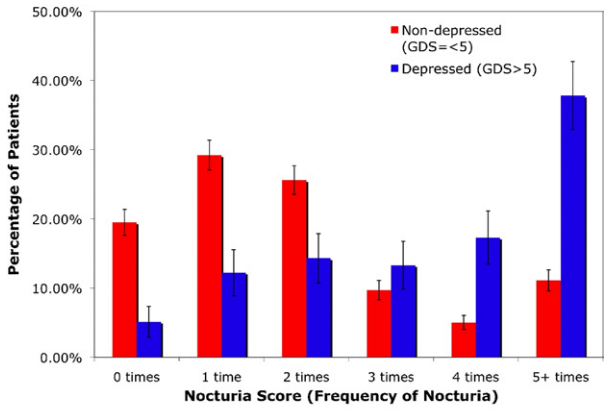
The 547 study participants reported a mean age (SD) of 58.1 years (15.1) and a mean education level (SD) of 13.8 years (3.4) (Table 1); 49% were "Black/African American," 44% were "White/Caucasian," and 7% were "Other." Approximately 90% reported English as their primary language, 43% were employed, and 7% were currently homeless. Of the entire cohort, 17% of patients screened positive for depression (GDS >5). Compared with nondepressed (GDS ≤5) patients, depressed (GDS >5) patients tended to have less education ($P = .013$), lower monthly income ($P = .002$), be African American ($P < .001$), self-report higher overall AUA-SI scores ($P < .001$), and report poorer QoL scores ($P < .001$).

Nocturia Symptom Severity by Depression Status

In addition to these differences, depressed patients (mean ± SD = 2.7 ± 1.4) self-reported significantly higher nocturia scores compared with nondepressed patients (mean ± SD = 1.9 ± 1.4) ($P < .001$) (Table 1). Depressed and nondepressed patients also exhibited significant differences in distribution of nocturia severity (P for trend <.001) (Figure 1A). The majority of nondepressed patients had 0-1 occurrence of nocturia, whereas most depressed patients had 4 or more episodes of nocturia. Differences in nocturia scores for depressed and nondepressed patients are significant ($P < .05$) for each response except "3 times" ($P = .300$). Represented differently, most patients with ≥4 episodes of nocturia had associated depressive symptoms, whereas a minority of patients with ≤1 occurrences of nocturia per night had no associated depressive symptoms (Figure 1B).

Binary Logistic Regression Analysis of Predictors of Depression

Significant univariate predictors of depression were included in binary logistic regression analysis with forward step-wise regression (Table 2). On multivariate analysis, only employment, nocturia, and QoL remained statistically significant after adjusting for age, education level, income, race, and overall AUA-SI score. Compared with patients without episodes of nocturia, patients with ≥5



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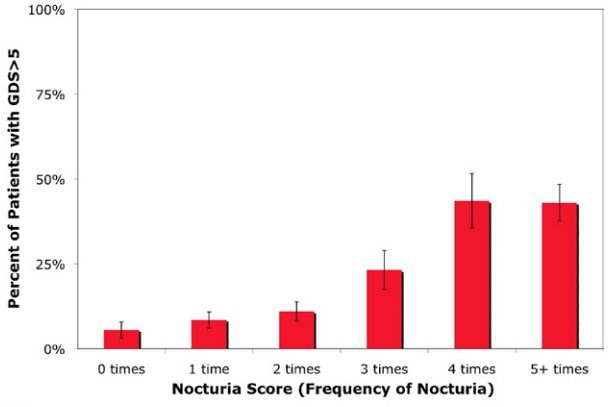

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Figure 1. (A) Distribution of nocturia frequency (episodes per night) by depression status. Differences in nocturia scores for depressed and nondepressed patients are significant ($P < .05$) for each response except "3 times" ($P = .300$). **(B)** Percentage of patients with GDS >5 by nocturia frequency (episodes per night).

episodes of nocturia had a 6.5-fold increased risk of depression (OR, 6.530; 95% CI, 2.107-20.239; $P < .001$).

COMMENT

Both nocturia and depressive symptoms affect a significant number of men worldwide.[2,5] Some studies suggest an association between these 2 disease states.[2,5] In these studies, depressed men had a 6.5-fold increased risk of nocturia.[5] Rapid screening of depression could prove useful in the urology clinic. Therefore, we conducted this investigation into the potential value of the AUA-SI's nocturia question in the screening of depressive symptoms among patients with nocturia.

Our findings suggest a strong association between the nocturia question, the seventh question of the AUA-SI and depressive symptoms. In particular, patients who report ≥5 episodes of nocturia have a 6.5-fold increased risk of depressive symptoms compared with patients without nocturia episodes (OR, 6.530; 95% CI, 2.107-20.239; $P < .001$) (Table 2). In fact, every increase in the number of nocturia episodes appears to increase the risk of depression (Figure 1).

The only investigation into the potential relationship before this study was conducted by Asplund et al. in 2004.[5] This study found an association between depression and nocturia. Unlike the previous study, our study involved an all-male population, our cohort was on average a decade older, and our methodology used the exact wording of the nocturia question from the AUA-SI. Consequently, this study adds support to the role of the nocturia question of the AUA-SI as a screening tool for depression.

Despite these differences, the findings of this study largely support the findings of Asplund et al.[5] Both studies suggest a direct relationship between episodes of nocturia and risk of depression. Moreover, both studies reveal that depression appears at the level of 2-3, or more, episodes of nocturia per night (Figure 1). Asplund et al. suggest that depression could increase the frequency of nocturia.[5] Specifically, depressed patients have higher overall levels of antidiuretic hormone (ADH), but lack the normal nocturnal elevation in the hormone. Subsequent loss of diurnal ADH may contribute to nocturia.[5,17] In addition, altered concentrations of monoamines could cause both depression and overactive bladder.[18] However, nocturia symptoms could by themselves cause depression. Several studies suggest that other causes of sleep disturbances, such as insomnia, can trigger depressive episodes.[19-23] Perhaps nocturia disrupts sleep, and this sleep disruption causes the associated depression.

Regardless of the mechanism, these findings offer significant implications for the clinical management and treatment of nocturia. Nocturia's negative impact on QoL remains undisputed.[2-5] The referral of patients with depressive symptoms for psychiatric evaluation may benefit patients.

Study Limitations

This study relied on a standard, validated screening tool for depression. However, we did not use in-depth psychiatric analysis. Consequently, further studies are needed to confirm these findings. In these studies, larger sample sizes might ensure narrower confidence intervals. In addition, we did not assess psychiatric medication usage. Specifically, patient compliance with BPH medications secondary to depressive symptoms could explain the relationship between nocturia and depression. In addition, the selection of our cohort could have introduced selection bias. Moreover, we did not control for comorbid conditions such as heart disease or diabetes. Finally, we did not assess the efficacy in treating depression among nocturia patients. Future studies are needed to assess the value in treating depression among this patient population.

CONCLUSIONS

Emerging evidence suggests a significant association between nocturia and depression. In this study, we demonstrated that depressed patients report significantly higher

Table 2. Binary logistic regression of depression (GDS > 5)

	Crude		Adjusted	
Variable	OR (95% CI)	*P* Value	OR (95% CI)*	*P* Value
Employment				
Employed	1		1	
Unemployed	3.004 (1.786-5.051)	<.001	2.529 (1.401-4.565)	.002
Nocturia score				
0—None	1		1	
1—One Time	1.600 (0.544-4.704)	.393	1.247 (0.399-3.892)	.704
2—Two times	2.131 (0.739-6.144)	.161	1.752 (0.567-5.409)	.330
3—Three times	7.600 (2.657-21.739)	<.001	4.469 (1.401-14.253)	.011
4—Four times	8.600 (2.706-27.329)	<.001	5.039 (1.405-18.074)	.013
5—Five times or More	12.988 (4.789-35.219)	<.001	6.530 (2.107-20.239)	<.001
Self-reported QOL				
0—Delighted	1		1	
1—Pleased	1.689 (0.418-6.822)	.462	1.047 (0.277-3.957)	.946
2—Mostly satisfied	3.395 (0.938-12.285)	.062	1.221 (0.351-4.248)	.753
3—Mixed	2.066 (0.523-8.152)	.300	0.802 (0.213-3.021)	.744
4—Mostly dissatisfied	4.167 (1.080-16.068)	.038	1.694 (0.455-6.307)	.432
5—Unhappy	5.042 (1.320-19.254)	.018	2.399 (0.657-8.750)	.185
6—Terrible	21.154 (5.910-75.718)	<.001	5.861 (1.660-20.689)	.006

* Adjusted for age, education, income, race, and self-reported AUA-SS score.

and more severe scores on the nocturia question of the AUA-SI score. These findings extend the utility of the AUA-SI beyond the diagnosis and management of nocturia to the screening of depressive symptoms, which could facilitate augmentation of current treatment to included treatment of depression. Further research is needed to confirm the relationship between nocturia and depression and to assess the efficacy of auxiliary depression treatment in nocturia patients.

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