Major Depression Drives Severity of American Urological Association Symptom Index

Timothy V. Johnson, Ammara Abbasi, Samantha S. Ehrlich, Renee S. Kleris, Siri L. Chirumamilla, Evan D. Schoenberg, Ashli Owen-Smith, Charles L. Raison, and Viraj A. Master

OBJECTIVES To evaluate the unclear relationship between depression and benign prostatic hyperplasia (BPH) by assessing depression's effect on the American Urological Association Symptom Index (AUA-SI) scores. Depression is a common illness associated with chronic inflammatory disease states. Data have suggested a significant role of inflammation in the progression of BPH.

METHODS The present prospective study involved 547 male patients who completed the Geriatric Depression Scale and the AUA-SI. We evaluated whether the mean AUA-SI score and the severity categories differed by the state of depression. We then conducted binary logistic regression analysis with forward stepwise regression to assess the relationship between depression and the severity symptoms as determined by the AUA-SI score.

RESULTS Of the cohort, 22% screened positive for depressive symptoms. The depressed patients (Geriatric Depression Scale score >5) reported significantly more severe symptoms (mean AUA-SI score 16.61 ± 9.89) compared with the nondepressed patients (Geriatric Depression Scale score of ≤5 and mean AUA-SI score 10.65 ± 7.29; F = 40.19, $P < .001$). After controlling for socioeconomic and demographic variables, depressed patients were 3 times more likely to present with severe symptoms (odds ratio 3.079, 95% confidence interval 1.129-8.402, $P = .028$).

CONCLUSIONS A significant association was found between depression and BPH. However, it remains unclear whether this relationship represents unidirectional or bidirectional causality. Additional research is imperative to assess the nature of this correlation, either to address comorbid depression in patients with BPH or to ensure that depressed patients do not report falsely elevated symptoms. UROLOGY 76: 1317–1320, 2010. © 2010 Published by Elsevier Inc.

Inflammation contributes to the pathophysiology of major depression.[1] Depressed patients often exhibit significant increases in inflammatory biomarkers such as C-reactive protein, interleukin-6, and tumor necrosis factor-α.[1,2] These inflammatory pathways might also contribute to the relationship between depression and other inflammatory disease states.[1] For example, evidence has suggested a strong association between depression and myocardial infarction, congestive heart failure, diabetes, and malignancy.[1-4] Some data have also suggested a bidirectional relationship between depression and inflammatory disease states.[5,6]

From the Departments of Urology and Psychiatry, Emory University School of Medicine, Atlanta, Georgia; and Department of Behavioral Sciences and Health Education, Emory University Rollins School of Public Health, Atlanta, Georgia

Reprint requests: Viraj A. Master, M.D., Ph.D., Department of Urology, Emory University School of Medicine, 1365 Clifton Road Northeast, Atlanta, GA 30322. E-mail: vmaster@emory.edu

Submitted: December 3, 2009, received (with revisions): January 27, 2010

Recent evidence has also suggested that depression might affect benign prostatic hyperplasia (BPH), another disease with inflammatory components.[7-9] Kok et al[10] recently reported a twofold increase in the risk of moderate or severe symptoms among patients taking antidepressants. However, studies have not directly examined the relationship between depression and BPH. Therefore, we conducted this cross-sectional study. We analyzed this potential relationship using the American Urological Association Symptom Index (AUA-SI), an assessment tool designed to determine the severity of BPH symptoms, stratify patients for future treatment, and monitor disease progression.[11] The European Association of Urology and AUA consider the AUA-SI a cornerstone of BPH management.[12,13] We hypothesized that depressed patients would report greater AUA-SI scores owing to the effect of depression on the patients' perceptions of suffering and social function.

0090-4295/10/$36.00

doi:10.1016/j.urology.2010.01.069

MATERIAL AND METHODS

Study Setting and Population

The present cross-sectional study enrolled 547 male patients from the urology clinics of Grady Memorial Hospital and Emory University Hospital. Grady Memorial Hospital, located in downtown Atlanta, is a tertiary care facility serving the needs of a primarily underprivileged urban patient population. Emory University's urology department is a tertiary care clinic. The exclusion criteria consisted of age <40 years and the inability to speak English. After complete description of the study to the subjects, all participants provided written informed consent. The institutional review board approved the present study.

Data Collection Procedures

The present protocol was adopted from previously published protocols.[14] The participants were first asked a series of demographic questions. The participants were then asked to self-administer the AUA-SI, which assesses the symptoms commonly associated with BPH, including incomplete emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia. Except for nocturia, the AUA-SI assesses the frequency with which patients experience the 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 summed to determine the severity of the patient's urinary symptoms: 0-7, mild; 8-19, moderate; and 20-35, severe.[11]

Finally, the participants were asked to complete the short version of the Geriatric Depression Scale (GDS). In response to the high prevalence and difficulty in diagnosing depression in the elderly, Yesavage et al[15] designed the GDS to be a rapid, reliable screening tool for geriatric depression. 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 suggestive of depression. The GDS has been widely validated among different cohorts of patients, including patients >40 years old.[16,17]

Statistical Analysis

The patients were initially grouped into 3 categories according to their GDS score: score ≤5, score >5, and score >10. However, subsequent analysis revealed no significant difference in the latter 2 groups of patients; thus, these groups were combined, resulting in 2 final groups of patients: nondepressed patients (GDS score of ≤5) and depressed patients (GDS score >5). Descriptive analyses and frequency analyses were conducted to assess the patient demographics. Paired-sample *t*-tests were conducted to evaluate whether the AUA-SI scores differed by mode of questionnaire delivery (self-administered versus interviewer administered) or the presence of depression. One-way analysis of variance was conducted to assess the difference in the distribution of the AUA-SI severity category by depression status. Finally, binary logistic regression analysis with forward stepwise regression was conducted to assess the relationship between depression and the severity of AUA-SI, controlling for patient age (as a continuous variable), education level, race, ethnicity, homeless status, native language, and employment status. All analyses were conducted using the Statistical Package for Social Sciences, version 15.0 (SPSS, Chicago, IL).

Table 1. Study population characteristics

Characteristic	Value
Total population	547
Average age (y)	59.1 ± 15.1
Education level (n)	
Less than high school	114 (21)
High school	433 (79)
Average monthly income (US$)	3319 ± 6155
Race (n)	
White	241 (44)
Black/African-American	268 (49)
Other	38 (7)
Native language (n)	
English	492 (90)
Other	55 (10)
Currently employed (n)	233 (43)
Currently homeless (n)	38 (7)
Depression (n)	
Depressed (GDS >5)	121 (22)
Nondepressed (GDS ≤5)	426 (78)

Data in parentheses are percentages.

Table 2. Comparison of American Urological Association Symptom Index scores among depressed and nondepressed men

Depression Status	Mean AUA-SI Score	F (df)	*P* Value
Depressed (GDS >5)	16.61 ± 9.89	40.19 (467)	<.001
Nondepressed (GDS ≤5)	10.65 ± 7.97		

AUA-SI = American Urological Association Symptom Index; GDS = Geriatric Depression Scale.

RESULTS

The 547 study participants reported a mean age of 59.1 ± 15.1 years and a mean education level of 13.8 ± 3.4 years (Table 1). Of the 547 men, 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, 22% of patients screened positive for depression (GDS >5).

Compared with nondepressed (GDS ≤5) patients (AUI-SI mean ± SD score 10.65 ± 7.97), depressed (GDS >5) patients self-reported significantly greater mean AUA-SI scores (16.61 ± 9.89; $F = 40.19$, $P < .001$; Table 2). Depressed and nondepressed patients also exhibited significant differences in the distribution of the AUA-SI severity categories ($P < .001$; Fig. 1). Of the nondepressed patients, almost three quarters presented with mild (43.4%) or moderate (40.4%) AUA-SI symptoms. Of the depressed patients, more than two thirds presented with moderate (37.5%) or severe (41.3%) AUA-SI symptoms.

On univariate logistic regression analysis, age ($P = .021$), income ($P = .023$), homelessness ($P = .020$), and depression ($P < .001$) were significant predictors of presenting with severe symptoms (Table 3). However, on

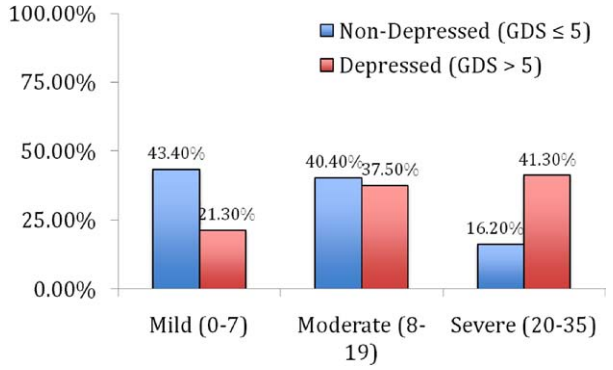

Figure 1. Distribution of AUA-SI severity categories by depression status. Scores grouped into mild (AUA-SI score 0-7), moderate (AUA-SI score 8-19), and severe (AUA-SI scores 20-35) according to AUA-SI severity category. Patients grouped into depressed (GDS >5) and nondepressed (GDS ≤5) according to GDS score. $P < .001$.

multivariate analysis, only depression remained statistically significant. After adjusting for age, education level, income, race, native language, employment, and homeless status, patients with depression were 3 times more likely to present with severe AUA-SI symptoms (odds ratio 3.079, 95% confidence interval 1.129-8.402, $P = .028$).

COMMENT

Increased Self-Reported AUA-SI Scores Among Depressed Patients

BPH and depression both affect a significant number of men worldwide. Moreover, inflammation contributes to the pathophysiology of both diseases. However, the present study is the first to investigate the relationship between BPH and depression directly. Our findings suggest a significant association between depression and BPH, as measured by the AUA-SI score. The depressed patients reported mean AUA-SI scores almost 156% greater than did the nondepressed patients (Table 2). Depressed patients also reported more severe AUA-SI scores (Fig. 1). Depressed patients experience a threefold increased risk (odds ratio 3.079, 95% confidence interval 1.129-8.402, $P = .028$) of presenting with severe BPH symptoms (Table 3).

Association but not Bidirectional Causation

Our findings have provided the first direct evidence of an association between BPH and depression. However, the direction of causation between the 2 disease states remains unclear. One hypothesis is that BPH causes depression. Studies have demonstrated that chronic illnesses can lead to depression.[18,19] Perhaps BPH also causes depression. Another hypothesis involves a bidirectional relationship between BPH and depression. Several studies have demonstrated that depression in the setting of cardiovascular disease and cancer actually worsens these chronic disease states.[5,6] Perhaps BPH symptoms cause depression, which in turn exacerbates the severity of the BPH.

Depression Might Alter Perception of BPH Severity

A final hypothesis in the association between depression and BPH concerns patients' perception of BPH severity. Our study required patients to self-report their BPH symptom severity by self-administering the AUA-SI. Although this method has accepted by the AUA and European Association of Urology in their BPH guidelines,[12,13] depression can prevent habituation of chronic pain.[20] Consequently, depressed patients might report subjective suffering or, in this case, greater AUA-SI scores, than represents their true pathologic state. Given the importance that the AUA and European Association of Urology have placed on the AUA-SI in the management of BPH, depressed patients who report falsely elevated AUA-SI scores might receive inappropriate treatment.[12,13]

Future Studies

Future studies are needed to evaluate these hypotheses. If a causative relationship truly exists between depression and BPH, whether unidirectional or bidirectional, changes in the management of BPH might be warranted. For example, perhaps men who screen positive for BPH should also be screened for depression. As a speculation, treatment might also be extended to include antidepressants. However, if depression falsely elevates AUA-SI scores, self-reported AUA-SI scores should be adjusted according to the results of the depression screening.

Study Limitations

The present hypothesis-generating study had important limitations. First, we only assessed symptoms. We did not quantitatively establish the presence of obstructive voiding on the basis of cystoscopy, uroflowmetry, or complex video urodynamics, which could be important adjuncts in the definitive establishment of a diagnosis of lower urinary tract symptoms. It is important to stress that the AUA-SI is a screening tool that only quantifies symptoms. It does not provide a true clinical diagnosis. Future studies should use these adjuncts to assess whether the high AUA-SI scores of depressed patients represent true pathologic features or whether depression leads to misperception of mild pathologic features. Finally, we did not account for the effect of psychiatric medication use.

CONCLUSIONS

Depression and BPH are common illnesses associated with inflammation. In the present hypothesis-generating study, we demonstrated that depressed patients reported significantly greater and more severe AUA-SI scores than did nondepressed patients. These findings suggest a significant correlation between depression and AUA-SI score. Additional research is imperative to assess the nature of this correlation, either to address comorbid depression in

Table 3. Binary logistic regression analysis with forward stepwise regression of likelihood of presenting with severe American Urological Association Symptom Index score (AUA-SI ≥20)

Variable	Crude HR	95% CI	*P* Value	Adjusted HR	95% CI	*P* Value
Age	1.006	1.001-1.012	.021	NS	NS	.159
Education	NS	NS	.390	NS	NS	.672
Monthly income	1.001	1.000-1.002	.023	NS	NS	.207
Race	NS	NS	.299	NS	NS	.700
Native language	NS	NS	.758	NS	NS	.477
Employment	NS	NS	.075	NS	NS	.491
Homeless status						
Not homeless	Referent			NS	NS	
Homeless	0.392	0.179-0.860	.020	NS	NS	.805
Depression						
Nondepressed (GDS ≤5)	Referent			Referent		
Depressed (GDS >5)	3.620	2.154-6.086	<.001	3.079	1.129-8.402	.028

HR, hazard ratio; CI, confidence interval; NS, not significant; GDS, Geriatric Depression Scale.

the presence of BPH or to ensure that depressed patients do not report falsely elevated symptoms.

References

1. Miller AH, Maletic V, Raison CL. Inflammation and its discontents: the role of cytokines in the pathophysiology of major depression. *Biol Psychiatry*. 2009;65:732-741.
2. Howren MB, Lamkin DM, Suls J. Associations of depression with C-reactive protein, IL-1, and IL-6: a meta-analysis. *Psychosom Med*. 2009;71:171-186.
3. Archer J, Hutchison I, Korszun A. Mood and malignancy: head and neck cancer and depression. *J Oral Pathol Med*. 2008;37:255-270.
4. Sobel RM, Markov D. The impact of anxiety and mood disorders on physical disease: the worried not-so-well. *Curr Psychiatry Rep*. 2005;7:206-212.
5. Lippi G, Montagnana M, Favaloro EJ, et al. Mental depression and cardiovascular disease: a multifaceted, bidirectional association. *Semin Thromb Hemost*. 2009;35:325-336.
6. Spiegel D, Giese-Davis J. Depression and cancer: mechanisms and disease progression. *Biol Psychiatry*. 2003;54:269-282.
7. Begley LA, Kasina S, MacDonald J, et al. The inflammatory microenvironment of the aging prostate facilitates cellular proliferation and hypertrophy. *Cytokines*. 2008;43:194-199.
8. Penna G, Fibbi B, Amuchastegui S, et al. Human benign prostatic hyperplasia stromal cells as inducers and targets of chronic immuno-mediated inflammation. *J Immunol*. 2009;182:4056-4064.
9. Yi FX, Wei Q, Li H, et al. Risk factors for prostatic inflammation extent and infection in benign prostatic hyperplasia. *Asian J Androl*. 2006;8:621-627.
10. Kok ET, Schouten BW, Bohnen AM, et al. Risk factors for lower urinary tract symptoms suggestive of benign prostatic hyperplasia in a community based population of healthy aging men: the Krimpen study. *J Urol*. 2009;181:710-716.
11. Barry MJ, Fowler FJ Jr, O'Leary MP, et al., for the Measurement Committee of the American Urological Association. The American Urological Association symptom index for benign prostatic hyperplasia. *J Urol*. 1992;148:1549-1557, 1564.
12. Madersbacher S, Alivizatos G, Nordling J, et al. EAU guidelines on assessment, therapy and follow-up of men with lower urinary tract symptoms suggestive of benign prostatic obstruction (BPH guidelines). *Eur Urol*. 2004;46:547-554.
13. Kaplan SA. Update on the American Urological Association guidelines for the treatment of benign prostatic hyperplasia. *Rev Urol*. 2006;8(suppl 4):S10-S17.
14. Johnson TV, Goodman M, Master VA. The efficacy of written screening tools in an inner city hospital: literacy based limitations on patient access to appropriate care. *J Urol*. 2007;178:623-629.
15. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res*. 1982;17:37-49.
16. Burke WJ, Roccaforte WH, Wengel SP. The short form of the geriatric depression scale: a comparison with the 30-item form. *J Geriatr Psychiatry Neurol*. 1991;4:173-178.
17. Fountoulakis KN, Tsolaki M, Iacovides A, et al. The validation of the short form of the geriatric depression scale (GDS) in Greece. *Aging*. 1999;11:367-372.
18. Fava GA, Sonino N, Morphy MA. Major depression associated with endocrine disease. *Psychiatr Dev*. 1987;5:321-348.
19. Lustman PJ, Griffith LS, Freedland KE, et al. The course of major depression in diabetes. *Gen Hosp Psychiatry*. 1997;19:138-143.
20. Katon WJ. Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. *Biol Psychiatry*. 2003;54:216-226.