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Association between physical activity, lower urinary tract symptoms (LUTS) and prostate volume

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Abstract

- To determine the association between lower urinary tract symptoms (LUTS) severity and physical activity (PA) across workplace, home, and leisure domains.
- To determine the mediating role of prostate enlargement on LUTS severity and PA.
- The study included 405 men without prostate cancer or prostatic intraepithelial neoplasia.
- LUTS severity was ascertained using the American Urological Association Symptom Index and prostate size by ultrasonography.
- PA was assessed using validated questionnaires, with conversion to metabolic equivalent of task (MET)-h/day to estimate leisure-time PA energy expenditure.
- Analysis used multivariable linear regression, controlling for body mass index (BMI), age, race, and treatment for benign prostatic hyperplasia, cardiovascular disease and diabetes.
- Higher leisure-time PA energy expenditure and light housework activities were significantly associated with lower LUTS severity.
- Prostate volume was not significantly associated with PA in adjusted analyses, and controlling for prostate volume did not affect the association between LUTS severity and PA.
- Stratification by BMI showed a moderate interaction ($P = 0.052$), suggesting that PA was more strongly associated with LUTS severity among obese men.
- In this cross-sectional analysis, leisure-time and home-time PA was inversely associated with LUTS severity.
- The association between PA and LUTS severity was stronger for irritative symptoms and among obese men, and was not mediated through changes in prostate size.
- Our results indicate the need for further detailed investigation of PA and LUTS.

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Conflicts of interest

None.

Keywords

lower urinary tract symptoms (LUTS); prostate enlargement; benign prostatic hyperplasia (BPH); physical activity; obesity

Introduction

LUTS, e.g. hesitancy, nocturia, urgency, or frequency, are common consequences of ageing and can lead to a diminished health-related quality of life [1]. Unfortunately, the extended underlying pathophysiologies leading to LUTS are unclear, although it is increasingly recognised that the causes of LUTS extend well beyond prostate enlargement and BOO [2]. The multiple pathways leading to LUTS onset and progression not only complicate diagnosis, but limit the overall effectiveness and satisfaction of targeted symptom management strategies [3].

Several epidemiological studies report that a lifestyle that includes moderate levels of leisure-time physical activity (PA) is associated with a lower risk of a BPH diagnosis or less severe LUTS [4–7]. However, our understanding of any relationship between PA and LUTS severity is at an early stage. PAs appropriate for older men and effective in LUTS management have not been identified, in part because of the difficulty in harmonising data from the different PA assessment methods across research studies. Additionally, studies differ in the ability to separate PA from obesity or other consequences of a sedentary lifestyle, and assessment methods may not be sufficiently sensitive to capture PA among older men expected to have lower overall activity levels.

This cross-sectional analysis further characterises the relationship between PA and LUTS severity through administration of multiple PA measures, allowing the separation of workplace activities, home activities (e.g. cleaning and washing), and more intensive sport and leisure activity and energy expenditure on LUTS severity. We also extend the investigation of mechanism by evaluating the association between PA and prostate volume as a possible mediator of the association between PA and LUTS severity. Patients with severe LUTS and willing to incorporate greater PA into their daily life may reduce the negative impact of severe LUTS, as well as reduce the risks from diabetes and cardiovascular disease (CVD). Our results may better characterize the intensity of PA associated with LUTS severity, and suggest whether PA influences prostate size to mediate these effects.

Patients and methods

The Nashville Men's Health Study is a multi-centred, rapid-recruitment protocol initiated in 2002 and targeting men seeking a diagnostic biopsy at Vanderbilt University Medical Center, the Tennessee Valley Veterans Administration Medical Center, and Urology Associates, a large community urology practice [8]. Exclusion criteria included age of < 40 years, a prior prostate cancer diagnosis, prior prostate surgery, use of androgen supplementation, or English language insufficient for informed consent. About 90% of eligible men approached for recruitment consented to participate, and a single pathologist reviewed biopsies for consistency. To focus on the non-malignant causes of LUTS, we excluded patients diagnosed with prostate cancer, prostatic intraepithelial neoplasia, or atypical or suspicious foci. All protocols were approved by the Institutional Review Boards at Vanderbilt University and the Tennessee Valley Veterans Administration.

Data abstraction from urology, surgery, and pathology medical reports included PSA test history, the number of prior biopsies, number of prostate cores collected at biopsy leading to

recruitment, prostate volume (mL) at biopsy ultrasonography, use of α -blockers or 5 α -steroid-reductase inhibitors, or use of medications to treat hypertension, hypercholesterolaemia, or diabetes. Weight (kg; no shoes, hospital gown) was measured on a calibrated scale, and height (within 0.1 cm) was measured by stadiometer at the time of recruitment by trained staff. A structured research questionnaire was also administered at the time of recruitment. LUTS severity was assessed using the AUA Symptom Index (AUA-SI) [9]. Leisure-time PA was assessed using the Baecke questionnaire [10], in which participants recorded the most frequent sport activities and other physically active activities in the preceding week. Participants also recorded the number of months per year participating in each of these activities. Annual metabolic equivalent of task (MET)-h/week were calculated using the Compendium of Physical Activities [11] standardised to the number of months per year participating in each activity. Total leisure PA energy expenditure (PAEE) was calculated as the sum of MET scores across all reported sports and other activities. Occupational activity was assessed by the Baecke Occupational Work Index, with queries about the frequency participants sit, stand, walk, lift heavy loads, and sweat at work [10]. Responses are scored as never, seldom, sometimes, often, and always. Household activity level in the past week included the frequency of dusting, washing dishes, washing windows, carrying trash, the number of rooms cleaned, number of meals prepared, number of stairs in the home, typical mode of transportation, and frequency of shopping trips and other common household activities among older persons [12]. Responses are coded from zero to three, and the sum of these scores provides an overall household activity score.

Preliminary analyses included describing the relationship between categories of PA, LUTS severity, and prostate volume. Because we began administering the AUA-SI in February 2009, we restricted all analyses to those participants recruited since that time. The AUA-SI scores were categorised as mild (score 0–7), moderate (8–19), or severe (20–35) for each patient. Prostate volume was categorised as < 40, 40–60 and > 60 mL to accommodate conservatively the skewed distribution in our analyses. Because our study included many sedentary participants, PA indices were first categorised as ‘none’, then at tertiles of distribution for non-sedentary participants. Chi-square (categorical variables), Wilcoxon rank-sum (numerical, two groups), and Kruskal–Wallis tests (numerical, three or more groups) were used to compare patient characteristics and PA levels across AUA-SI or prostate volume outcomes. Multivariable regression was used to determine the association between each PA metric with AUA-SI or prostate volume. Initial models controlled for age, body mass index (BMI), race, and current use of medications to treat BPH, CVD, and diabetes. However, diabetes and CVD medication uses did not affect our results and were excluded from the final model. We repeated each analysis stratifying by BPH medication use, and evaluated the interaction cross-product term of BPH treatment and PA, to consider the consistency of the PA and LUTS/volume analysis. Similarly, analyses were stratified by BMI categories to explore the effects of PA intensity with LUTS severity within obese and non-obese men.

Results

Participants ranged in age from 40 to 93 years, and $\approx 5\%$ reported a race/ethnicity other than White (predominately African-American; Table 1). BMI ranged from 18.9 to 53.1 kg/m², with the median BMI among obese men (BMI ≥ 30 kg/m²) of 32.6 kg/m². Moderate or severe LUTS severity was reported by $\approx 55\%$ of the study population. More severe LUTS was significantly associated with taking BPH medications. Prostate volume ranged from 5.5 to 213 mL, and the median prostate volume within each prostate volume category (< 40, 40–60, and > 60 mL) was 30.0, 48.4, and 80.9 mL, respectively. Prostate volume was significantly associated with age, BMI, and use of BPH medication.

There was a high prevalence of sedentary or low levels of PA across all PA indices (Table 2). In crude analyses, PA was not associated with LUTS severity, while a higher level of workplace activity was significantly associated with a smaller prostate volume. However, after controlling for age, BMI, race, and BPH treatment, PA levels were no longer associated with prostate volume (Table 3). Furthermore, increasing housework activity and PAEE were significantly associated with a lower LUTS severity. The results were similar for participants receiving vs not receiving BPH medication, and controlling for prostate volume did not affect the association between PA and LUTS severity. We further found greater PA significantly associated with irritative, but not for obstructive, LUTS severity.

Interestingly, the inverse association between PAEE and LUTS severity was most evident among obese men (i.e., BMI > 30 kg/m²; Figure 1). The interaction between BMI and PAEE approached statistical significance ($P = 0.052$), and the effect was consistent among men receiving and not receiving BPH treatment.

Discussion

Past studies of PA and BPH have produced mixed results. In the present study greater PA was associated with lower LUTS severity. Although the cross-sectional design of the present analysis limits our ability to conclude that PA reduces LUTS, our results are consistent with a systematic review and meta-analysis of PA and BPH performed by Parsons and Kashefi [13] that included 43–083 participants across 11 observational studies. Eight studies reported an inverse relationship between PA and LUTS, while two showed no relationship, and one was equivocal. The results of these studies were pooled through meta-analysis using four PA categories: sedentary, light, moderate and heavy PA. Compared with the sedentary group, the odds ratio for LUTS was 0.70, 0.74 and 0.74 for the light, moderate and heavy PA groups, respectively, with statistically significant associations for the moderate and heavy PA groups.

The present analysis extends previous investigations of PA and BPH to include PA assessment to relatively moderate activities, e.g. household work, and found men participating in household activities, such as cleaning or yard work, reported significantly fewer LUTS events on the AUA-SI. Similarly, less severe LUTS was associated with PAEE estimated as MET-h/day through sport or other activities. The present analysis suggested that a moderate level of PA beyond a sedentary state, whether from household activities or leisure activities, would yield a benefit.

From a patient care perspective, it must be recognised that incorporating greater PA into daily living is a challenge for many patients. Attempts may fail if benefits are not seen within an expected period or are only modestly effective and not seen as worth the time and effort. Thus, the present results suggesting that obese men (BMI > 30 kg/m²) or men experiencing urgency or other irritative symptoms provide clinicians with information to better target and personalise referrals and recommendations to increase PA in a diverse patient population. Combining PA with pharmaceutical approaches toward BPH, such as finasteride or an α -blocker, may improve patient outcomes, as LUTS is the cumulative manifestation of multiple disorders affecting the prostate, bladder, urethra, and kidney, and the present data suggest the possibility that recommendations for greater PA may have an impact beyond the drug-targeted pathway to improve patient response.

Obesity is one of the more consistent comorbidities of BPH, associated with prostate enlargement [14] and LUTS severity [15]. Adipocytes alter steroid hormone metabolism, induce oxidative stress, and release inflammatory cytokines to potentially advance BPH progression [16, 17], and insulin, HbA1c, or fasting glucose levels are also associated with

BPH symptoms, treatment, and prostate volume [18–24]. However, although we can understand that there is an intimate relationship between obesity and PA; the present results suggest that PA and obesity operate through separate mechanisms. PA levels were not associated with prostate size, and controlling for BMI or prostate size did not alter the relationship between PA and LUTS severity. PA is thought to suppress sympathetic nervous system activity [25], critical in urine storage through increasing urethral resistance and depressing detrusor contractions. Simultaneously, ischaemia may have an important role in bladder dysfunction [26], and increasing PA and overall blood flow and blood oxygen levels to the bladder may in turn decrease bladder muscle ischaemia and inhibit muscle atrophy. However, we also cannot exclude the possibility from the present study that PA instead improves psychological well-being, separate from physical health, such that more physically active men do not perceive LUTS severity in the same way as less active men.

The present analysis had several strengths but also limitations. The primary limitation was that the temporal relationship between PA and LUTS could not be definitely determined. It is thus possible that men are more physically active because they have less severe LUTS. Certainly future analyses should query patients to determine the impact of LUTS on their ability to participate in PA. We used multiple PA assessment instruments, including instruments validated specifically for older persons, to evaluate multiple domains of PA. However, the validity and sensitivity of assessment instruments in the present population is unknown, and it was not feasible for us to request participants to wear PA monitors for an extended period in this large sample. The present analyses controlled for BPH treatment, BMI, and treatment for CVD and diabetes, and men diagnosed with prostate cancer or PIN were excluded. However, there also may be error associated with reporting LUTS on the AUA-SI that is otherwise not controlled here [27].

In conclusion, increased levels of household and leisure-time PA were associated with lower LUTS severity, independent of prostate size, BMI, or other BPH treatments.

Acknowledgments

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Abbreviations

AUA-SI	AUA Symptom Index
BMI	body mass index
CVD	cardiovascular disease
PA(EF)	physical activity (energy expenditure)

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What's known on the subject? and What does the study add?

Greater leisure-time physical activity (PA) levels or a lower body mass index have previously been associated with a lower risk of benign prostatic hyperplasia or less severe lower urinary tract symptoms (LUTS). However, separating the effects of PA from obesity can be difficult, and the types of PA and the mechanisms underlying any association with LUTS among older men are unclear.

The present analysis used multiple validated instruments to measure PA domains across workplace, leisure time, and home domains, and finds that PAs ranging from sports to light housework are associated with lower LUTS severity. The benefits of PA were seen with irritative symptoms, and also among obese men. Furthermore, this analysis begins the investigation of mechanism by finding that the relationship between PA and LUTS is not mediated by prostate enlargement.

Figure 1.

PAEE and LUTS severity, stratified by BMI and BPH treatment. Association between PA and LUTS severity by BMI category (black $\leq 25.0\text{ kg/m}^2$; red 25–29.9 kg/m^2 ; green $\geq 30\text{ kg/m}^2$) and current BPH treatment (solid lines, yes; dotted lines, no BPH treatment). LUTS severity among men reporting no sport or other PA is represented by box plots for each BMI category. $P = 0.052$ for interaction between PAEE and BMI (controlling for age, race, and BPH treatment).

Table 1
LUTS severity and prostate volume with BMI and study population description

LUTS severity:		Prostate volume (mL):				
	mild (0–7)	moderate (8–20)	severe (21–35)	<40	40–60	>60
All, n (%)	180 (100)	176 (100)	49 (100)	151 (100)	143 (100)	111 (100)
Age (years), n (%)						
40–49	7 (4)	11 (6)	1 (2)	14 (9)	4 (3)	1 (1)
50–59	49 (27)	35 (20)	14 (29)	55 (36)	31 (22)	12 (11)
60–69	74 (41)	79 (45)	16 (33)	52 (34)	66 (46)	51 (46)
70–93	50 (28)	51 (29)	18 (37)	30 (20)	42 (29)	47 (42)
Median (IQR)	63.7 (58.2, 70.5)	65.5 (59.5, 71.0)	67.0 (59.3, 71.6)	61.0 (54.8, 67.5)	64.3 (60.3, 70.6)	68.9 (64.0, 72.5)
BMI (kg/m ²), n (%)						
<25.0	34 (19)	25 (14)	6 (12)	32 (21)	21 (15)	21 (11)
25.0–29.9	70 (39)	76 (43)	25 (51)	69 (46)	62 (43)	40 (36)
30	76 (42)	74 (42)	18 (37)	50 (33)	60 (42)	58 (53)
Median(IQR)	28.9 (25.7, 31.9)	29.1 (26.2, 31.3)	28.3 (26.4, 31.8)	28.0 (25.2, 31.1)	28.8 (26.5, 31.3)	30.1 (26.8, 32.8)
Race, n (%)						
White	172 (96)	168 (95)	44 (90)	148 (98)	132 (92)	104 (94)
Other	8 (4)	8 (5)	5 (10)	3 (2)	11 (8)	7 (6)
Education, n (%)						
HS	64 (36)	67 (38)	25 (51)	56 (37)	51 (36)	49 (44)
> HS	116 (64)	109 (62)	24 (49)	95 (63)	92 (64)	62 (56)
BPH treatment, n (%)						
Yes	30 (16)	70 (36)	31 (60)	29 (19)	40 (28)	50 (45)
No	160 (84)	122 (64)	21 (40)	122 (81)	103 (72)	61 (55)
Diabetes treatment, n (%)						
Yes	22 (12)	22 (13)	8 (16)	16 (11)	18 (13)	18 (16)
No	158 (88)	154 (87)	41 (84)	135 (89)	125 (87)	93 (84)
CVD treatment, n (%)						
Yes	104 (58)	98 (56)	30 (61)	76 (50)	82 (57)	74 (67)
No	76 (42)	78 (44)	19 (39)	75 (50)	61 (43)	37 (33)

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IQR, interquartile range; HS, high school; *P*-value from chi-square test or Kruskal–Wallis rank-sum test.

Table 2

LUTS severity or prostate volume by PA level

PA level N (%):	LUTS severity:		Prostate volume (mL):					
	mild (0–7)	moderate (8–20)	severe (21–35)	P	<40	40–60	>60	P
Sport (S):								
none	108 (60)	113 (64)	36 (73)		94 (62)	88 (62)	75 (58)	
low	22 (12)	24 (14)	5 (10)		18 (12)	17 (12)	16 (14)	
med	30 (17)	15 (9)	5 (10)		19 (13)	19 (13)	12 (11)	
high	20 (11)	24 (14)	3 (6)	0.21	20 (13)	19 (13)	8 (7)	0.72
Leisure (L):								
low	59 (36)	49 (30)	20 (48)		51 (37)	43 (33)	34 (35)	
med	59 (36)	57 (35)	15 (36)		49 (35)	44 (33)	38 (39)	
high	48 (29)	55 (34)	7 (17)	0.17	39 (28)	45 (34)	26 (27)	0.72
Work (W):								
none	60 (34)	63 (37)	20 (41)		40 (28)	50 (35)	53 (48)	
low	34 (19)	31 (18)	11 (22)		27 (19)	31 (22)	18 (16)	
med	40 (23)	38 (22)	8 (16)		36 (25)	31 (22)	19 (17)	
high	41 (23)	40 (23)	10 (20)	0.94	41 (28)	30 (21)	20 (18)	0.04
Total (S+L+W):								
low	54 (31)	52 (31)	19 (41)		45 (31)	32 (24)	48 (46)	
med	58 (34)	59 (36)	16 (35)		48 (33)	54 (40)	31 (30)	
high	60 (35)	55 (33)	11 (24)	0.62	53 (36)	48 (36)	25 (24)	<0.01
Household:								
low	55 (33)	49 (31)	16 (40)		46 (34)	44 (33)	30 (31)	
med	50 (30)	40 (32)	13 (32)		39 (29)	41 (31)	33 (34)	
high	63 (38)	59 (37)	11 (28)	0.76	51 (38)	48 (36)	34 (35)	0.94
PAEE (MET-h/day):								
<3	69 (38)	63 (36)	25 (51)		58 (38)	56 (39)	43 (39)	
3–9	7 (4)	6 (3)	3 (6)		8 (5)	5 (3)	3 (3)	
9.1–18	24 (13)	25 (14)	3 (6)		22 (15)	17 (12)	13 (12)	
18.1–27	13 (7)	15 (9)	4 (8)		9 (6)	12 (8)	11 (10)	

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pA level N (%):	LUTS severity:		Prostate volume (mL):			
	mild (0–7)	moderate (8–20)	severe (21–35)	P	<40	40–60
>27	67 (37)	67 (38)	14 (29)	0.62	54 (36)	53 (37)
					41 (37)	41 (37)

P-values from chi-square test.

Table 3

Association between PA, LUTS severity, and prostate volume

Outcome:	AUA-SI score			Obstructive symptoms			Irritative symptoms			Prostate volume		
	Coefficient	SE	P	Coefficient	SE	P	Coefficient	SE	P	Coefficient	SE	P
Base model:												
Age (years)	0.550	0.432	0.012	0.132	0.213	0.537	0.418	0.260	0.108	9.694	1.452	<0.001
Race (White: other)	-1.970	1.601	0.219	-0.765	0.790	0.333	-1.206	0.963	0.211	-2.533	5.382	0.638
BMI (kg/m ²)	0.065	0.072	0.369	-0.024	0.036	0.496	0.089	0.043	0.041	1.101	0.243	<0.001
BPH treatment (Yes:No)	-5.133	0.797	<0.001	-2.341	0.393	<0.001	-2.791	0.480	<0.001	-7.622	2.680	0.005
PA added to base model:												
Work	0.139	0.286	0.626	0.028	0.141	0.843	0.111	0.172	0.518	0.534	0.955	0.576
Leisure	-0.219	0.612	0.721	-0.123	0.303	0.680	-0.095	0.371	0.797	3.564	2.113	0.093
Sport	-0.149	0.080	0.065	-0.068	0.040	0.089	-0.081	0.048	0.094	-0.295	0.271	0.276
Total	-0.185	0.178	0.300	-0.118	0.088	0.183	-0.067	0.107	0.533	0.169	0.606	0.780
Housework	-0.142	0.061	0.021	-0.056	0.030	0.061	-0.086	0.037	0.021	-0.119	0.208	0.566
PAEE (MET-h/day)	-0.025	0.012	0.041	-0.010	0.006	0.088	-0.014	0.007	0.046	-0.046	0.040	0.256