

Prior studies suggest that oversensitivity of the presumed site of pain generation is a possible mechanism for the development of chronic pain syndromes such as IC/PBS [5], irritable bowel syndrome [6], fibromyalgia [7] and vulvodynia [8]. In a study examining tolerance to bladder filling on filling cystometry, women with interstitial cystitis had significantly lower volumes and more pain with bladder filling than healthy controls [9]. The joint report [9] of the International Urogynecologic Association and International Continence Society has defined bladder oversensitivity as symptoms of frequency and/or nocturia, reduced average voided volume in the bladder diary and increased perceived bladder sensation during filling cystometry with no abnormal increase in detrusor pressure and in the absence of known or suspected bladder infection.

The aim of the present study was to compare the average voided volume and bladder sensation during filling cystometry in women with recurrent UTIs and controls. Our hypothesis is that women with recurrent UTIs have increased bladder sensation compared with women without a history of recurrent UTI.

### PATIENTS AND METHODS

Following institutional review board approval by the University of Pennsylvania, a retrospective case-control study was performed. Cases were women with recurrent UTIs. Recurrent UTI was defined as the presence of lower urinary tract symptoms (urgency, frequency or dysuria) and three documented positive urine cultures >10<sup>5</sup> colonies/mL on a voided urine specimen in the previous 12 months [9]. Controls were women with stress urinary incontinence and no history of recurrent infections and absence of urge incontinence. The 2-day diary by averaging data over 2 days. Bladder diary data were described using standard definitions for the following variables: the number of daytime and night-time voids, mean voided volume and maximum voided volume [9]. The number of voids per litre of fluid intake, previously reported as a stable measure of urinary frequency [13], was also calculated.

The electronic medical records of consecutive women in the age group 18–40 years attending the Urogynecology Clinic of the University of Pennsylvania between December 2009 and September 2010 were reviewed. Women with a final clinical diagnosis of recurrent UTI or stress urinary incontinence, as defined above, were identified. We limited inclusion to women in the age group 18–40 years to avoid the

confounding effect of aging and menopause on bladder sensitivity. Additional inclusion criteria were availability of a bladder diary and filling cystometry data, negative office cystoscopy for cases, negative dipstick urine for cases preceding bladder diary and filling cystometry testing, and one documented negative urine culture for controls.

We excluded women with conditions known to be associated with bladder hypersensitivity. These included age greater than 40 years, known diagnosis of IC/PBS, urge urinary incontinence (as determined by a positive response to the urge incontinence question on the UDI-6) [10], pelvic organ prolapse stage 2 or greater on clinical examination based on the pelvic organ prolapse quantification system [11], neurological disorder known to affect the lower urinary tract, previous hysterectomy or surgery for incontinence or pelvic organ prolapse, current or recent vaginal pessary use, other known urinary tract pathologies such as calculus and urethral diverticulum, history of pelvic cancer or radiation to the pelvis and diabetes mellitus.

The data of validated questionnaires (O'Leary-Sant Interstitial Cystitis Symptom and Problem Index) [12], pelvic organ prolapse stage, bladder diary, filling cystometry and cystoscopy were extracted from the medical records.

### BLADDER DIARY

Women had collected bladder diary data using a log and a container in the 2 days immediately preceding the filling cystometry. Since a negative urine dipstick was documented on the day of filling cystometry, this ensured that cases had not maintained the bladder diary during an episode of infection. Daily values were calculated from the 2-day diary by averaging data over 2 days. Bladder diary data were described using standard definitions for the following variables: the number of daytime and night-time voids, mean voided volume and maximum voided volume [9]. The number of voids per litre of fluid intake, previously reported as a stable measure of urinary frequency [13], was also calculated.

### FILLING CYSTOMETRY

In this study, we only included subjects for whom filling cystometry data were available.

Cystometry had been performed in women with recurrent UTI if they had complained of urinary symptoms of uncertain diagnosis, e.g. persistent urinary frequency and/or nocturia in the absence of a recent (less than 6 weeks) UTI. The purpose of the filling cystometry in women with recurrent UTI was to rule out the presence of detrusor overactivity.

Negative urine dipstick had been documented in all women prior to filling cystometry. Filling cystometry was performed in the sitting upright position using an air-charged (T-Doc) catheter and Duet<sup>®</sup> Logic G/2 (Medtronic Inc., Minneapolis, MN, USA). Following spontaneous voiding, postvoid residual volume was measured and the bladder was filled at 50 mL/min using warm sterile water intra-abdominal pressure was measured using a rectal catheter. The first desire to void (volume of filling associated with the first need to urinate but voiding can be delayed if necessary), strong desire to void (persistent desire to pass urine without fear of leakage), maximum tolerated volume (filling volume at which the patient feels she can no longer delay micturition) and change in detrusor pressure (from the start of bladder filling to maximum cystometric capacity) were recorded. All terminology and methods are in accordance with International Continence Society nomenclature [9] unless specified otherwise.

Data were analysed using SAS (version 9.2, SAS Institute, Inc.). They were described using mean, median or percentages. We compared urinary symptom and quality of life scores, bladder diary and filling cystometry data between cases and controls using the Wilcoxon rank-sum test for continuous data and the chi-squared test for categorical data. We examined the relationship between maximum voided volume and maximum cystometric capacity using the Pearson correlation coefficient. A 0.05 significance level was used for all statistical tests.

We based our sample size calculation on a previously reported mean voided volume of 220 ± 84 mL in the bladder diary in women with stress urinary incontinence [14]. This is similar to the mean voided volume in asymptomatic women [15]. Based on these data, we estimated that we needed 50 women in each group at an  $\alpha$  of 0.05 and