The Distribution of Post-Void Residual Volumes in People Seeking Care in the Symptoms of Lower Urinary Tract Dysfunction Network Observational Cohort Study With Comparison to Asymptomatic Populations


OBJECTIVE To describe the distribution of post-void residual (PVR) volumes across patients with and without lower urinary tract symptoms (LUTS) and examine relationships between self-reported voiding symptoms, storage symptoms, and PVR.

METHODS PVR and demographic data were obtained from the Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN) observational cohort study. Self-reported symptoms were collected using the American Urological Association Symptom Index and the LUTS Tool. PVR values were obtained from 2 other cohorts: living kidney donors with unknown LUTS from the Renal and Lung Living Donors Evaluation Study (RELIVE), and continent women in the Establishing the Prevalence of Incontinence (EPI) study, a population-based study of racial differences in urinary incontinence prevalence.

RESULTS Across the 3 studies, median PVRs were similar: 26 mL in LURN (n = 880, range 0-932 mL), 20 mL in EPI (n = 166, range 0-400 mL), and 14 mL in RELIVE (n = 191, range 0-352 mL). In LURN, males had 3.6 times higher odds of having PVR > 200 mL (95% CI = 1.72-7.48). In RELIVE, median PVR was significantly higher for males (20 mL vs 0 mL, P = .004). Among women, only the intermittency severity rating was associated with a probability of an elevated PVR. Among men, incomplete emptying and burning severity rating were associated with a higher odds of elevated PVR, but urgency severity ratings were associated with lower odds of elevated PVR.

CONCLUSION Care-seeking patients have PVRs similar to those in people with unknown history of LUTS (RELIVE) and without self-reported LUTS (EPI). Although PVR was correlated with voiding symptoms, the mean differences only explain ~2% of the variance. UROLOGY 130: 22−28, 2019. © 2019 Elsevier Inc.

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The initial evaluation of lower urinary tract symptoms (LUTS) includes a history, physical examination, urinalysis, and post-void residual (PVR), measured by bladder scan or straight catheterization.\(^1\)\(^,\)\(^2\) Conventional wisdom states that elevated PVR may correlate with clinically-relevant issues, such as risk of urinary tract infection (UTI) and the severity of LUTS, and may be an indication for clinical intervention. However, there is no standard for what constitutes an abnormal PVR.\(^3\)\(^,\)\(^4\) or at what volume residual urine may cause symptoms. In the available literature, the definition of urinary retention has been pragmatically set as a PVR volume ranging from 100 mL to 500 mL.\(^5\) While this is still debated, current expert opinion defines urinary retention as an elevated PVR of >300 mL, without differentiation among males and females.\(^5\)\(^-\)\(^10\) There is no guideline or evidence stronger than expert panel consensus to establish the use of PVR as a clinical tool.

Given this knowledge gap, we assessed PVR and patient-reported urinary symptoms in the Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN) and compared them with PVR distributions in other large cohorts with and without LUTS. We hypothesized that: (1) there would be wide variation in retained urine volume, with a substantial number having what is currently considered to be a clinically-significant elevated PVR; and (2) absolute PVR volume would not correlate with self-reported storage and voiding symptoms.

MATERIALS AND METHODS

Study Design and Population

Data were obtained from the LURN Observational Cohort Study, which has been described previously. Briefly, men and women presenting to a physician at 1 of 6 LURN tertiary care centers were recruited between June 2015 and January 2017. These persons were free of major neurologic diseases or injuries known to directly affect bladder function, as outlined in the LURN protocol for inclusion and exclusion.\(^11\) Patients were not excluded if they had already sought care from another provider, such as primary care practitioners, urologists, or gynecologists for LUTS. At the baseline visit, participants completed a medical history and clinical examination as well as questionnaires related to LUTS, bowel function, sexual function, and psychological health.

Additional data for patients without LUTS were obtained from 2 prior published studies: the Renal and Lung Living Donors Evaluation (RELIVE) study and the Establishing the Prevalence of Incontinence (EPI) study. The RELIVE study explored long-term outcomes, including measured iothalamate glomerular filtration rates, for living kidney donors who donated between 1963 and 2007 at 3 large US transplant centers.\(^12\) Calculation of the iothalamate glomerular filtration rates required several complete urine voids, with a PVR measured after each void. The first PVR measurement was used for the current analysis. The RELIVE study had no information about urinary symptoms. The EPI study’s primary purpose was to estimate the prevalence of incontinence in black and white women in southeast Michigan using population-based samples. Women aged between 35 and 64 years were recruited between 2002 and 2004 and completed telephone surveys. A subset was invited to the clinic for urodynamic and pelvic floor testing where the PVR was obtained.\(^13\)

Procedures and Measures

At the LURN baseline clinical visit, comorbidities were assessed using the Functional Comorbidity Index.\(^1\)\(^-\)\(^3\), 4-7, 8-10, 11-13, and 14 or more times per day and never, 1, 2, 3, or 4 or more times per night, respectively.

Statistical Analysis

Demographic and clinical characteristics of LURN participants with measured PVR are presented by sex using frequencies and percentages for categorical variables, and means and standard deviations (SD) or median and interquartile ranges (IQR) for continuous variables. Differences between sexes and between participants with and without PVR were assessed using chi-square and Wilcoxon 2-sample tests for categorical and continuous variables, respectively.

Potential associations between measured PVR and self-reported responses from the LUTS Tool and the AUA-SI were assessed descriptively by sex using box plots of PVR by self-reported symptom rating and Pearson correlation. The distribution of PVR by presence and absence of LUTS was explored using medians and IQRs of PVR and Wilcoxon 2-sample tests. Multivariable Weibull and logistic regression was used to test for adjusted associations between multiple LUTS and PVR as a continuous variable and probability of elevated PVR (defined a priori as PVR > 200 mL) by sex. Weibull regression is an accelerated failure time model commonly used for survival analysis. It specifies that the covariates act multiplicatively on the outcome; in this case, measured PVR model selection was guided by the method of best subsets. P values were adjusted for multiple comparisons by controlling the false discovery rate using the method developed by Benjamini and Hochberg.\(^16\) All analyses were completed using SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

Of the 1064 participants in the LURN Observational Cohort Study, 880 had PVR measured at enrollment. Participants with measured PVR were more likely to be female (53% vs 44%, P= .03), but were similar on all other demographic and clinical characteristics. In the cohort with PVR data recorded, women were younger than men (mean age [SD] 56.6 [14.5] vs 61.0 [13.7], P < .001, Table 1). Anticholinergic or anticholinesterase medication use was similar between men and women, while alpha-blocker use was higher in men (40% vs 2%), and 15% of men reported using 5-alpha reductase inhibitors. Forty-eight percent of women reported more than 2 UTIs in the past year,
and 22% of men reported ever having at least 1 UTI within their lifetime.

In LURN, PVR measurement was done predominately by ultrasound for men (99%). Among women, 61% of measured PVR was obtained by ultrasound, and median PVR was 10 mL lower for those measured with ultrasound (median [IQR] = 20 [0-52] for ultrasound, 30 [10-70] for catheter, \( P = .001 \)). Other demographics and LUTS severity did not differ by method of PVR measurement. The median PVR in the LURN cohort was 26 mL (IQR 6-67 mL, range 0-932 mL, Supplemental Fig. 1).

The distribution of PVR was similar by sex (median PVR = 27 mL [IQR = 0-78.5 mL] in men, 25 mL [IQR = 10-60 mL] in women), but the maximum PVR observed was higher in men (932 mL vs 420 mL).

Observed PVR in RELIVE (n = 413) and EPI (n = 166), although statistically significantly lower, was clinically similar to LURN, with medians of 14 mL (IQR = 0-42 mL) and 20 mL (IQR = 10-35 mL), respectively (Fig. 1A). Elevated PVR (defined as PVR > 200 mL) was more prevalent in LURN (5.2%) compared with RELIVE (1.6%) and EPI (0.6%, \( P = .004 \)). In RELIVE, PVR was statistically lower in women (median PVR 0 mL IQR = 0-32 mL compared with 20 mL IQR = 0-51 mL in men, Fig. 1B). No association between PVR and age was detected in any of the studies (Fig. 1C).

Correlations between PVR and symptom severity ratings on the LUTS Tool and AUA-SI ranged from −0.1 to 0.2, demonstrating weak correlation (Fig. 2). In men, voiding and postmicturition symptoms of incomplete emptying, delay, and weak stream showed very weak positive correlation with PVR; nocturia demonstrated weak negative correlation. In women, delay, straining, and intermittency were weakly positively correlated with PVR; symptoms of stress urinary incontinence were weakly negatively correlated. When men taking outlet medications were excluded, results were unchanged (Supplemental Fig. 2).

When comparing the distribution of PVR by symptom presence or absence, only straining and hesitancy in women and

| Table 1. Demographics and medical history of LURN participants with measured PVR by sex |
|-----------------|-----------------|-----------------|
| Age mean (SD)   | 61.0 (13.7)     | 56.6 (14.5)     |
| Male (n = 416)  | Female (n = 464) |
| Race n (%)      |                 |
| African-American| 39 (9%)         | 59 (13%)        |
| Other           | 43 (10%)        | 32 (7%)         |
| White           | 333 (80%)       | 373 (80%)       |
| Ethnicity n (%) |                 |
| Hispanic/Latino | 17 (4%)         | 18 (4%)         |
| Non-Hispanic/Non-Latino | 390 (94%)  | 435 (94%)       |
| Ethnicity unknown | 9 (2%)          | 11 (2%)         |
| BMI median (IQR) | 28.6 (25.6-32.7) | 29.3 (24.9-35.0) |
| Diabetes n (%)  | 80 (19%)        | 68 (15%)        |
| Anticholinergic medication use n (%) | 13 (3%) | 10 (2%) |
| Anticonstipation medication use n (%) | 36 (9%) | 28 (6%) |
| Alpha blocker use n (%) | 168 (40%) | 9 (2%) |
| 5-alpha reductase inhibitor use n (%) | 64 (15%) |
| Functional comorbidity index median (IQR) | 2.0 (1.0-3.0) | 2.0 (1.0-4.0) |
| History of UTI** n (%) | 90 (22%) | 219 (48%) |

BMI, body mass index; IQR, interquartile range; LURN, Symptoms of Lower Urinary Tract Dysfunction Research Network; PVR, post-void residual volumes; SD, standard deviation; UTI, urinary tract infection.

* \( P \) value from chi-square or Wilcoxon 2-sample test.

** History of UTI assessed as more than two UTIs in the past year for women and any previous UTIs for men.

Figure 1. Comparison of PVR across 3 studies. Boxplots show the distribution of PVR in LURN, RELIVE, and EPI overall and by sex. Relationships between age and PVR in each study are shown using scatter plots. \( P \) values from nonparametric analysis of variance (ANOVA; Kruskal-Wallis tests) are shown testing for differences in distributions across the studies (A) and differences in distributions by sex within each study (B). \( P \) values (C) are from Pearson correlations between age and PVR within each study.
intermittency, weak stream, and delay in men demonstrated statistically significant differences in PVR, compared with those without symptoms; however, the maximum difference in PVR between symptom presence and absence was only 20 mL (Supplemental Table 1). A comparison of symptom ratings between participants with and without elevated PVR (>200 mL) showed higher median scores for incomplete emptying (AUA-SI), weak stream (AUA-SI and LUTS Tool), and delay (LUTS Tool) reported for male participants with elevated PVR (Supplemental Table 2). Among women, higher incomplete emptying (AUA-SI), straining (AUA-SI and LUTS Tool), and intermittency (AUA-SI and LUTS Tool) ratings were observed for those with elevated PVR (Supplemental Table 3).

In women, intermittency severity on the LUTS Tool and sensation of incomplete emptying on the AUA-SI were associated with elevated PVR (26% increase in PVR per unit increase in intermittency severity rating, 95% confidence interval [CI] 13%-42%, P < .001, Table 2a). Higher nocturia severity, leakage just after voiding, and spraying severity ratings were associated with lower measured PVR (range 8%-11% decrease in PVR).

Among men, self-reported incomplete emptying on the AUA-SI and weak stream severity ratings on the LUTS Tool were associated with higher PVR (21% increase in PVR per unit increase in incomplete emptying severity rating, 95% CI = 11%-31%, P < .001, 19% increase in PVR per unit increase in weak stream severity rating, 95% CI = 8%-32%, P < .001, Table 2b). Higher urgency severity rating on the AUA-SI and bladder pain rating on the LUTS Tool were associated with lower PVR.

Among women, only intermittency rating on the LUTS Tool was associated with probability of elevated PVR (odds ratio [OR] = 1.49, 95% CI = 1.06-2.10, P = .02). Among men, each unit increase in incomplete emptying severity rating on the AUA-SI was associated with a 50% increase in odds of elevated PVR (OR = 1.50, 95% CI = 1.17-1.92, P = .001). In addition,
higher severity ratings of burning during urination were associated with higher odds of elevated PVR (OR = 1.40, 95% CI = 0.98-2.01), while higher urgency severity ratings on the AUA-SI were associated with 24% lower odds of elevated PVR (OR = 0.76, 95% CI = 0.60-0.97, P = .03).

We further performed a subgroup analysis of all patients in LURN taking medications that may affect PVR, including alpha blockers; 5-alpha reductase inhibitors; and bladder relaxants, such as anticholinergic medications and beta-3 agonists. Among men taking alpha-blockers or 5-alpha reductase inhibitors, the median PVR was 41 mL (IQR 15-119) for those on an alpha blocker alone (n = 127), 27 mL (IQR 0-88) for those on 5-alpha reductase inhibitors alone (n = 23), and 28 mL (IQR 13-92) for men on both medications (n = 41), compared with a median PVR of 21 mL (0-53) for men not taking either medication (P < .001). The proportion of men with elevated PVR (>200 mL) did not differ between the 4 groups (P = .27). In men and women, there was no statistically significant difference in PVR between those on any form of bladder relaxant medications (19 men, 11 women) and those not taking these medications (median PVR in men = 14.5 mL on bladder relaxant vs 27 mL not on bladder relaxant, P = 0.19, median PVR in women = 26 mL on bladder relaxant vs 25 mL not on bladder relaxant, P = .74).

### COMMENT

In our treatment-seeking population from LURN, median PVR was clinically similar to the other community populations (RELIVE and EPI), while the range was wider and slightly higher in the LURN cohort. We identified statistically significant but very weak correlations between symptom severity and PVR in both sexes that endorsed a sensation of incomplete emptying.

The proportions of people seeking care for LUTS with elevated PVR, as defined by >300 cc in prior studies, were lower than anticipated at less than 2%. Using lower thresholds of PVR (ie, 250 mL, 200 mL, and 150 mL) found only 3%, 5%, and 9% of care-seeking patients in these groups respectively (Fig. 1A). Most importantly, the subgroup analysis of those patients with PVR greater than 200 mL did not show any clinically-relevant association between symptoms when compared with the overall cohort.

Other longitudinal community-based studies associating PVR with LUTS have yielded weak associations as well. In a study of 329 men, baseline PVRs were measured, and patients were followed for 5 years. In those with PVR of <400 cc, the rates of proceeding to prostate surgery and/or the need for indwelling or intermittent catheterization ranged from 4% (<200 cc) to 18% (200-400 cc). However, when the baseline PVR was over 400, it was found that over 75% of these men ultimately underwent interventions, suggesting that a PVR <400 cc may only need intervention in less than a quarter of patients. Our cohort had very few men with PVR >400, and we did not follow men longitudinally, so cannot comment on the natural history for elevated PVR.

In a separate study of 1688 asymptomatic community-dwelling men, PVR, along with 6 other factors, including family history of an enlarged prostate or LUTS, were associated with the future development of symptomatic LUTS. However, in a different study of randomly-selected men, PVR alone was not associated with present or future symptoms, similar to our findings. Finally, in a longitudinal study of community-dwelling men that measured PVR every 2 years for up to 12 years, the average yearly increase in PVR was only 2.2%. However, there was significant variability in PVR trajectory where a rapid rise, not just the overall 1-time PVR, was associated with higher baseline AUA-SI. These studies all agree with our findings that symptoms alone may not be able to predict the presence of an elevated PVR.

This observational cohort gives notable information on a large group of care-seeking patients with respect to measured PVR values. We acknowledge certain limitations in our research. Notably, the control groups (those from RELIVE) were not prospectively enrolled in the study at the same time as the cases (LURN and EPI), and we drew their data from other studies. In the LURN cohort, we do not have longitudinal PVR data to track changes over time, or with respect to various treatments, age and time, bladder volume, medications, and infections. Because of this, multiple sets of measurements with analysis of median values would be valuable. The RELIVE cohort was not confirmed to be free of LUTS, just presumed to be asymptomatic because they were not care-seeking individuals. The EPI patients were only women who may have had LUTS other than incontinence. There may be a difference between the ultrasound measurements and the

### Table 2b. Multivariable associations with PVR among male LURN participants

<table>
<thead>
<tr>
<th>Covariate</th>
<th>% change or OR</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weibull model of continuous PVR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete emptying (AUA-SI)</td>
<td>+21%</td>
<td>+11%</td>
<td>+31%</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Urgency (AUA-SI)</td>
<td>–11%</td>
<td>–18%</td>
<td>–4%</td>
<td>.002</td>
</tr>
<tr>
<td>Pain (LUTS tool)</td>
<td>–15%</td>
<td>–26%</td>
<td>–4%</td>
<td>.011</td>
</tr>
<tr>
<td>Weak stream (LUTS tool)</td>
<td>+19%</td>
<td>+8%</td>
<td>+32%</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Logisitc model of probability of PVR &gt; 200</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete emptying (AUA-SI)</td>
<td>1.50</td>
<td>1.17</td>
<td>1.92</td>
<td>.001</td>
</tr>
<tr>
<td>Urgency (AUA-SI)</td>
<td>0.76</td>
<td>0.60</td>
<td>0.97</td>
<td>.027</td>
</tr>
<tr>
<td>Burning (LUTS tool)</td>
<td>1.40</td>
<td>0.98</td>
<td>2.01</td>
<td>.066</td>
</tr>
</tbody>
</table>

AUA-SI, American Urological Association-Symptom Index; CI, confidence interval; IQR, interquartile range; LURN, Symptoms of Lower Urinary Tract Dysfunction Research Network; LUTS, lower urinary tract symptoms; OR, odds ratio; PVR, post-void residual volume.
volumes obtained by catheterization; ultrasound measurements are more operator-dependent, and the catheterization result is more difficult to be confounded by other physical issues, such as pelvic masses, ovarian cysts, etc.

A portion of the observational cohort (184 participants, or 17%) did not have PVR measurements and were not included in this analysis. The absence of this group may have biased the analysis; however, these patients were demographically and clinically similar to included LURN participants. Finally, we did not exclude patients who had already obtained specialty care elsewhere with either primary care practitioners, gynecologists, or urologists. This contributed a small cohort that were already on medicines, such as alpha blockers and 5-alpha reductase inhibitors. Inclusion of this group could have skewed the PVR downward due to prior treatment or upward due to recalcitrant symptoms that prompted additional care-seeking. However, exclusion of these participants did not change the results of the whole cohort.

CONCLUSIONS

This study demonstrates that the proportions of men and women seeking care for LUTS with an elevated PVR were lower than we anticipated, making up less than 2% of the cohort. Also in this cohort, self-reported LUTS are only lower than we anticipated, making up less than 2% of the women seeking care for LUTS with an elevated PVR. However, exclusion of these participants did not change the results of the whole cohort.

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SUPPLEMENTARY MATERIALS

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Editorial Comment

Obtaining a Post-void Residual (PVR) is one of the most common procedures performed in Urology. In a subspecialty replete with uncomfortable and potentially embarrassing tests, measuring PVR using ultrasound is arguably unique in its minimally-invasive nature, reproducibility, and ability to deliver objective data. It is a technique which has been universally adopted and employed, albeit with little data to guide the user in interpreting its results. Indeed, several guideline statements deemed obtaining a PVR a Clinical Principle, a statement for which there may or may not be evidence in the medical literature that is widely agreed upon by clinicians.1–3

The current study explored the relationship between PVR and LUTS in several large cohorts and delivered 3 key findings. First, the incidence of elevated PVR in men and women seen for LUTS varies by the definition of “elevated.” When PVR exceeded 300 mL the incidence was 2% and rose to 9% when the threshold was lowered to 150 mL. Second, and not unexpectedly, voiding symptoms had a greater association with elevated PVR than storage symptoms. Third, the association between self-reported LUTS and PVR was weak, at best. Regardless of the threshold, it is reassuring to know that relatively few patients with LUTS have “elevated” PVRs; however, this finding, unfortunately, gets us no closer to advancing PVR beyond its current Clinical Principle status. A threshold, clinically-significant elevation in PVR that automatically triggers a “red flag” for the practitioner remains elusive.

As it stands, PVR can be viewed in 2 ways. On one hand, if viewed in a vacuum, PVR is either a source of comfort or potential concern. If low, the practitioner is more confident about proceeding with medical or surgical treatment of LUTS associated with BPE, SUI, or OAB. Conversely, when high, the practitioner is more likely to engage in additional work-up or monitoring. While not a surrogate for progression or stability of a urologic condition, obtaining serial PVR measurements can further bolster the practitioner’s confidence in maintaining or changing their treatment course. On the other hand, PVR can be considered a part of a greater whole in evaluating LUTS. Thus, management and additional work-up can be guided by the patients’ history, physical examination, PVR, and other testing such as uroflowmetry and urodynamics.

The authors’ conclusion that “the measurement of a PVR during the initial evaluation of all patients with LUTS is advisable” is on the money. While the absolute threshold for guiding work-up and treatment of LUTS is yet unresolved, PVR continues to be a low-risk, high-reward tool in improving the practitioner’s confidence and guiding the decision to perform further testing.

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