Relationship Between Central Obesity, General Obesity, Overactive Bladder Syndrome and Urinary Incontinence Among Male and Female Patients Seeking Care for Their Lower Urinary Tract Symptoms


OBJECTIVES
To describe the relationship between metabolic factors and lower urinary tract symptoms, overactive bladder syndrome (OAB) and urinary incontinence (UI).

METHODS
Adult male and female patients who presented to a clinician from the symptoms of lower urinary tract dysfunction research network were recruited. Urinary symptoms (presence of OAB, any UI, stress UI (SUI), urgency UI (UUI), urgency, frequency, and nocturia) were assessed with the lower urinary tract symptoms tool. Metabolic factors assessed included central obesity (waist circumference, using the Adult Treatment Panel III, the International Diabetes Federation thresholds, and waist circumference as a continuous variable), general obesity (body mass index as dichotomous or continuous variables), diabetes mellitus, hypertension, and dyslipidemia. Multivariable logistic regression was used to test for associations.

RESULTS
920 participants were studied. In multivariable analyses, central obesity (per 10 cm larger waist) was associated with higher odds of UI in both sexes (odds ratio [OR] = 1.16, \( P = .008 \)), SUI in females (\( OR = 1.27, P = .008 \)), UUI in both sexes (\( OR = 1.24, P = .001 \)), OAB in females (\( OR = 1.248, P = .003 \)), as well as frequency and nocturia. General obesity (5-unit increase in body mass index) was associated with UI, UUI, urgency and frequency in both sexes, and with SUI and OAB in females. We did not find associations between central or general obesity and OAB in males. Dyslipidemia was associated with nocturia \( \geq 2 \).

CONCLUSION
In patients, central and general obesity were key metabolic factors associated with UI in both males and females, and with OAB in females but not in males. The association between dyslipidemia and nocturia \( \geq 2 \) needs further research.

The prevalence of metabolic factors such as obesity and diabetes in the United States has been increasing. The morbidity and mortality associated with metabolic factors are costly and pose a serious burden to society. Recent studies suggest that metabolic factors may play a role in the development of overactive bladder syndrome (OAB), urinary incontinence (UI) and other lower urinary tract symptoms (LUTS). However, the literature has major knowledge gaps. For females, studies have shown high body mass index (BMI) to be a risk factor for UI. However, the relationships between obesity and OAB are less clear. The results are conflicting; some studies showed that high BMI was associated...
with OAB while other studies\textsuperscript{8,9} showed no association. For males, studies have reported associations between metabolic factors and higher American Urological Association Symptom Index scores.\textsuperscript{10–13} However, the relationships between metabolic factors and UI and OAB in males have not been well studied. In addition, most studies were community-based; thus it is unclear whether the findings would apply to patients seeking care for their LUTS.\textsuperscript{2,3,5–8,10–12,14–19} Among studies that have examined obesity, most have only reported on BMI.\textsuperscript{5,7,8,15–18} Few studies have specifically evaluated central obesity for its association with urinary symptoms.\textsuperscript{6,9}

The Symptoms of lower urinary tract dysfunction research network (LURN)\textsuperscript{20,21} sought to address these knowledge gaps by recruiting a large cohort of male and female patients who were seeking care for their LUTS. We assessed multiple metabolic factors (including 3 measures of central obesity, 3 measures of BMI, diabetes, hypertension, and dyslipidemia), and their relationships to OAB, UI, and other LUTS. We expect to gain insights into the relevant and modifiable metabolic factor(s) associated with these LUTS that may inform future primary and secondary management and prevention strategies.

**MATERIALS AND METHODS**

**Study Design and Population**

The LURN Observational Cohort Study\textsuperscript{20,21} recruited adult male and female patients over the age of 18 who presented to a urologist or urogynecologist for treatment of their LUTS between June 2015 and January 2017 at 1 of 6 LURN clinical centers in the United States. Participants were followed prospectively for 1 year, although data reported herein only include baseline data. The inclusion and exclusion criteria and details of the study design have been previously reported.\textsuperscript{21} Participants with neurogenic conditions or neurogenic bladder were excluded. The following data were collected at the baseline visit: urinary symptoms, medical history, medication use, systolic and diastolic blood pressure, BMI, and waist circumference measurements. All participants provided informed consent. The protocol was approved by the institutional review boards of all participating research sites.

**Measures**

Central obesity was assessed based on waist circumference measurements. Three measures of central obesity were used: (1) the Adult Treatment Panel III (ATP III) Guidelines of ≥102 cm for males, ≥88 cm for females;\textsuperscript{1} (2) the 2004 Consensus Statement from the International Diabetes Federation (IDF) of ≥94 cm for white males, ≥80 cm for white females;\textsuperscript{12} and (3) waist circumference as a continuous variable. Body weight and height were also measured, and BMI was calculated as the weight in kilograms divided by the square of the height in meters. General obesity was defined as BMI ≥30; overweight was defined as BMI ≥25; and BMI was also used as a continuous variable.

The majority of studies in the literature have only assessed BMI. Since central obesity is a key component of metabolic syndrome, we have also included measures of central obesity in addition to BMI. We have included the 2 most commonly used definitions of central obesity (ATP III and IDF) to be comprehensive. The ATP III definition used the same waist circumference cutoffs regardless of race, while the newer IDF definition used race-specific waist circumference cutoffs. Also, the IDF used lower cutoffs to include subjects who are overweight but not yet considered obese.

Hypertension was defined by a measured systolic pressure ≥130 mm Hg, diastolic pressure ≥85 mm Hg, or self-reported medication(s) to treat hypertension. Dyslipidemia was defined by self-reported medication(s) taken to treat elevated serum cholesterol or triglycerides. Diabetes was defined by a self-reported medical history of diabetes mellitus.

Urinary symptoms were assessed using the LUTS Tool\textsuperscript{22} with a 1-week recall period. Seven LUTS Tool questions addressed UI; participants with responses of “rarely” or “never” to all seven UI questions were classified as “without UI” and responses of “sometimes” or greater to at least 1 symptom of UI were classified as “with UI.” Two LUTS Tool questions addressed stress urinary incontinence (SUI), leakage while exercising or during a laugh, cough, or sneeze. Participants who classified as having SUI if they had responses of “sometimes” or more to at least 1 of 2 leakage questions. Participants who answered “sometimes” or more to a sudden need to rush to urinate were classified as having urgency. A follow-up question asked about urinary leakage due to a sudden feeling of needing to rush to urinate; those who responded “sometimes” or more were classified as having urgency urinary incontinence (UUI).

Participants who reported that they “sometimes,” “often” or “almost always” urinate too frequently were classified as having frequency. Those who reported that they wake up because of the need to urinate 1 or 2 times a night or more were classified as having nocturia ≥1 or nocturia ≥2 respectively. Participants who answered affirmatively to the urgency question, and who also reported frequency and/or nocturia were classified as having overactive bladder syndrome (OAB), in accordance with the definition of the International Continence Society.\textsuperscript{24} Among those with OAB, they were further classified into 2 groups: with UI (also referred as “OAB-wet”) or without UI ("OAB-dry").

**Statistics**

Demographics and other participant characteristics are shown as means and standard deviations, or medians and interquartile ranges, as appropriate, for continuous variables and as frequencies and percentages for categorical variables.

Multivariable logistic regression models were fitted to test associations between metabolic factors and the LUTS groups described above. For each outcome (e.g., UI, OAB), regression models were developed using the following metabolic predictors: central obesity cutoffs defined by ATP III or by IDF, waist circumference as a continuous variable, general obesity (BMI ≥30), overweight status (BMI ≥25), BMI as a continuous variable, hypertension, diabetes, and dyslipidemia. Additional candidate covariates included sex, age, race, ethnicity, and smoking status. Menopausal status, hormonal use, parity, and pelvic organ prolapse quantification classification were also included for females using interactions with sex. Model selection was guided by the method of best subsets. Interactions between sex and waist circumference/BMI (both continuous and dichotomous versions) were tested in all models and are presented when statistically significant ($P < .05$). All $P$ values were adjusted for multiple comparisons using the false discovery rate correction. Models are shown with the adjusted odds ratios and 95% confidence.
levels. All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

Among the 1064 participants recruited into the LURN Observa-
tional Cohort Study, 920 had complete data on metabolic fac-
tors and had complete responses to at least 15 out of 22
questions on the LUTS Tool. Demographics and characteris-
tics of these 920 participants (456 males and 464 females) are
included in the Supplemental Table. The mean age was 59.1 ±
13.9 years; 81.5% were white, most had central obesity per ATP
III definition (60.4%) or IDF definition (70.2%), 43.4% had
general obesity (BMI ≥30), 76.5% were overweight (BMI ≥25),
65.2% had hypertension, 31.5% had dyslipidemia, and 17.1% had
diabetes mellitus. The lower percentage with central obesity
using the ATP III vs the IDF definition was due to higher cutoff
values with ATP III. Regarding incontinence, 33.1% had no UI,
7.4% had SUI, 20.4% had mixed UI, and 13.0% had other UI; 63.4% of participants had OAB (urgency
plus either frequency or nocturia). Among those with OAB,
66.4% had OAB with UUI (“OAB-wet”), and 33.6% had OAB
without UUI (“OAB-dry”).

Table 1 shows the relationships between central obesity and
LUTS (multivariable logistic regression). We include the results
from all 3 obesity measures in the table (central obesity cutoffs
defined by ATP III, defined by IDF, and waist circumference as a
continuous variable), but will describe the results of the continu-
ous predictors in more detail below, keeping in mind that the
dichotomous predictors also identify several significant predic-
tors.

Higher waist circumference was associated with higher
odds of having any UI (OR = 1.16 per 10 cm increase, 
\( P = .008 \)) and UUI (OR = 1.24 per 10 cm increase, 
\( P = .001 \)) in both sexes, and SUI in females (OR = 1.27 per 10 cm
increase, \( P = .008 \)). In females, there was a relationship
between waist circumference and OAB (OR = 1.25/10 cm
increase, \( P = .003 \)), however the relationship was not
detected in males (OR = 1.02/10 cm increase, \( P = .73 \)). Among participants with OAB, higher waist circumference
was associated with UUI vs without UUI (“OAB-wet” vs
“OAB-dry,” OR = 1.26/5 unit increase, \( P = .006 \)). Dyslipidemia
was also associated with nocturia \( \geq 2 \) in this model (OR = 1.48,
\( P = .021 \)). Of the other covariates, older age, female sex, and
African American race were also associated with multiple uri-
inary symptoms (Tables 1 and 2).

DISCUSSION

Previous community-based studies have demonstrated
relationships between high BMI and UI in females,\(^2,3\) and
between metabolic factors and higher AUA Symptom
Index in males.\(^4\) However, the relationships between
metabolic factors and OAB in females were less clear.\(^5\)
Also the relationships between metabolic factors and UI
and OAB in males have not been well studied. In this
study we found associations between both central and
general obesity and OAB in females, and UI and its sub-
types in males and females. We did not find association
between central or general obesity and OAB in males.
We also found an association between dyslipidemia and
nocturia \( \geq 2 \) in the clinical population.

Our observations in the clinical cohort were consistent to
those reported in the Boston Area Community Health (BACH)
population-based cohort.\(^6\) In the BACH Study, the
odds of having OAB increased with waist circumference
and with BMI in females. However, in males, there
were negative associations up to 100 cm waist circumference
or a BMI of 27.5, and then positive associations
beyond those thresholds.\(^6\) In longitudinal studies, Dal-
losso et al also showed that obesity at baseline was associ-
ated with new onset of OAB 1 year later in women\(^18\); however obesity at baseline was not associated with new
onset of OAB 1 year later in men.\(^17\) Taken together, the
data suggested that there might be important sex differ-
ence in the relationships between obesity and OAB.

This sex difference raises some interesting research pos-
sibilities. For example, hormonal factors may play a role.
Anatomic factors may account for some of the sex differ-
ences. Increased abdominal pressure from central (vis-
ceral) obesity could increase the pressure on the bladder,
stretch the pelvic floor, or trigger urine entry into the
proximal urethra, which could in turn cause prolapse, ure-
thral hypermobility, and OAB symptoms in females.
Males however are less susceptible to these anatomic
forces since males do not develop prolapse, urethral hyper-
mobility, or an open bladder neck. Besides local mechani-
ical forces, systemic factors such as neuroendocrine,
vascular or inflammatory processes can provide a link
between obesity and OAB. Adipose tissue produces leptin,
which can stimulate the sympathetic nervous system activ-
ity, and exacerbate urinary frequency.\(^25,26\) The generation
of inflammatory factors (e.g. cytokines, C-reactive protein)
from visceral adipose tissue may also influence bladder sen-
sory function. Obesity is also associated with vascular dys-
function and ischemia. Vascular ischemia in pelvic
structures including the bladder has been demonstrated to
drive detrusor overactivity and OAB in animal models.\(^27\)
In summary, the pathophysiology that links obesity and
Table 1. Relationships between central obesity (waist circumference) and LUTS (multivariable logistic regression)

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Variable</th>
<th>Models Using Central Obesity ATP III Definition (Yes vs No)</th>
<th>Models Using Central Obesity IDF Definition (Yes vs No)</th>
<th>Models Using Waist Circumference (Continuous Measures)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Odds Ratio (OR) Lower 95% CI Upper 95% CI FDR adjusted P value</td>
<td>Odds Ratio (OR) Lower 95% CI Upper 95% CI FDR adjusted P value</td>
<td>Odds Ratio (OR) Lower 95% CI Upper 95% CI FDR adjusted P value</td>
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<td>UI (odds of having any UI)</td>
<td>Central Obesity</td>
<td>1.411 1.009 1.973 .058</td>
<td>Central Obesity</td>
<td>0.872 0.585 1.300 .637</td>
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<td>Female vs Male</td>
<td>4.572 3.223 6.487 &lt;.001</td>
<td>Female vs Male</td>
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<td>Female vs Male</td>
<td>5.262 3.733 7.418 &lt;.001</td>
<td>Female vs Male</td>
<td>1.271 1.08 1.495 .008</td>
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<td>SU1 (in females only)*</td>
<td>Central Obesity</td>
<td>1.716 1.175 2.507 .011</td>
<td>Central Obesity</td>
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<td>Female vs Male</td>
<td>7.174 4.868 10.572 &lt;.001</td>
<td>Female vs Male</td>
<td>7.761 5.302 11.359 &lt;.001</td>
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<td>Female vs Male</td>
<td>1.248 1.093 1.426 .003</td>
<td>Female vs Male</td>
<td>1.248 1.093 1.426 .003</td>
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<td>UUI</td>
<td>Central Obesity</td>
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<td>Central Obesity</td>
<td>1.232 0.837 1.814 .407</td>
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<td>Female vs Male</td>
<td>1.232 0.837 1.814 .407</td>
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<td>2.493 1.530 4.063 .001</td>
<td>Female vs Male</td>
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<td>2.493 1.530 4.063 .001</td>
<td>Female vs Male</td>
<td>2.493 1.530 4.063 .001</td>
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<td>OAB</td>
<td>Central Obesity - Males</td>
<td>1.174 1.050 1.312 .011</td>
<td>Female vs Male</td>
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<td>Central Obesity - Females</td>
<td>1.149 1.117 1.293 .034</td>
<td>Female vs Male</td>
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<td>Central Obesity - Females</td>
<td>1.149 1.117 1.293 .034</td>
<td>Female vs Male</td>
<td>1.197 1.137 1.263 .004</td>
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<td>1.149 1.117 1.293 .034</td>
<td>Female vs Male</td>
<td>1.197 1.137 1.263 .004</td>
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<td>OAB with UUI vs without UUI (among those with OAB only)</td>
<td>Central Obesity</td>
<td>1.422 0.931 2.172 .123</td>
<td>Central Obesity</td>
<td>1.159 0.685 1.96 .681</td>
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<td>Female vs Male</td>
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<td>Female vs Male</td>
<td>1.327 0.96 1.834 .108</td>
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<td>3.142 2.008 4.385 &lt;.001</td>
<td>Female vs Male</td>
<td>3.142 2.008 4.385 &lt;.001</td>
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Table 1. Continued

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Models Using Central Obesity ATP III Definition (Yes vs No)</th>
<th>Models Using Central Obesity IDF Definition (Yes vs No)</th>
<th>Models Using Waist Circumference (Continuous Measures)</th>
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<td>Black vs Non-Black</td>
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<td>Black vs Non-Black Hypertension (Yes vs No)</td>
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<td>Nocturia ≥1 Males</td>
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<td>Central Obesity - Females</td>
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<td>Age (per 10 years)</td>
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<td>Black vs Non-Black Dyslipidemia (Yes vs No)</td>
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<td>1.703</td>
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Abbreviations: CI = confidence limit; FDR = false discovery rate; OAB = overactive bladder syndrome; SUI = stress urinary incontinence; UI = urinary incontinence; UUI = urgency urinary incontinence

* Males with a history of prostate cancer were excluded from the study. Since male SUI was rare, only female SUI was analyzed.

Comparing OAB with UUI vs OAB without UUI (“OAB-wet” vs “OAB-dry”).
<table>
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<tr>
<th>Models Using General Obesity</th>
<th>Odds Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>FDR adjusted P value</th>
<th>Variable</th>
<th>Models Using Overweight Status</th>
<th>Odds Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>FDR adjusted P value</th>
<th>Variable</th>
<th>Models Using BMI (Continuous Measures)</th>
<th>Odds Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>FDR adjusted P value</th>
<th>Variable</th>
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<td>(BMI ≥30 vs &lt;30)</td>
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<td>UI (odds of having any UI)</td>
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<td>Female vs Male</td>
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<td>SUI (in females only)*</td>
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<tr>
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<td>Hypertension (Yes vs No)</td>
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<td>Female vs Male</td>
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<td>2.960</td>
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<tr>
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<td>1.699</td>
<td>.502</td>
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<td>OAB General Obesity - Females</td>
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<td>3.753</td>
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<tr>
<td>OAB vs without UUI (among those with OAB only)†</td>
<td>1.148</td>
<td>1.129</td>
<td>1.507</td>
<td>&lt;.001</td>
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<tr>
<td>General Obesity - Males</td>
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<td>.007</td>
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<td>General Obesity - Females</td>
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<td>2.222</td>
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<tr>
<td>Age (per 10 years)</td>
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Abbreviations: CI = confidence limit; FDR = false discovery rate; OAB = overactive bladder syndrome; SUI = stress urinary incontinence; UI = urinary incontinence; UUI = urgency urinary incontinence
* Males with a history of prostate cancer were excluded from the study. Since male SUI was rare, only female SUI was analyzed.
† Comparing OAB with UUI vs OAB without UUI (“OAB-wet” vs “OAB-dry”).
OAB is poorly understood, and the mechanisms behind the sex differences need to be further examined.

Among participants with OAB, increases in continuous BMI and waist circumference were associated with UUI vs without UUI (“OAB-wet” vs “OAB-dry”). Our results were in contrast to a Korean community study which showed that high BMIs were associated with “OAB-dry” but not “OAB-wet.” Our clinical cohort consisted of patients who presented to tertiary urology and urogynecology clinics seeking care for their LUTS; thus, it was possible that the community sample may have less severe UUI, and therefore did not permit the discovery of an association.

Although a number of measures of adiposity are available that account for different aspects of obesity, they have rarely been evaluated together for their associations with urinary symptoms. Among studies that have examined obesity, most have only reported on BMI. Since the distribution of fat in the abdominal viscera—central obesity—is a key component of metabolic syndrome, and central obesity is more predictive of cardiovascular risk than high BMI, we have specifically examined 3 measures of central obesity (the ATP III definition, the IDF definition, and waist circumference as a continuous measure) and 3 measures of BMI (general obesity [BMI ≥30], overweight status [BMI ≥25], and BMI as a continuous measure), to assess differences among these measures of obesity with respect to their relationships to UI and OAB. Overall the continuous measures of waist circumference or BMI showed the strongest relationships with incontinence measures, followed by central obesity (ATP III) and general obesity (BMI ≥30). As shown in Figure 1, there was high correlation between waist circumference and BMI in our care seeking cohort. No associations were found with central obesity defined by IDF, which has lower cutoffs than ATP III. This is likely due to the distribution of waist circumference in the LURN sample resulting in similar odds of LUTS when participants are grouped using the IDF definition despite a positive association with waist circumference (as a continuous variable). This is illustrated in Figure 2 using UUI in males as an example. It is also possible that the positive association is less strong at lower values of waist circumference, however we did not have adequate sample size to detect this difference. Despite this limitation, the use of continuous predictor variables for waist circumference and BMI revealed the substantial gain in power over use of dichotomized variables, and may explain some of the conflicting results from prior studies that used dichotomous predictors. For similar reasons, overweight status was not associated with many LUTS due to lower BMI cutoffs, even though there were positive associations with higher BMI (as a continuous variable).

In this study we were not able to demonstrate any relationships to other metabolic factors including diabetes and hypertension. A novel association between dyslipidemia and nocturia ≥2 was observed, that to our knowledge has never been reported in the literature. One study from Taiwan (n = 1827) found an increased odds of OAB in individuals with dyslipidemia. In the BACH Study, the use of statins was associated with lower prevalence of LUTS among older men but not among women or younger men. Unfortunately neither of these studies had looked specifically at nocturia. The significance of the potential link between nocturia and dyslipidemia is unclear at this time and should be further investigated.

Our data showed that obesity is a key modifiable metabolic factor associated with UI, SUI, UUI, and OAB.

**Figure 1.** Scatterplots of body mass index (BMI) by waist circumference for males and females, with Pearson correlation coefficients (both P < .001). Dashed lines show the ATP III criteria for central obesity (waist circumference ≥102 cm for males, ≥88 cm for females) and the general obesity criterion of BMI ≥30.
This finding may have important implications for primary and secondary preventive strategies to reduce the prevalence and burden of OAB and UI. Weight loss interventions targeting physical activity and healthy diet might be considered as an adjuvant therapy in OAB and UI patients who are obese. A 2015 Cochrane systematic review concluded that the therapeutic effect of weight loss on UI is building and should be a research priority.  

The strength of the study included: enrollment of a large cohort (>900) of patients who were seeking care for their LUTS at 6 clinical centers; inclusion of both males and females; and measurement of both waist circumference and BMI so we could examine various measures of obesity along with other metabolic factors. Our use of continuous predictor variables for waist circumference and BMI also revealed the substantial gain in power over use of dichotomized variables. There are several potential weaknesses of the study. We did not collect fasting glucose, hemoglobin A1c, HDL-cholesterol, or triglyceride serum levels to fully assess metabolic syndrome. For participants who took medications for hypertension, dyslipidemia or diabetes, we did not further subcategorize them into those whose conditions were poorly controlled vs well controlled. Also, instead of using multiple instruments to assess different LUTS (e.g. OAB-q for OAB), we chose to use 1 instrument (LUTS Tool) as a comprehensive tool to assess a variety of LUTS. Only participants from specialty clinics (urology, urogynecology) in tertiary academic medical centers were enrolled, which may limit the generalizability of the findings. Finally our cross-sectional data does not permit one to draw inference on causality or temporal relationships.

**CONCLUSION**

In care-seeking patients with LUTS, central obesity and general obesity were key metabolic factor associated with UI in both males and females, and with OAB in females. We did not demonstrate association between obesity and OAB in males. The association between dyslipidemia and nocturia ≥2 needs further research. Weight loss is a promising therapeutic intervention. Future research could focus on optimizing this intervention.

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SUPPLEMENTARY MATERIALS


References