The Persistency Index: A novel screening tool for identifying myofascial pelvic floor dysfunction in patients seeking care for lower urinary tract symptoms

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BACKGROUND: Patients with myofascial pelvic floor dysfunction often present with lower urinary tract symptoms, such as urinary frequency, urgency, and bladder pressure. Often confused with other lower urinary tract disorders, this constellation of symptoms, recently termed myofascial urinary frequency syndrome, is distinct from other lower urinary tract symptoms and optimally responds to pelvic floor physical therapy. A detailed pelvic floor myofascial examination performed by a skilled provider is currently the only method to identify myofascial urinary frequency syndrome. Despite a high influence on quality of life, low awareness of this condition combined with no objective diagnostic testing leads to the frequent misdiagnosis or underdiagnosis of myofascial urinary frequency syndrome.

OBJECTIVE: This study aimed to develop a screening measure to identify patients with myofascial urinary frequency syndrome (bothersome lower urinary tract symptoms secondary to myofascial pelvic floor dysfunction) from patient-reported symptoms.

STUDY DESIGN: A population of patients with isolated myofascial urinary frequency syndrome was identified by provider diagnosis from a tertiary urology practice and verified by standardized pelvic floor myofascial examination and perineal surface pelvic floor electromyography. Least Angle Shrinkage and Selection Operator was used to identify candidate features from the Overactive Bladder Questionnaire, Female Genitourinary Pain Index, and Pelvic Floor Distress Index predictive of myofascial urinary frequency syndrome in a pooled population also containing subjects with overactive bladder (n=42), interstitial cystitis/bladder pain syndrome (n=54) (derivation cohort). A simple, summated score of the most discriminatory questions separating a population of women seeking care for lower urinary tract symptoms with myofascial urinary frequency syndrome was more prevalent in younger subjects, the inclusion of an age penalty (3 points added if under the age of 50 years) improved the area under the curve to 0.8. This score was defined as the Persistency Index (possible score of 0–15). The Youden Index was used to identify the optimal cut point Persistency Index score for maximizing sensitivity and specificity.

RESULTS: Using a development cohort of 215 subjects, the severity (Pelvic Floor Distress Index 5) and persistent nature (Female Genitourinary Pain Index 5) of the sensation of incomplete bladder emptying and dyspareunia (Female Genitourinary Pain Index 2b) were the most discriminatory characteristics of the myofascial urinary frequency syndrome group, which were combined with age to create the Persistency Index. The Persistency Index performed well in a validation cohort of 719 patients with various lower urinary tract symptoms, including overactive bladder (n=285), interstitial cystitis/bladder pain syndrome (n=53), myofascial urinary frequency syndrome (n=111), controls (n=209), and unknown diagnoses (n=61), exhibiting an area under the curve of 0.74. A Persistency Index score ≥7 accurately identified patients with myofascial urinary frequency syndrome from an unselected population of individuals with lower urinary tract symptoms with 80% sensitivity and 61% specificity. A combination of the Persistency Index with the previously defined Bladder Pain Composite Index and Urge Incontinence Composite Index separated a population of women seeking care for lower urinary tract symptoms into groups consistent with overactive bladder, interstitial cystitis/bladder pain syndrome, and myofascial urinary frequency syndrome phenotypes with an overall diagnostic accuracy of 82%.

CONCLUSION: Our study recommends a novel screening method for patients presenting with lower urinary tract symptoms to identify patients with myofascial urinary frequency syndrome. As telemedicine becomes more common, this index provides a way of screening for myofascial urinary frequency syndrome and initiating pelvic floor physical therapy even before a confirmatory pelvic examination.

Key words: benign urological conditions, interstitial cystitis, lower urinary tract symptoms, nomogram, overactive bladder, persistency

Introduction

Lower urinary tract symptoms (LUTS), such as urinary frequency, urgency, and bladder discomfort, are common and affect most individuals during their life. Despite this high prevalence, diagnostic tools are sparse and rely heavily on clinician judgment. This lack of objective criteria leads to an inadequately defined diagnostic schema, which classifies patients into symptom clusters such as overactive bladder (OAB) and interstitial cystitis (IC) or bladder pain syndrome (BPS) that do not specify underlying pathophysiology. Such contemporary allocation strategies for LUTS do not effectively differentiate subsets of patients that require different treatment approaches. Therefore, most patients with LUTS fail to respond to initial treatment approaches and are frequently lost to care. Better tools to recognize more homogeneous LUTS phenotypes would dramatically improve both the recognition and management of patients with LUTS by primary care and specialist providers.
Why was this study conducted?
This study developed an algorithmic screening measure based on patient-reported symptoms to identify patients with urinary symptoms related to myofascial pelvic floor dysfunction.

Key findings
The study algorithm separated populations of women, a total of 1084, in both derivation and validation cohorts who were seeking care for lower urinary tract symptoms into groups consistent with overactive bladder, interstitial cystitis/bladder pain syndrome, and myofascial urinary frequency syndrome phenotypes with an overall diagnostic accuracy of 82%.

What does this add to what is known?
This screening approach will help identify patients with myofascial pelvic floor dysfunction who would likely benefit from myofascial-directed therapies. The early identification of such patients would facilitate targeted therapy, expedite recovery, and minimize unnecessary pharmacologic and procedural interventions.

We recently described a novel LUTS diagnosis termed “myofascial urinary frequency syndrome” (MUFS). This prevalent condition, frequently seen in individuals with urinary frequency without true urgency, occurs when dysfunctional pelvic muscles result in a range of bothersome urinary complaints. Prominent features of MUFS include a sensation of incomplete bladder emptying (without true urinary retention), urinary frequency, and a persistent desire to urinate prompted more by pressure, fullness, or discomfort than fear of incontinence—a symptom complex we dubbed “persistency.” Affected subjects display myofascial pelvic floor dysfunction (increased tone with or without pelvic floor trigger points) on examination and perineal surface electromyography (EMG) and improve with myofascial release-based physical therapy or biofeedback.

Despite being exceedingly common, because of the vague mix of uncomfortable bladder sensations and urinary complaints, MUFS is often mistaken for other symptom complexes, such as IC or BPS, OAB, pelvic organ prolapse (POP), or even urinary tract infection. No specific International Classification of Diseases, Tenth Revision, code specifies this diagnosis, making epidemiologic assessment and surveillance difficult. Given the nonspecific constellation of symptoms, MUFS can be challenging for providers to recognize, as this diagnosis requires a detailed pelvic examination, sufficient understanding of the global symptom complex, and ruling out confounding conditions. Given these challenges, which are compounded by increasing reliance on telemedicine and limited visit times, improved tools are required to assist providers in recognizing MUFS. A symptoms-based measure associated with the MUFS phenotype could greatly assist providers in suspecting a myofascial origin to a patient’s urinary symptoms, thus focusing on physical assessment and possible treatments.

As initial characterization of MUFS revealed a consistent pattern of associated symptoms across multiple independent cohorts, we hypothesized that it would be feasible to construct a symptoms-based measure to identify patients with MUFS. With a patient-derived indicator identifying these patients, earlier interventions with appropriate treatment (ie, pelvic floor physical therapy [PFPT]) can be achieved, even when providers are less facile at making the diagnosis.

Therefore, we sought to develop a screening index to identify patients with possible MUFS for use in telemedicine and by providers unskilled with discriminate pelvic examination. By comparing a population of patients with MUFS vs patients with OAB or IC or BPS, we developed a novel measure, termed the “Persistency Index (PI),” to screen for this underrecognized type of LUTS. We further propose a modified diagnostic nomogram incorporating this measure that is capable of differentiating this cohort of patients from classical OAB and IC or BPS.

Materials and Methods

Study inclusion
After local institutional review board (IRB#00040261) approval, female subjects presenting for care in a specialized urogynecology clinic were included (Figure 1). At initial consultation, all subjects were given 3 validated questionnaires: the (1) Female Genitourinary Pain Index (fGUPI), (2) Overactive Bladder Questionnaire (OAB-q), and (3) Pelvic Floor Distress Inventory 20 (PFDI-20). The fGUPI measures the nature and severity of genitourinary pain. The OAB-q symptom questions (1–8) assess continent and incontinent OAB symptoms. The PFDI-20 measures pelvic floor symptoms in 3 domains, assessing (1) urinary (Urinary Distress Inventory 6 [UDI-6]), (2) defecatory (Colorectal-Anal Distress Inventory 8 [CRADI-8]), and (3) prolapse (Pelvic Organ Prolapse Distress Inventory 6 [POPDI-6]) symptoms.

Study cohorts
A derivation cohort of 215 subjects from a single-center urogynecology practice between January 2018 and December 2018 was employed to develop the PI. This population contained 68 subjects with urinary symptoms determined to be derived from myofascial dysfunction by the assessing physician. Myofascial dysfunction was confirmed on standardized pelvic floor examination with the observation of overactivity on perineal surface pelvic floor EMG. Myofascial dysfunction was secondarily verified as the source of their symptomatology by demonstrable improvements in urinary symptoms after myofascial release-based PFPT. This group was composed of 2 other groups with LUTS: (1) 42 subjects diagnosed
with OAB who endorsed substantial urgency incontinence (UI), displayed detrusor overactivity on urodynamic evaluation, and lacked bladder pain (BP) on examination or questionnaire assessment and (2) 51 subjects with a clinical diagnosis of IC or BPS with marked BP on physical examination, who reported pain with bladder filling on validated questionnaires, and who lacked any incontinence. An additional 54 subjects with asymptomatic questionnaire responses seeking care for asymptomatic conditions (commonly microhematuria) served as controls.

A validation cohort of 719 subjects evaluated consecutively between January 2019 and December 2019 served to assess the performance of candidate symptomatic measures in an unselected population. This cohort contained 111 subjects with diagnosed MUFS (subjects with pelvic floor increased tone or trigger points on examination, presenting with urinary frequency, persistent bladder pressure, and a sensation of incomplete bladder emptying who bore a primary diagnosis of high-tone pelvic floor dysfunction), 285 subjects with OAB, 53 with IC or BPS, 209 subjects with minimal bother, and 61 subjects with more than 1 of these diagnoses. Moreover, this cohort was given the O’Leary-Sant Indices, which include the Interstitial Cystitis Symptom Index (ICSI) and Interstitial Cystitis Problem Index (ICPI), that measure the severity and bother of urinary frequency, urgency, nocturia, and BP.

**Derivation of the Persistency Index**

We used the derivation cohort to create a measure of urinary symptoms associated with a myofascial origin—the PI. The Least Angle Shrinkage and Selection Operator (LASSO) identified candidate predictors from individual questionnaire features. Of note, 10-fold cross-validation was used to determine the appropriate shrinkage parameter ($\lambda = 0.01307$), which identified 20 of 41 variables as potential predictors (ie, nonzero coefficients). From these, variables with positive standardized shrunken coefficients of $>0.4$ that had acceptable face validity for capturing the underlying clinical phenotype (eg, which were in agreement with previously defined phenotypic characteristics) were used in a multivariable logistic regression model. Statistically significant, positive model coefficients were retained, resulting in a reduced model consisting of 3 predictors (Pelvic Floor Distress Index 5 [PFDI-5], Female Genitourinary Pain Index 5 [fGUPI5], and Genitourinary Pain Index 2b [GUPI2b]). As reduced age was substantially associated with myofascial dysfunction, age was added to the model. To increase the usability of this model, we generated a simple summated score of these questions weighted approximately by their coefficients from the multivariable model. The smallest coefficient was normalized to 1, and other coefficients were scaled to the nearest integer to preserve their relative relationships. That adjustment resulted in a score using the original scaling of the PFDI-5 (0–4) and GUPI5 (0–5) with a modified scaling of GUPI2b (0 or 3 if positive) and an age penalty for subjects aged <50 years (3 points added if under the age of 50 years), with a maximal possible score of 15.

**Modification of diagnostic nomogram**

The PI was added to the previous diagnostic nomogram to classify OAB vs IC or BPS to generate the phenotyping comprehensive lower urinary symptoms (p-CLUS) nomogram. In this

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**FIGURE 1**

**Study design**

A screening measure associated with myofascial urinary frequency syndrome (MUFS), termed the “Persistency Index,” has been derived. This measure was composed of the most salient features of MUFS identified by comparison of a group of subjects with LUTS, abnormal pelvic floor findings on examination, and EMG findings of a tonically contracted pelvic floor to asymptomatic subjects and patients with OAB and IC or BPS (derivation cohort). The real-world performance of this measure in classifying subjects with MUFS from a large population of individuals presenting to a urogynecology clinic (validation cohort) has been determined.

BPS, bladder pain syndrome; EMG, electromyography; IC, interstitial cystitis; LUTS, lower urinary tract symptom; MUFS, myofascial urinary frequency syndrome; OAB, overactive bladder.

nomogram, the PI, Bladder Pain Composite Index (BPCI), Urgency Incontinence Composite Index (UICI), and Bother Index in combination classify patients as nonbothered subjects, IC or BPS, OAB, and MUFs. Inaccuracy was calculated as the percentage of subjects incorrectly classified by the nomogram to a diagnosis different from physician-assigned diagnosis.

Statistical analysis

Bivariate differences between groups were examined using the Welch t test and chi-square test in the derivation and validation cohorts. P values were adjusted using the Holm-Bonferroni correction for multiple comparisons.14 All analyses were performed using Stata (version 16.1; StataCorp, College Station, TX).

Results

Myofascial urinary frequency syndrome subjects are a distinct subset of subjects with lower urinary tract symptoms

The derivation cohort (Table and Supplemental Table 1) consisted of patients presenting for care in a tertiary urogynecology practice in 2018. Subjects with confirmed MUFs (n=68), in whom myofascial dysfunction was confirmed on physical examination and pelvic floor EMG, were compared with a population of controls (n=54) and cases with OAB (n=42) or IC or BPS (n=51). Subjects with MUFs exhibited similar levels of urinary frequency and urge as both subjects with OAB and subjects with IC or BPS, but lacked UI (approximated of the original scaling of the PFDI-5 (red), GUP5 (blue), and GUP12b) resulted in a reduced model with an in-sample area under the curve (AUC) of 0.75 (95% confidence interval [CI], 0.68—0.83) (Supplemental Table 3).

Age is a valuable predictor of myofascial urinary frequency syndrome

As subjects with MUFs were noted to be considerably younger than subjects with OAB with similar severity of urinary symptoms, we evaluated the use of including age as a predictor of MUFs. The inclusion of age in the multivariable regression model substantially increased the AUC to 0.8 (95% CI, 0.73—0.87) (Supplemental Table 4). To simplify this model for ease of clinical use, regression coefficients were scaled to generate a simple, summed score of these questions. A total possible score of 15 included the original scaling of the PFDI-5 (0—4) and fGUPI5 (0—5), a modified scaling of GUPI2b (0 or 3 if positive), and an age factor for subjects aged <50 years (3 points added if under the age of 50 years). Moreover, this simplified, summed score showed an in-sample AUC of 0.79 (95% CI, 0.72—0.87) (Supplemental Table 4). Given greater ease of use to the simple, summed score with minimal loss of performance, this simple score was defined as the PI.

The Persistency Index can identify the myofascial urinary frequency syndrome phenotype from unselected lower urinary tract symptoms patients

The PI was used in a validation cohort consisting of 719 patients who consecutively sought care in 2019. This cohort included subjects with MUFs (n=111), OAB (n=285), and IC or BPS (n=53); controls (n=209); and subjects with LUTS of unclear etiology (n=61). The out-of-sample AUC for the simple, summed PI in the validation cohort was 0.74 (95% CI, 0.67—0.83) (Supplemental Table 5). Sensitivity and specificity were calculated for each PI score in the validation cohort (Supplemental Table 6). The Youden Index was used to identify the optimal cut point for maximizing sensitivity and specificity, which was found to be a simple, summed score of ≥7, which had 80% sensitivity and 61% specificity. Overall accuracy of diagnosis at this score was 65% (Supplemental Table 6 and Figure 3).

Phenotyping comprehensive lower urinary symptoms nomogram can distinguish different etiologies of lower urinary tract symptoms patients

Application of these 4 indices (Bother, BPCI, UICI, and PI) to this unselected population was able to separate the population into phenotypic groups, which correlated well with specialist-assigned diagnoses of OAB, IC or BPS, and MUFs (Figure 4). Subjects identified as patients with MUFs using PI of ≥7 (n=125) were highly bothered subjects (median Bother Index, 9.0; range, 8.0—10.0) with low scores on the UICI (median Bother Index, 2.0; range, 1.3—2.7) and BPCI (median Bother Index, 0.6; range, 0.6—1.2) and elevated PCI scores (median Bother Index, 8.4; range, 6.8—10.3). This independent population of subjects with MUFs exhibited the same pattern of symptomatology on their patient-reported questionnaires as observed in the initial description of MUFs; questions describing pelvic pressure and heaviness (POPDI-6 1 and 2), straining to defecate (CRADI-8 1), urinary frequency (UDI-6 1, ICSI 2, ICPI 1, fGUPI 6), incomplete emptying (UDI-6 5), and bladder or pelvic discomfort (UDI-6 6, fGUPI 1, fGUPI 4, ICPI 4) were substantially increased over controls in this population (Supplemental Table 7). The algorithm categorized subjects with a known MUFs diagnosis with good overall accuracy; only 18% of subjects overall had a discordant nomogram classification to the physician-assigned diagnosis (15% inaccuracy for IC or BPS,
<table>
<thead>
<tr>
<th>Variable</th>
<th>Question</th>
<th>Scale</th>
<th>MUFS (n=68)</th>
<th>Asymptomatic control (n=54)</th>
<th>OAB (n=42)</th>
<th>IC or BPS (n=51)</th>
<th>Adjusted $P$ value (MUFS vs asymptomatic control, OAB, or IC or BPS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age $^a$</td>
<td></td>
<td></td>
<td>43.62 (14.89)</td>
<td>54.22 (15.26)</td>
<td>64.03 (11.40)</td>
<td>49.05 (13.70)</td>
<td>&lt;.001 &lt;.001 .054</td>
</tr>
<tr>
<td>OAB-q2</td>
<td>An uncomfortable urge to urinate</td>
<td>1—6</td>
<td>3.72 (1.34)</td>
<td>1.69 (1.16)</td>
<td>4.08 (1.56)</td>
<td>3.65 (1.57)</td>
<td>&lt;.001 .214 .784</td>
</tr>
<tr>
<td>OAB-q3</td>
<td>A sudden urge to urinate</td>
<td>1—6</td>
<td>2.29 (1.50)</td>
<td>1.39 (0.81)</td>
<td>4.43 (1.19)</td>
<td>2.08 (1.38)</td>
<td>&lt;.001 &lt;.001 .423</td>
</tr>
<tr>
<td>OAB-q4</td>
<td>Accidental loss of small amounts of urine</td>
<td>1—6</td>
<td>1.91 (1.47)</td>
<td>1.63 (0.78)</td>
<td>4.29 (1.38)</td>
<td>1.47 (0.67)</td>
<td>.206 &lt;.001 .049</td>
</tr>
<tr>
<td>OAB-q5</td>
<td>Nighttime urination</td>
<td>1—6</td>
<td>2.87 (1.64)</td>
<td>2.09 (1.33)</td>
<td>4.00 (1.86)</td>
<td>2.98 (1.63)</td>
<td>.006 .001 .712</td>
</tr>
<tr>
<td>OAB-q6</td>
<td>Waking at night because you had to urinate</td>
<td>1—6</td>
<td>3.29 (1.65)</td>
<td>2.38 (1.44)</td>
<td>4.44 (1.55)</td>
<td>3.29 (1.59)</td>
<td>.002 &lt;.001 1.000</td>
</tr>
<tr>
<td>OAB-q8</td>
<td>Urine loss associated with a strong desire to urinate</td>
<td>1—6</td>
<td>1.53 (1.13)</td>
<td>1.30 (0.57)</td>
<td>4.36 (1.39)</td>
<td>1.31 (0.65)</td>
<td>.168 &lt;.001 .224</td>
</tr>
<tr>
<td>fGUPI1a $^{a,b}$</td>
<td>Pain or discomfort at the entrance to the vagina</td>
<td>0—1</td>
<td>0.51</td>
<td>0.07</td>
<td>0.05</td>
<td>0.43</td>
<td>&lt;.001 &lt;.001 .372</td>
</tr>
<tr>
<td>fGUPI1b $^{a,b}$</td>
<td>Pain or discomfort in the vagina</td>
<td>0—1</td>
<td>0.49</td>
<td>0.07</td>
<td>0.07</td>
<td>0.43</td>
<td>&lt;.001 &lt;.001 .563</td>
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<tr>
<td>fGUPI1c $^{a,b}$</td>
<td>Pain or discomfort in the urethra</td>
<td>0—1</td>
<td>0.44</td>
<td>0.04</td>
<td>0.05</td>
<td>0.59</td>
<td>&lt;.001 &lt;.001 .114</td>
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<tr>
<td>fGUPI1d $^{a,b}$</td>
<td>Pain or discomfort below the waist or in the pubic or bladder area</td>
<td>0—1</td>
<td>0.42</td>
<td>0.08</td>
<td>0.10</td>
<td>0.90</td>
<td>&lt;.001 &lt;.001 &lt;.001</td>
</tr>
<tr>
<td>fGUPI2a $^{a,b}$</td>
<td>Pain or burning during urination</td>
<td>0—1</td>
<td>0.44</td>
<td>0.02</td>
<td>0.10</td>
<td>0.62</td>
<td>&lt;.001 &lt;.001 .055</td>
</tr>
<tr>
<td>fGUPI2b $^{a,b}$</td>
<td>Pain or discomfort during or after sexual intercourse</td>
<td>0—1</td>
<td>0.52</td>
<td>0.09</td>
<td>0.12</td>
<td>0.47</td>
<td>&lt;.001 &lt;.001 .581</td>
</tr>
<tr>
<td>fGUPI2c $^{a,b}$</td>
<td>Pain or discomfort as your bladder fills</td>
<td>0—1</td>
<td>0.09</td>
<td>0.00</td>
<td>0.00</td>
<td>0.92</td>
<td>.025 .048 &lt;.001</td>
</tr>
<tr>
<td>fGUPI2d $^{a,b}$</td>
<td>Pain or discomfort relieved by voiding</td>
<td>0—1</td>
<td>0.23</td>
<td>0.06</td>
<td>0.05</td>
<td>0.73</td>
<td>.009 .011 &lt;.001</td>
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<tr>
<td>fGUPI3</td>
<td>Frequency of pain or discomfort over the last week</td>
<td>0—5</td>
<td>3.00 (1.43)</td>
<td>0.37 (0.66)</td>
<td>0.68 (0.91)</td>
<td>3.00 (1.31)</td>
<td>&lt;.001 &lt;.001 1.000</td>
</tr>
<tr>
<td>fGUPI4</td>
<td>Number that best describes average pain or discomfort</td>
<td>0—10</td>
<td>3.85 (2.23)</td>
<td>0.39 (1.08)</td>
<td>1.43 (1.74)</td>
<td>5.91 (2.31)</td>
<td>&lt;.001 &lt;.001 &lt;.001</td>
</tr>
<tr>
<td>fGUPI5</td>
<td>Frequency of sensation of incomplete emptying</td>
<td>0—5</td>
<td>2.76 (1.25)</td>
<td>0.39 (0.60)</td>
<td>1.39 (1.18)</td>
<td>2.12 (1.48)</td>
<td>&lt;.001 &lt;.001 .011</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
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</tr>
</thead>
<tbody>
<tr>
<td>fGUPI6</td>
<td>Need to urinate &lt;2 h after last urinating</td>
<td>0−5</td>
<td>3.19 (1.21)</td>
<td>1.04 (1.06)</td>
<td>3.19 (1.40)</td>
<td>3.06 (1.52)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>fGUPI7</td>
<td>Have your symptoms kept you from doing the kinds of things you would usually do?</td>
<td>0−3</td>
<td>1.49 (1.03)</td>
<td>0.04 (0.19)</td>
<td>1.45 (1.15)</td>
<td>1.51 (1.12)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>fGUPI8</td>
<td>How much did you think about your symptoms?</td>
<td>0−3</td>
<td>2.50 (0.70)</td>
<td>0.37 (0.52)</td>
<td>2.43 (0.70)</td>
<td>2.51 (0.76)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>fGUPI9</td>
<td>Satisfaction with current symptoms</td>
<td>0−6</td>
<td>4.59 (1.22)</td>
<td>1.59 (1.11)</td>
<td>4.62 (1.10)</td>
<td>5.04 (1.02)</td>
<td>&lt;.001</td>
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<tr>
<td>POPDI-1</td>
<td>Pressure in the lower abdomen</td>
<td>0−4</td>
<td>1.83 (1.42)</td>
<td>0.34 (0.83)</td>
<td>0.85 (1.21)</td>
<td>1.80 (1.37)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>POPDI-2</td>
<td>Heaviness or dullness in the lower abdomen</td>
<td>0−4</td>
<td>1.46 (1.45)</td>
<td>0.23 (0.64)</td>
<td>0.62 (1.11)</td>
<td>1.84 (1.43)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>POPDI-3</td>
<td>A bulge or something falling out that can be seen or felt in the vaginal area</td>
<td>0−4</td>
<td>0.36 (0.99)</td>
<td>0.20 (0.74)</td>
<td>0.29 (0.72)</td>
<td>0.16 (0.50)</td>
<td>.326</td>
</tr>
<tr>
<td>POPDI-4</td>
<td>A need to push on the vagina or around the rectum to have a complete bowel movement</td>
<td>0−4</td>
<td>0.42 (0.89)</td>
<td>0.31 (0.89)</td>
<td>0.68 (1.25)</td>
<td>0.45 (1.10)</td>
<td>.527</td>
</tr>
<tr>
<td>CRADI-8-1</td>
<td>A need to strain too hard to have a bowel movement</td>
<td>0−4</td>
<td>1.31 (1.43)</td>
<td>0.20 (0.63)</td>
<td>1.10 (1.34)</td>
<td>0.80 (1.28)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CRADI-8-2</td>
<td>A feeling that you have not completely emptied your bowels after a bowel movement</td>
<td>0−4</td>
<td>1.33 (1.37)</td>
<td>0.36 (0.83)</td>
<td>0.83 (1.10)</td>
<td>0.80 (1.20)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CRADI-8-3</td>
<td>Losing stool without control when stools are well formed</td>
<td>0−4</td>
<td>0.12 (0.56)</td>
<td>0.11 (0.60)</td>
<td>0.32 (0.85)</td>
<td>0.10 (0.50)</td>
<td>.938</td>
</tr>
<tr>
<td>CRADI-8-4</td>
<td>Losing stool without control when stool is loose or liquid</td>
<td>0−4</td>
<td>0.27 (0.77)</td>
<td>0.15 (0.76)</td>
<td>0.83 (1.25)</td>
<td>0.24 (0.74)</td>
<td>.392</td>
</tr>
</tbody>
</table>

### TABLE
Symptomatic features of the derivation cohort by diagnosis (continued)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Question</th>
<th>Scale</th>
<th>MUFS (n=68)</th>
<th>Asymptomatic control (n=54)</th>
<th>OAB (n=42)</th>
<th>IC or BPS (n=51)</th>
<th>Adjusted P value (MUFS vs asymptomatic control, OAB, or IC or BPS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRADI-8-5</td>
<td>Losing gas from the rectum without control</td>
<td>0—4</td>
<td>0.71 (1.22)</td>
<td>0.31 (0.73)</td>
<td>0.98 (1.33)</td>
<td>0.31 (0.73)</td>
<td>.045 .279 .045</td>
</tr>
<tr>
<td>CRADI-8-6</td>
<td>Pain with passing stools</td>
<td>0—4</td>
<td>0.34 (0.91)</td>
<td>0.00 (0.00)</td>
<td>0.27 (0.71)</td>
<td>0.16 (0.64)</td>
<td>.007 .654 .217</td>
</tr>
<tr>
<td>CRADI-8-7</td>
<td>A strong sense of urgency and have to rush to the bathroom to have a bowel movement</td>
<td>0—4</td>
<td>0.70 (1.18)</td>
<td>0.30 (0.85)</td>
<td>0.81 (1.15)</td>
<td>0.41 (0.85)</td>
<td>.040 .640 .141</td>
</tr>
<tr>
<td>CRADI-8-8</td>
<td>Stool passes through the rectum and bulges outside during or after a bowel movement</td>
<td>0—4</td>
<td>0.24 (0.87)</td>
<td>0.13 (0.58)</td>
<td>0.22 (0.61)</td>
<td>0.04 (0.20)</td>
<td>.444 .919 .116</td>
</tr>
<tr>
<td>UDI-6-1</td>
<td>Bothered by frequent urination</td>
<td>0—4</td>
<td>2.16 (1.40)</td>
<td>0.74 (1.12)</td>
<td>2.95 (1.27)</td>
<td>2.46 (1.18)</td>
<td>&lt;.001 .004 .225</td>
</tr>
<tr>
<td>UDI-6-2</td>
<td>Bothered by leakage related to feeling of urgency</td>
<td>0—4</td>
<td>0.41 (0.78)</td>
<td>0.31 (0.72)</td>
<td>3.12 (0.92)</td>
<td>0.69 (0.79)</td>
<td>.482 &lt;.001 .060</td>
</tr>
<tr>
<td>UDI-6-3</td>
<td>Bothered by leakage related to physical activity, coughing, or sneezing</td>
<td>0—4</td>
<td>0.79 (1.13)</td>
<td>0.83 (1.16)</td>
<td>2.00 (1.47)</td>
<td>0.63 (1.00)</td>
<td>.863 &lt;.001 .404</td>
</tr>
<tr>
<td>UDI-6-4</td>
<td>Bothered by small amounts of leakage (drops)</td>
<td>0—4</td>
<td>0.76 (1.27)</td>
<td>0.42 (0.84)</td>
<td>2.26 (1.48)</td>
<td>0.31 (0.73)</td>
<td>.090 &lt;.001 .027</td>
</tr>
<tr>
<td>UDI-6-5</td>
<td>Bothered by difficulty emptying bladder</td>
<td>0—4</td>
<td>1.61 (1.37)</td>
<td>0.15 (0.53)</td>
<td>0.74 (1.27)</td>
<td>1.45 (1.39)</td>
<td>&lt;.001 .001 .546</td>
</tr>
<tr>
<td>UDI-6-6</td>
<td>Bothered by pain or discomfort in the lower abdominal or genital area</td>
<td>0—4</td>
<td>1.65 (1.52)</td>
<td>0.19 (0.62)</td>
<td>0.51 (1.05)</td>
<td>2.10 (1.43)</td>
<td>&lt;.001 &lt;.001 .110</td>
</tr>
</tbody>
</table>

Data are presented as mean (standard deviation) for all interval variables, except for the binary variables, which document the population proportions scoring positive for each individual feature. Pairwise comparison of interval variables was performed using the Welch t test, and binary variables (designated with “b”) were examined using the chi-square test.

BPS, bladder pain syndrome; CRADI-8, Colorectal-Anal Distress Inventory 8; fGUPPI, Female Genitourinary Pain Index; IC, interstitial cystitis; ICPI, Interstitial Cystitis Problem Index; iCSI, Interstitial Cystitis Symptoms Index; MUFS, myofascial urinary frequency syndrome; NS, not significant; OAB, overactive bladder; OAB-q, Overactive Bladder Questionnaire; POPDI-6, Pelvic Organ Prolapse Distress Inventory 6; UDI-6, Urinary Distress Inventory 6.

*Variables used to create the Persistency Index; * Binary variables: the values noted are proportions of each population answering “yes” to the symptomatic feature.

**FIGURE 2**
Persistency Index describes unique features of myofascially-derived LUTS

<table>
<thead>
<tr>
<th>Instruments</th>
<th>LASSO Selection</th>
<th>Factor Reduction</th>
<th>Number</th>
<th>Question</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFDI20</td>
<td>PFDI20</td>
<td>PFDI20</td>
<td>PFDI20</td>
<td>PFDI20q1</td>
<td>p=0.00007</td>
</tr>
<tr>
<td>OABq</td>
<td>OABq</td>
<td>OABq</td>
<td>OABq</td>
<td>OABq</td>
<td></td>
</tr>
<tr>
<td>fGUPI</td>
<td>fGUPI</td>
<td>fGUPI</td>
<td>fGUPI</td>
<td>fGUPI2b</td>
<td>p=0.00004</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>fGUPI5</td>
<td>p=0.00001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>fGUPI6</td>
<td>p=0.0004</td>
</tr>
</tbody>
</table>

A. Least Angle Shrinkage and Selection Operator with 10-fold cross-validation ($\lambda=0.01307$) identified 20 of 41 variables from the OAB-q, fGUPI, and PFDI as potential predictors. Of note, 5 of these variables with a positive standardized shrunken coefficient of $>0.4$ and a face validity for capturing the underlying clinical phenotype were used in a multivariable logistic regression model. Variables with statistically significant model coefficients (PFDI-5, GUPI5, and GUPI2b) were retained, resulting in a reduced model consisting of these 3 predictors weighted based on these coefficients, composing the Persistency Index.

fGUPI, Female Genitourinary Pain Index; GUPI, Genitourinary Pain Index; GUPI2b, Genitourinary Pain Index 2b; GUPI5, Genitourinary Pain Index 5; OAB-q, Overactive Bladder Questionnaire; PFDI, Pelvic Floor Distress Index; PFDI-20, Pelvic Floor Distress Inventory 20; PFDI-5, Pelvic Floor Distress Index 5.


**FIGURE 3**
Performance of the PI

A. Distribution of persistency across the pooled population of 215 subjects by diagnosis (derivation dataset). Positivity on the PI was defined as $>7$, which best defined the population with MUFS. B. Sensitivity, specificity, and overall accuracy of the PI in identifying MUFS in the validation dataset. A summated score of 7 denotes the cutoff threshold that maximizes both sensitivity and specificity.

BPS, bladder pain syndrome; IC, interstitial cystitis; MUFS, myofascial urinary frequency syndrome; OAB, overactive bladder; PO, Persistency Index.

Comment

Principal findings

MUFS, a symptom complex of urinary frequency, bladder pressure, sensation of incomplete emptying, and persistent desire to urinate associated with myofascial dysfunction, is common in patients presenting for urogynecologic care but remains underrecognized. Currently, most diagnostic approaches to LUTS only marginally address pelvic floor myofascial dysfunction as an independent contributor to urinary symptomatology. However, the pelvic floor plays a central role in pelvic, visceral function, and dysregulation can provoke pelvic pain syndromes and urinary complaints, improving with myofascial physical therapy. Although muscle laxity is widely acknowledged as a contributor to POP or stress urinary incontinence, increased muscle tone or discoordination is rarely recognized in nonpainful LUTS. Although understood to contribute to functional voiding, dyssynergia of the pelvic floor can demonstrate a vast spectrum of clinical presentations. Widely fluctuating estimates of its prevalence are indicative of a high rate of misdiagnosis and poor understanding of the contribution of the pelvic floor to urinary complaints. However, a growing body of evidence suggests that increased pelvic floor tone underlies many urinary, gastrointestinal, and sexual complaints, even in the absence of pain.

Results in the context of what is known

In the colorectal literature, a high-tone or hypertonic pelvic floor is well understood to result in symptoms of fecal urgency, stool frequency, and obstructive defecation, which can often present as chronic, idiopathic constipation. As in defecation, normal urinary function similarly requires appropriate relaxation and coordination of the pelvic floor muscles, including urinary sphincters. Thus, a growing body of evidence suggests that a high-tone pelvic floor (“nonrelaxing” or fixed) can result in
analogous symptoms in the urinary tract, embodied in the clinical phenotype of MUFS.3,4,6,20–22

MUFS is prevalent in individuals highly bothered by their LUTS. In our unselected population of subjects seeking care in a pelvic medicine specialty clinic, MUFS cases consisted of more than 20% of subjects presenting with LUTS, a similar prevalence to that seen in the initial cohort used to describe this condition.3 This is similar to the prevalence of pelvic floor dysfunction (dysynergic defecation) in 22% to 27% of patients presenting with chronic, idiopathic constipation.23,24 However, increasing awareness of this prevalent cause of pelvic symptomatology may not be sufficient to improve care; additional tools and standards for diagnosis are needed.

Clinical implications
The screening measure developed in this study, the PI, performs well in a real-world, unselected population of patients seeking care for LUTS to identify MUFS with an overall accuracy of 65%. This accuracy reflects the fact that the chosen threshold for diagnosis tends to overpredict the likelihood of MUFS (Supplemental Figure 1) but misses a few with true MUFS, as evidenced by 80% sensitivity. As the likely outcome of obtaining a diagnosis of MUFS would be a referral to PFPT, a treatment that carries very few side effects and the potential for symptomatic improvements even in patients with other diagnoses, the risks of overdiagnosing MUFS are minimal. This risk-to-benefit ratio reflects the optimal features of a screening measure, especially for an underrecognized condition that could assist providers in identifying patients that would benefit from consideration of myofascial-directed therapies and perhaps avoid unnecessary pharmacologic or even surgical interventions.

The addition of the PI to our previously described LUTS diagnostic nomogram provided a new diagnostic algorithm, the p-CLUS nomogram. The application of this classification method provided an overall accuracy of LUTS classification in an unselected population of care-seeking women of 82% (Supplemental Figure 2), using only 11 symptomatic questions and patient age. As this information can be obtained without in-person assessment, this clinical tool could be used by providers across a range of disciplines, even when assessing patients by telemedicine, to help with initial diagnostic evaluation and treatment assignment.

Research implications
As this dataset included only women, using validated questionnaires that are specific to pelvic symptomatology in women, it is not clear how these symptoms manifest in men or the prevalence of myofascial dysfunction as a cause for LUTS. A comprehensive myofascial pelvic examination is more challenging in men, as an internal assessment can only be performed during a digital rectal examination, which is frequently perceived as uncomfortable and may provoke reflexive pelvic floor contraction confounding the use of examination.

Strengths and limitations
Such discomfort on examination confounding assessment may manifest in women. The accuracy of the PI at diagnosing MUFS was determined without an objective gold standard for diagnosis; the comparative measure determining whether a subject’s urinary symptoms derived from a myofascial origin was based on symptom assessment and subjective pelvic floor examination by a board-certified urogynecologist. This method, despite being the current diagnostic standard, is itself an inconsistent measure.25–27 It is possible that the real accuracy of the PI in identifying MUFS is greater than anticipated, as patients with MUFS may be misclassified by this subjective approach. In a 3-dimensional graphic representation of patient symptoms (Figure 4), a substantial number of patients diagnosed with OAB are noted within the region of the graph with a high PI, low BPCI (BP), and low UICI (urgency or UI). Although it is possible the PI is not accurate in such patients, it remains equally plausible that these patients represent misdiagnosed cases of MUFS, which could have been recognized by using a screening method, such as the PI. This lack of objective tests to identify MUFS may, in part, explain the discrepancy between physician-assigned diagnosis and PI classification.

Conclusions
Our study provides a screening measure helpful in identifying patients with MUFS, which would likely benefit from myofascial-directed therapies. Although the diagnostic use of the PI will require further evaluation in prospective studies examining improvements in MUFS identification and treatment assignment, we anticipate that early identification of such patients will facilitate targeted therapy, expedite recovery, and minimize unnecessary pharmacologic and procedural interventions.

GLOSSARY
AUC: area under the curve
BP: bladder pain
BPS: bladder pain syndrome
BPCI: Bladder Pain Composite Index
CRADI-8: Colorectal-Anal Distress Inventory 8
EMG: electromyography
fGUPI: Female Genitourinary Pain Index
fGUPI5: Female Genitourinary Pain Index 5
GUPI2b: Genitourinary Pain Index 2b
IC: interstitial cystitis
ICPI: Interstitial Cystitis Problem Index
ICSI: Interstitial Cystitis Symptom Index
LASSO: Least Angle Shrinkage and Selection Operator
LUTS: lower urinary tract symptoms
MUFS: myofascial urinary frequency syndrome
OAB: overactive bladder
OAB-q: Overactive Bladder Questionnaire
PI: Persistency Index
POP: pelvic organ prolapse
POPD1: Pelvic Organ Prolapse Distress Inventory 6
UDI-6: Urinary Distress Inventory 6
UI: urgency incontinence
UICI: Urge Incontinence Composite Index
References


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