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Obesity Increases and Physical Activity Decreases Lower Urinary Tract Symptom Risk in Older Men: The Osteoporotic Fractures in Men Study

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Abstract

Background: Two potential targets for preventing chronic lower urinary tract symptoms (LUTS) in older men are obesity and physical activity.
Objective: To examine associations of adiposity and physical activity with incident LUTS in community-dwelling older men.
Design, setting, and participants: The Osteoporotic Fractures in Men Study (MrOS) is a prospective cohort of men ≥65 yr of age. MrOS participants without LUTS and a history of LUTS treatment at baseline were included in this analysis.
Measurements: Adiposity was measured with body mass index (BMI), physical activity with the Physical Activity Scale for the Elderly (PASE) and self-report of daily walking, and LUTS with the American Urological Association Symptom Index.
Results and limitations: The mean age (standard deviation [SD]) of the 1695 participants was 72 (5) yr at baseline. At a mean (SD) follow-up of 4.6 (0.5) yr, 524 (31%) of men reported incident LUTS. In multivariate analyses, compared with men of normal weight at baseline (BMI <25 kg/m^2), overweight (BMI: 25.0–29.9 kg/m^2) and obese (≥ 30 kg/m^2) men were 29% (adjusted odds ratio [OR_{adj}]: 1.29; 95% confidence interval [CI], 1.00–1.68) and 41% (OR_{adj}: 1.41; 95% CI, 1.03–1.93) more likely to develop LUTS, respectively. Men in the highest quartile of physical activity were 29% (OR_{adj}: 0.71; 95% CI, 0.53–0.97) and those who walked daily 20% (OR_{adj}: 0.80; 95% CI, 0.65–0.98) less likely than their sedentary peers to develop LUTS, adjusting for BMI. The homogeneous composition of MrOS potentially diminishes the external validity of these results.
Conclusions: In older men, obesity and higher physical activity are associated with increased and decreased risks of incident LUTS, respectively. Prevention of chronic urinary symptoms represents another potential health benefit of exercise in elderly men.

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1. Introduction

Lower urinary tract symptoms (LUTS) occur among 15–80% of men >40 yr of age [1–4] and exert a substantial, and often underappreciated, negative effect on public health. LUTS are independently associated with increased mortality, an increased risk of falls, a substantially diminished quality of life, and depression [5–7]. The costs associated with diagnosis and treatment exceed $6 billion each year in the United States [1,8].

Relatively little research, however, has focused on prevention. Emerging data intimate that metabolic disturbances, and the lifestyle factors that modulate these disturbances, potentially contribute substantially to LUTS onset and progression. These observations are clinically important because they suggest the existence of modifiable pathways that might provide novel targets for LUTS prevention.

Two modifiable factors possibly involved with LUTS development are obesity and physical activity. Obesity has been associated with increased likelihood; conversely, increased physical activity has been associated with decreased likelihood [9–11]. Observations, however, are inconsistent [12–15]. These data are based predominantly on cross-sectional studies that did not explore the effects of obesity and exercise on the natural history of LUTS onset in asymptomatic men, investigate potential links between these two highly interrelated variables, or include detailed assessments of related metabolic factors that could confound or modify these associations.

Longitudinal analyses of obesity and exercise with incident LUTS, incorporating comprehensive evaluation of prevalent demographic and health conditions, would provide valuable insight by identifying at-risk individuals and elucidating behavior-related prevention strategies. Therefore, we examined the associations of adiposity and physical activity with incident LUTS in a large cohort of community-dwelling older men.

2. Methods

2.1. *Study population and design*

The Osteoporotic Fractures in Men Study (MrOS) is an institutional review board approved, prospective cohort study of community-dwelling older men designed to identify risk factors for falls, fractures, and other important conditions of aging. The MrOS study protocol includes a prospective collection of extensive information on prostate disease and LUTS [16].

2.2. *Demographic, lifestyle, and medical factors*

Participants provided information regarding age, race/ethnicity (white, black/African American, Asian, Hispanic, other), education level, marital status, socioeconomic status, self-reported health status, lifestyle measures (cigarette smoking and current alcohol consumption), medical history, benign prostatic hyperplasia (BPH) diagnosed by a doctor or other health care provider, and BPH treatment [16,17].

2.3. *Medication and supplement use*

Based on the information recorded at the baseline visit, participants were classified as currently using herbal supplements for urinary symptoms if they reported using saw palmetto, South African star grass, stinging nettle, rye grass pollen, pumpkin seed, African plum, or any other herb or supplement. Participants were classified as currently taking prescription urologic medications if they reported use of finasteride or if they had a prescription for 5α-reductase inhibitors (finasteride or dutasteride; dutasteride was included under medications at follow-up but was not available at baseline), α-blockers, or urinary-specific antispasmodics.

2.4. *Assessment of urinary symptoms*

LUTS were measured at two study time points, baseline and a follow-up visit, using the American Urological Association Symptom Index (AUA-SI).

2.5. *Assessments of adiposity and physical activity*

During the baseline study visit, participants were measured for height (centimeters) and weight (kilograms). Body mass index (BMI; kilograms per square meter) was calculated from the height and weight measures and categorized as normal (<25.0 kg/m^2), overweight (25.0–29.9 kg/m^2), or obese ($\geq$30 kg/m^2) [18]. Adipose tissue distribution in the whole body and the trunk was obtained with dual-energy x-ray absorptiometry (DXA) [19,20]. Percentage total body fat, percentage trunk fat, and the ratio of total trunk fat to total arm and leg fat were assessed; for the analysis each was scored by quartiles of the sample population.

Physical activity at baseline was self-reported using two assessments. First, participants provided a detailed assessment of their household, leisure, and occupational activities in the past 7 d on the 12-item Physical Activity Scale for the Elderly (PASE) [21]. Second, participants were asked, "Do you take walks for exercise, daily or almost every day? (yes or no)."

2.6. *Insulin and glucose*

At the baseline visit, blood was drawn while the subject was in a fasting state. For insulin, we stratified by quartiles. For fasting glucose, we stratified by quartiles and also by the American Diabetic Association guidelines as follows: normal, <100 mg/dl (<5.6 mmol/l); prediabetes, 100–125 mg/dl (5.6–6.9 mmol/l); and diabetes, $\geq$126 mg/dl ($\geq$7 mmol/l). We combined insulin and glucose measures using the homeostatic model assessment for insulin resistance (HOMA-IR), calculated as fasting serum insulin (mU/l) $\times$ fasting serum glucose (mmol/l)/22.5. Using this approach, insulin resistance is defined as having a HOMA-IR value $\geq$3.0 [7,22].

2.7. *Analytic cohort and primary outcome*

We restricted the analytic cohort to men with an AUA-SI of 0–7 at baseline and who reported no history of any treatment for BPH, no current use of herbal supplements for prostate symptoms, and no current prescription urologic medication. To avoid including symptoms associated with incident prostate cancer, we further excluded adjudicated incident prostate cancer cases occurring between baseline and the second clinic visit.

We defined onset of LUTS as any of the following at the follow-up clinic visit: an AUA-SI $\geq$8; documented current use of prescription medications including α-adrenergic blockers, urinary antispasmodics, and 5α-reductase inhibitors for urinary symptoms; or self-report of past use of prescription medications or noncancer surgery of the prostate.

2.8. Statistical analysis

Continuous variables were coded into sample quartiles or categorized using previously published cut points. For categorical variables, categories were sometimes combined to have sufficient sample sizes within each group. Baseline variables were tested for univariate association with incident LUTS using the Pearson chi-square test. For the primary variables of interest measuring physical activity levels, body composition (BMI, percentage body fat) and insulin and glucose metabolism, univariate association with incident LUTS was also assessed using the Cochran-Armitage test of trend across increasing categories [23]. Variables significant at the 10% level were carried forward for assessment in the final multivariate logistic regression models. Because PASE score and self-reported walking are two instruments that assess the same underlying construct (level of physical activity), in the final logistic regression models each was included in a separate model. Variables with p values <0.05 were retained in the model. Analyses were performed with SAS statistical software v.9.2 (SAS, Cary, NC, USA).

3. Results

3.1. Study population

Of the 5994 men enrolled in MrOS, 1695 (28%) reported a baseline AUA-SI <8, did not have a history of LUTS or treatment for LUTS, were not taking urologic medications at baseline, were not diagnosed with prostate cancer during follow-up, and had complete baseline and follow-up visit data (Fig. 1). The baseline mean age (standard deviation [SD]; range) of this analytic cohort was 72 (5; 65–91) yr. Mean (SD; range) follow-up time in the analytic cohort was 4.6 (0.5; 3.7–6.0) yr between baseline and the follow-up clinic visit.

3.2. Demographic, health, and lifestyle characteristics at baseline

At the follow-up clinic visit, 524 (31%) of the participants who were asymptomatic at baseline reported new-onset LUTS (175 treatment with surgery or medications and 349 with an AUA-SI ≥8). These men at baseline older, more likely to report at least one chronic medical condition, had lower PASE scores, and were less likely to walk daily than the men who did not report LUTS onset. There was no association of LUTS onset with race, educational attainment, socioeconomic status, diabetes, smoking status, or level of alcohol consumption (Table 1).

3.3. Metabolic characteristics

Men who reported incident LUTS had higher BMI than those who did not (Cochran-Armitage test for trend; $p = 0.02$). There were no associations of LUTS onset with body fat distribution as measured by DXA scanning or multiple measures of glucose homeostasis including fasting glucose, fasting insulin, or HOMA-IR (Table 2).

3.4. Multivariate models of body mass index, Physical Activity Scale for the Elderly score, and walking

The baseline measures indicating study site, age, presence of at least one medical condition, BMI, PASE, and self-reported

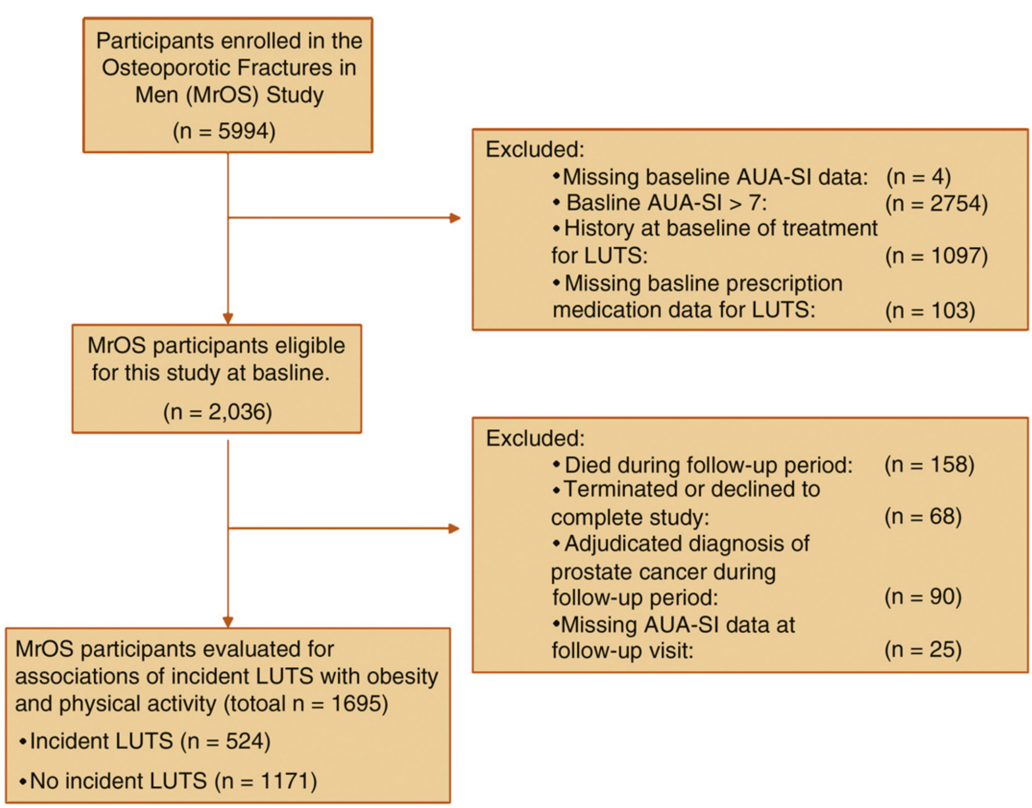

Fig. 1 – Study population.

Table 1 – Baseline demographic characteristics of the study population and onset of lower urinary tract symptoms at the second study visit (mean: 4.6 yr of follow-up)

	No.	Percentage with LUTS (n = 524), %	Percentage without LUTS (n = 1171), %	p value
Age, yr				0.02
65–69	675	29.0	71.0	
70–79	852	30.5	69.5	
≥80	168	40.5	59.5	
Race				0.47
White	1502	30.6	69.4	
Nonwhite	193	33.2	66.8	
Education				0.13
High school or less	398	33.9	66.1	
Some college or college degree	706	31.6	68.4	
Some graduate school or graduate degree	591	28.1	71.9	
SES (compared with United States)*				0.60
Below median	829	30.3	69.7	
Median and above	854	31.5	68.5	
Diabetes				0.23
No diabetes	1523	30.5	69.5	
Diabetes	172	34.9	65.1	
Chronic medical conditions†				0.01
Reported none	765	27.8	72.2	
Reported at least one	930	33.4	66.6	
Smoking status**				0.73
Never	672	30.2	69.8	
Former	948	31.7	68.4	
Current	74	28.4	71.6	
Alcohol consumption‡				0.82
Nondrinker	549	31.7	68.3	
Average <1 drink per day	680	30.3	69.7	
Average 1 to <2 drinks per day	242	29.3	70.7	
Average ≥2 drinks per day	223	32.7	67.3	
PASE*** score, quartile				0.06
<111.5	423	34.8	65.1	
111.5–150.9	422	29.9	70.1	
151.0–196.6	422	32.5	67.5	
>196.6	427	26.5	73.5	
Walking				0.02
Do not walk daily for exercise	839	33.6	66.4	
Walk daily for exercise	856	28.3	71.7	

LUTS = lower urinary tract symptoms; SES = socioeconomic status; PASE = Physical Activity Scale for the Elderly.
* Self-reported; 12 with missing data.
† Dizziness, diabetes, heart attack, stroke, or high blood pressure.
‡ One with missing data.
** One with missing data.
*** PASE; one with missing data.

walking were carried forward to the multivariate logistic regression models. In addition, because of significant differences between sites in educational levels, we retained educational level in the final models. Because PASE score and self-reported walking are two instruments that assess the same underlying construct (level of physical activity), we included each in a separate model (Table 3). Whether using PASE score or self-reported daily walking, overweight and obese (BMI ≥25 kg/m^2) participants were significantly more likely to report LUTS onset than normal (BMI <25 kg/m^2) participants (Table 3). Compared with those in the lowest quartile, participants in the highest quartile of physical activity as measured by PASE score were 29% less likely to report LUTS onset. Similarly, those who walked were 20% less likely to report LUTS symptoms compared with those who did not walk.

4. Discussion

To our knowledge, this is the first prospective study to investigate the associations of obesity and physical activity with incident urinary symptoms in a cohort of community-dwelling elderly men. In this cohort, compared with men of normal BMI, men who were overweight or obese had 29% (OR_{adj}: 1.29) and 41% (OR_{adj}: 1.41) higher odds, respectively, of developing LUTS over the approximate 5-yr study period.

Table 2 – Baseline metabolic characteristics of the study population and onset of lower urinary tract symptoms at the second study visit (mean: 4.6 yr of follow-up)

	No.	Percentage with LUTS (n = 524), %	Percentage without LUTS (n = 1171), %	p value
BMI, kg/m^2				0.06
<25	439	26.7	73.3	
25–29.9	884	31.7	68.3	
≥30	372	34.1	65.9	
Percentage total body fat, quartile				0.11
<22.7	421	31.1	68.9	
22.7–26.2	422	26.8	73.2	
26.3–29.9	421	33.7	66.3	
>29.9	422	31.5	68.5	
Missing	9	55.6	44.4	
Percentage trunk fat, quartile				
<24.8	421	31.4	68.6	0.17
24.8–29.1	422	27.3	72.7	
29.2–33.3	421	33.3	66.7	
>33.3	422	31.3	68.7	
Missing	9	55.6	44.4	
Fasting glucose, quartile, mg/dl				0.31
<93	355	31.3	68.7	
93–99	390	28.2	71.8	
100–109	389	30.9	69.2	
>109	408	34.6	65.4	
Missing	153	27.5	72.5	
Fasting glucose, cut points, mg/dl				0.44
Normal	745	29.7	70.3	
Prediabetic	617	32.9	67.1	
Diabetic	180	32.2	67.8	
Missing	153	27.5	72.5	
Fasting insulin, quartile, μIU/ml				0.72
<5.56	385	32.7	67.3	
5.6–8.2	385	30.4	69.6	
8.3–12.1	385	32.2	67.8	
>12.1	387	29.7	70.3	
Missing	153	27.5	72.5	
HOMA-IR, quartile				0.85
<1.34	385	31.9	68.1	
1.34–2.06	386	32.1	67.9	
2.07–3.25	385	30.6	69.4	
>3.26	386	30.3	69.7	
Missing	153	27.5	72.5	
HOMA-IR, cut points				0.42
Normal (<3)	1093	31.9	68.1	
Insulin resistant (≥3)	449	29.6	70.4	
Missing	153	27.5	72.5	

LUTS, lower urinary tract symptoms; BMI = body mass index; HOMA-IR = Homeostatic Model Assessment for Insulin Resistance.

In contrast, compared with men in the lowest quartile of physical activity as assessed by PASE score, men in the highest quartile were 29% less likely to develop LUTS (OR_{adj}: 0.71). The apparent protective association with increased physical activity remained significant in a model adjusted for BMI, suggesting that increased physical activity may have significantly diminished the probability of symptom onset even among overweight and obese men. Additionally, those who walked daily for exercise were 20% less likely to report LUTS compared with those who did not walk daily (OR_{adj}: 0.80).

Our results are consistent with the hypothesis that excess body weight may promote and exercise may protect against the onset of LUTS in older men. LUTS prevention thus represents another potential health benefit of exercise in elderly men. Because more than one in three men in the entire cohort developed LUTS within 5 yr, our data represent substantial, clinically relevant variations in risk with potentially important applications to medical practice.

These data are consistent with prior studies of LUTS, obesity, and physical activity. In prior cross-sectional analyses, obesity was associated with increased prevalence of LUTS [7,9] and related outcomes including BPH surgery [7,9] and prostate enlargement [11]. In the only previous prospective study, obese men (as determined by BMI at

Table 3 – Multivariable-adjusted odds ratios for lower urinary tract symptoms progression by physical activity as measured by the Physical Activity Scale for the Elderly score and daily walking

Variable	Model 1: Physical activity				Model 2: Walking			
	OR	95% CI		*p* value	OR	95% CI		*p* value
Age, yr								
65–69	Ref	–	–	–	Ref	–	–	–
70–79	1.03	0.82	1.29	0.80	1.05	0.84	1.31	0.68
≥80	1.53	1.06	2.21	0.02	1.65	1.15	2.38	0.007
Education								
High school or less	Ref	–	–	–	Ref	–	–	–
Some college or college degree	0.98	0.74	1.29	0.87	0.99	0.75	1.31	0.96
Some graduate school or graduate degree	0.86	0.64	1.16	0.33	0.87	0.65	1.18	0.38
Chronic medical conditions[†]								
No medical condition	Ref	–	–	–	Ref	–	–	–
Any medical condition	1.20	0.97	1.49	0.09	1.22	0.98	1.51	0.07
BMI, kg/m^2								
<25	Ref	–	–	–	Ref	–	–	–
25–29.9	1.29	1.00	1.68	0.05	1.29	1.00	1.68	0.05
>30	1.41	1.03	1.93	0.03	1.40	1.02	1.91	0.04
PASE score								
<111.5	Ref	–	–	–	–			
111.5–150.9	0.80	0.60	1.08	0.15	–	–	–	–
151.0–196.6	0.95	0.71	1.27	0.72	–	–	–	–
>196.6	0.71	0.53	0.97	0.03	–	–	–	–
Walking								
No daily walking	–	–	–	–	Ref	–	–	–
Daily walking	–	–	–	–	0.80	0.65	0.98	0.03

CI = confidence interval; OR = odds ratio; BMI = body mass index; PASE = Physical Activity Scale for the Elderly.
* Models are controlled for study site in addition to all the variables listed in the body of the table.
[†] Including diabetes, heart attack, stroke, high blood pressure, or trouble with dizziness.

study entry) were up to 30% more likely to be diagnosed subsequently with BPH [14]. Conversely, exercise and increased physical activity have been linked, in many of the same study populations, with a decreased likelihood of LUTS [24]. A meta-analysis of eight cross-sectional studies indicated that moderate to vigorous physical activity reduced the prevalence of BPH or LUTS by up to 25% relative to a sedentary lifestyle [25]. The one prospective analysis of exercise observed no associations with incident BPH [14]. Other, smaller studies have noted equivocal [26] or null cross-sectional associations of obesity with LUTS and related outcomes. It is possible that the same potential mechanisms by which obesity increases LUTS risk, including inflammatory pathways and alterations in endogenous sex steroid hormone levels, may be counterbalanced by exercise [25].

A preponderance of the existing literature supports a positive association of LUTS-related outcomes with prevalent diabetes and blood markers of disruptions in glucose homeostasis, including elevated fasting glucose, elevated insulin, and HOMA [27].We did not observe a higher risk of incident LUTS with any of these variables.

LUTS affect millions of older men and generate substantial medical and economic costs. Both the prevalence and incidence of LUTS and BPH in the United States are steadily increasing (http://www.UDAonline.net) [28]. Prior clinical research has focused almost exclusively on treatment with surgery or medication. Walking once daily is simple, straightforward, and beneficial to global health. Indeed, walking is the most common form of exercise among older adults [29]. Thus, in counseling older men about the favorable outcomes of walking and other forms of physical exercise, clinicians should consider including LUTS prevention as part of the discussion.

Our study has several strengths that distinguish it from prior investigations. First, it explored the natural history of urinary symptom onset in initially asymptomatic men. Second, it examined effects of adiposity and physical activity in the same analytical models. Third, it incorporated a comprehensive array of demographic and metabolic variables not included in previous analyses. DXA scanning allowed us to examine the association of adipose tissue distribution, particularly in the abdomen, with LUTS, a novel and important study characteristic, given the biologic relation of adipose tissue distribution to insulin and glucose [30]. Finally, our study is the first to use the PASE questionnaire to assess quantitatively the effect of physical activity on urinary symptoms. The merit of the validated PASE instrument is that it assesses the types of activities commonly engaged in by elderly adults [21].

A potential limitation of this analysis is that the homogeneous composition of MrOS—predominantly healthy, white, well-educated volunteers–potentially diminishes the external validity of the results. Another possible limitation is the absence of urinary bother, storage, and voiding symptom analyses. Finally, our models were not able to take into account the following variables that may potentially affect LUTS: sexual health, hormones, phosphodiesterase type 5 inhibitor and diuretic therapy, incident neurologic disease, renal function, sleep apnea, fluid intake, prostate volume measures, prostate-specific antigen, or urodynamics.

5. Conclusions

In older men, modest amounts of physical activity and walking appear to be associated with a reduction in the 5-yr incidence of LUTS. Although randomized trials may be needed to establish definitively the efficacy of exercise and other forms of increased physical activity for LUTS prevention and control, there are no drawbacks to discussing the potential urinary health benefits of exercise with older male patients. Given the high prevalence of LUTS among older men, exercise has the potential to substantially reduce the burden of urinary disease in older men.

Author contributions: J. Kellogg Parsons had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Parsons, Marshall.
Acquisition of data: Marshall.
Analysis and interpretation of data: Parsons, Marshall, White, Messer.
Drafting of the manuscript: Parsons.
Critical revision of the manuscript for important intellectual content: Messer, Barrett-Connor, Bauer, Marshall.
Statistical analysis: Messer, White, Marshall.
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