Comparison of nocturia etiology in black and white male patients

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Introduction: *Much of what is known about the etiology of nocturia (i.e., nocturnal polyuria [NP], small bladder capacity [SBC], etc.) at the population level stems from the Krimpen study, which enrolled aging males from a homogenous municipality in the Netherlands. Given the higher prevalence of benign prostatic hyperplasia and overactive bladder in black versus white males in population research, we aim to test the hypothesis that black males seeking treatment for lower urinary tract symptoms (LUTS) are more likely to have nocturia owing to SBC.*

Materials and methods: *We retrospectively analyzed 24 hour frequency-volume charts (FVCs) completed by males seeking treatment for LUTS at a Veterans Affairs urology clinic from 2008-2016. Patients were included if they were ≥ 18 years, identified as either Caucasian or African American, and had a complete baseline FVC showing ≥ 1 nocturnal void. Patients were stratified by race and classified as having nocturia owing to SBC (defined by a maximum voided volume < 200 mL or a nocturnal bladder capacity index > 1.3); NP (defined by a nocturnal polyuria index > 0.33); "mixed" (SBC + NP); or "other" (neither SBC nor NP).*

Results: *Between white and black patients, 28 (24%) versus 28 (26%) had NP, 32 (27%) versus 33 (30%) had SBC, and 35 (30%) versus 30 (28%) had mixed nocturia. Overall, there was no difference in distribution of underlying etiology by race (p = 0.51).*

Conclusions: *Our results demonstrate no difference in the etiology of nocturia between black and white males. Accordingly, race should not play a role in the evaluation of patients seeking treatment for nocturia.*

Key Words: BPH, disparity, LUTS, nocturia, OAB, race

Introduction

Nocturia, defined as waking to void during the hours of intended sleep, is among the most common and bothersome urological complaints in the general population.[1] At least 1 in 6 people below the age of 40 consistently wake to void twice each night, and the prevalence of nocturia further increases with age, affecting 56% of patients 75 years or older in the National Health and Nutrition Examination Survey (NHANES).[1-3]

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Several population-based surveys have identified a robust association between nocturia and race—an effect which is particularly pronounced among black men.[4-6] Moreover, the literature shows a well-established difference in the prevalence of lower urinary tract symptoms (LUTS) between black and white men. Black men are more likely to have both benign prostatic hyperplasia (BPH) and overactive bladder (OAB) compared to white men. In the placebo arm of the Prostate Cancer Prevention Trial, black men had a 41% higher risk of BPH, and a 68% higher risk of severe BPH compared to white men.[7] Likewise, the nationally-representative OAB-POLL study determined that race is a strong predictor of OAB, with black men significantly more likely than white men to have OAB, despite having a lower prevalence of self-reported comorbidities and known risk factors.[8]

Nocturia is a complex and multifactorial disease. The etiologies of nocturia can be broadly divided into global polyuria, nocturnal polyuria (NP), small bladder capacity (SBC), and mixed etiology.[9] SBC can be due to impaired bladder emptying or filling, most commonly related to BPH and/or irritative symptoms, which cause patients to void at sub-optimal bladder volumes.[9] Although via different mechanisms, both OAB and BPH predominantly give rise to a SBC nocturia phenotype, which is readily apparent as small voided volumes upon analysis of the frequency-volume chart (FVC).

Given the higher prevalence of BPH and OAB in black men, it stands to reason that there may be a corresponding increase in the prevalence of nocturia due to SBC in black versus white men. Thus, we aim to test the hypothesis that, among patients seeking treatment for LUTS at a urology clinic, black men have a greater prevalence of nocturia caused by SBC compared to white men.

Materials and methods

Patients

Patients who had established care for LUTS at a Veterans Affairs urology clinic from 2008 to 2016 were asked to complete a 24 hour FVC according to best practice standards in the evaluation of LUTS. The FVC is an objective record of the timing and volume of every void during a 24 hour period. This instrument provides valuable insight regarding global and nocturnal urine output, bladder capacity, and urinary frequency, and can be used to identify the primary mechanism underlying a patient's nocturnal voiding.[10] A FVC database was approved by the Veterans Affairs New York Harbor Healthcare System Institutional Review Board, and a waiver of informed consent was granted for retrospective analysis.

Study design and procedures

Patients were included if they were ≥ 18 years of age, identified as either Caucasian or African American (as documented in Veterans Affairs medical records), and had a complete FVC showing ≥ 1 nocturnal void. Patients were excluded if they were biracial. Only baseline FVCs were included from patients with multiple complete entries.

Patients were split into two cohorts: those who identified as Caucasian and those who identified as African American. A complete overview of patient demographics, comorbid conditions, and urological treatment history by race is provided in Table 1.

Parameters used in the comparison of nocturia by race included 24 hour urine volume, number of voids in 24 hours, actual nocturnal voids (ANV), first uninterrupted sleep period (FUSP), maximum voided volume (MVV), nocturnal bladder capacity index (NBCi), nocturnal maximum voided volume (NMVV), nocturnal polyuria index (NPi), and nocturnal urine volume (NUV). An overview of standard FVC parameter definitions and derivations is provided in Table 2.

TABLE 1. **Patient demographics by race**

	White (n = 117)	Black (n = 109)
Age	68.0 (52.0-84.0)	67.0 (53.0-81.0)
Medications		
Alpha-blocker	72 (61.5)	50 (45.9)
Anti-muscarinic	15 (12.8)	13 (11.9)
B3-agonist	0 (0.0)	2 (1.8)
Surgery		
RRP	6 (5.1)	4 (3.7)
TURP	6 (5.1)	7 (6.4)
Urethroplasty	1 (0.9)	1 (0.9)
Radiation		
EBRT	2 (1.7)	13 (11.9)
Brachytherapy	4 (3.4)	3 (2.8)
Comorbidities		
Hypertension	81 (69.2)	88 (80.7)
Diabetes	30 (25.6)	30 (27.5)
Sleep apnea	24 (20.5)	16 (14.7)

RRP = radical retropubic prostatectomy; TURP = transurethral resection of the prostate; EBRT = external beam radiation therapy age reported as median (interquartile range); categorical variables reported as frequency (proportion)

Patients were further stratified based on underlying etiology of their nocturia. Patients were classified as having SBC if they had either a MVV < 200 or NBCi > 1.3.[11] Patients met the criteria for NP with an NPi > 0.33.[12] Patients were classified as "mixed" if their FVC showed features of both SBC and NP, or "other" if they showed neither.

Statistical analysis

For categorical variables, the chi-squared test was used to determine significance between groups, and results were reported as frequency (percentage). Continuous variables were reported as median (interquartile range), and the Wilcoxon rank-sum test was used to determine significance. A correction for multiple comparisons was not employed to demonstrate the lowest possible threshold for significance. All tests were two-sided and a p value < 0.05 was deemed statistically significant.

TABLE 2. **Frequency-volume chart (FVC) parameters**

Parameter	Definition
Actual number of nightly voids (ANV)	The number of voids recorded from the time the individual goes to bed with the intention of sleeping, to the time the individual wakes with the intention of rising
24 hour total urine volume (TUV)	Total volume of urine produced during a 24 hour period
Nocturnal urine volume (NUV)	Total volume of urine passed during the night, including the first morning void
Maximum voided volume (MVV)	The single largest voided volume passed in a 24 hour period
Nocturnal maximum voided volume (NMVV)	The single largest voided volume passed during the night
Nocturnal urine production (NUP)	NUV/(sleeping hours); if NUP ≥ 90mL/h, patient has nocturnal polyuria
Nocturnal polyuria index (NPi)	NUV/TUV; if NPi > 0.20-0.33 (age-dependent), patient has nocturnal polyuria
Nocturnal bladder capacity index (NBCi)	(ANV – Ni – 1); NBCi > 0 indicates that nocturia occurs at voided volumes less than MVV; NBCi > 2 is associated with severe nocturia
First uninterrupted sleep period (FUSP)	Number of hours between the time the individual goes to bed with the intention of sleeping to the time of first awakening

Modified from van Kerrebroeck P. Standardization of terminology in nocturia: commentary on the ICS report. *BJU Int* 2002; 90(Suppl 3):16-17.

Results

Our study included 117 white men and 109 black men. A complete overview of FVC results by race is provided in Table 3. In the span of 24 hours, white men and black men voided a median 11 and 10 times, respectively (p = 0.061), with white men producing 1800 mL and black men producing 1900 mL of urine (p = 0.37). The median

TABLE 3. **Frequency-volume chart parameters by race**

	White (n = 117)	Black (n = 109)	p value
Age	68 (65-81)	67 (60-74)	0.064
24 hour volume	1800 (1400-2700)	1900 (1400-2400)	0.37
Voids in 24 hours	11 (9-14)	10 (8-12)	0.061
ANV	3 (2-4)	2 (1-3)	0.24
FUSP	2.3 (1.5-3.4)	2.2 (1-3.8)	0.83
MVV	300 (210-400)	300 (200-380)	0.29
NBCi	1.1 (0.63-1.8)	1 (0.4-1.5)	0.11
NMVV	250 (180-380)	240 (150-300)	0.14
NPi	0.37 (0.27-0.5)	0.39 (0.26-0.49)	0.79
NUV	670 (500-1100)	660 (420-990)	0.15

variables defined and derived in Table 2. ANV = actual nocturnal voids; FUSP = first uninterrupted sleep period, hours; MVV = maximum voided volume; NBCi = nocturnal bladder capacity index; NMVV = nocturnal maximum voided volume, ml; NPi = nocturnal polyuria index; NUV = nocturnal urine volume, mL

TABLE 4. **Nocturia etiology by race**

	White (n = 117)	Black (n = 109)	p value
Small bladder capacity	28 (24%)	28 (26%)	0.51
Nocturnal polyuria	32 (27%)	33 (30%)	
Mixed	35 (30%)	30 (28%)	
Other	22 (19%)	18 (17%)	

variables reported as frequency (percentage). Small bladder capacity (SBC) defined as a nocturnal bladder capacity index (NBCi) > 1.3 or 24 hour maximum voided volume (MVV) < 200. Nocturnal polyuria (NP) defined as a nocturnal polyuria index (NPi) > 0.33. All variables defined and derived in Table 2.

ANV was 3 in white men and 2 in black men (p = 0.24), with white men producing a NUV of 670 mL, similar to the 660 mL NUV passed by black men (p = 0.15). The FUSP was 2.3 hours in white men and 2.2 hours in black men (p = 0.83).

MVV and NMVV were also similar between cohorts. White and black subjects both demonstrated a median MVV of 300 mL (p = 0.29). NMVV was 250 mL in white subjects compared to 240 mL in black subjects (p = 0.14). Median NBCi was 1.1 in white men and 1.0 in black men (p = 0.11). The NPi was 0.37 among white subjects and 0.39 among black subjects (p = 0.79).

Amongst white subjects, 28 (24%) had NP, 32 (27%) had SBC, and 35 (30%) had nocturia owing to mixed etiology, Table 4. In black subjects, 28 (26%) had NP, 33 (30%) had SBC, and 30 (28%) had nocturia owing to mixed etiology. Overall, there was no statistical difference in the distribution of underlying nocturia etiology by race (p = 0.51).

Discussion

In this study, no differences were observed in any of the standard FVC parameters between white and black subjects. There were no significant differences in (1) overall fluid intake, evidenced by 24 hour volume, (2) bladder filling or bladder emptying, evidenced by MVV, NBCi, and NMVV, and (3) nocturnal urine production or nocturnal fluid intake, demonstrated by NPi, NUP, and NUV. Additionally, no significant difference was found in nocturia severity, as measured by ANV.

Our findings suggest that the distribution of mechanistic etiologies of nocturia in males who identify as black is similar to that of males who identify as white. This finding does not support the hypothesis that nocturia owing to SBC is more common in black versus white urology patients. Although past studies have demonstrated a predisposition for BPH and OAB among black males, it seems that these conditions do not weigh significantly on the underlying causes of nocturia in males seeking care in the outpatient clinical setting.[7,8]

Much of what is known about the etiology of nocturia stems from the Krimpen study, a landmark FVC-based longitudinal evaluation of an aging male population in the Netherlands.[13,14] Given the homogeneous patient population of the Krimpen study, it is unknown if these findings are generalizable to a more diverse patient population. To our knowledge, our study is the first to compare nocturia subtypes between races.

Limitations of this study include possible errors in self-reported FVCs, and the use of FVCs limited to 24 hours, which are considered to be less reliable than FVCs 3-5 days in duration.[15,16] Additionally, our data are derived from older males seeking treatment for LUTS at a urological clinic, and, thus, may not be generalizable with respect to nocturia at the population level. Further population research using FVCs to study the effect of race on the etiology of nocturia is warranted.

Conclusions

Our study demonstrates that frequency-volume chart parameters do not vary between black and white males. Accordingly, race should not be used as a factor for informing the management of nocturia in these populations in the outpatient urology setting. □

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