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ORIGINAL ARTICLE

Correlations between bladder wall thickness and clinical manifestations in female patients with detrusor underactivity and detrusor overactivity–with–detrusor underactivity

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Abstract

Background: Among female patients with lower urinary tract symptoms, detrusor underactivity (DU), and detrusor overactivity–with–detrusor underactivity (DO-DU) are two common diagnoses. Here, we investigated the correlations between bladder wall thickness (BWT) and clinical manifestations of the two diagnoses.

Methods: From 2011 to 2016, female patients with DU or DO-DU, diagnosed at our institute, were recruited. We analyzed their urodynamic parameters and collected three questionnaires (IPSS, UDI-6, OABSS). Using transabdominal sonography, the BWT was recorded. DU was defined as follows: maximum free flow rate (Q_{max}) ≤ 15 cc/s; detrusor pressure at maximum flow ($P_{detQmax}$) ≤ 20 cmH_2O; bladder capacity > 150 cc. DO-DU was defined as follows: Q_{max} ≤ 15 cc/s; $P_{detQmax}$ ≤ 20 cmH_2O; bladder capacity ≤ 150 cc. The BWTs of the two groups were compared using the Mann–Whitney *U* test; the correlations among the BWTs and the results of three questionnaires were analyzed using Spearman's rank correlation coefficient.

Results: Forty-eight female patients with DU and 13 with DO-DU were recruited. Demographic data revealed no differences between the two groups. The mean BWT of the DO-DU patients was significantly larger than that of the DU patients (4.11 vs 3.42 mm; $p = 0.001$). In the DO-DU group, a high correlation existed between the BWT and some of the UDI-6 items (urgency incontinence: $r = 0.831$, $p = 0.006$; incontinence related to activity: $r = 0.884$, $p = 0.002$; small amounts of leakage: $r = 0.809$, $p = 0.008$). The BWT of the DO-DU patients also exhibited a moderate correlation with the urgency incontinence from the OABSS questionnaire ($r = 0.679$; $p = 0.044$). No correlations existed between the BWT of the DU patients and any of the data from the three questionnaires.

Conclusion: The BWT in the DO-DU patients was significantly thicker than that in the DU patients. The DO-DU patients with thicker bladder walls also had higher UDI-6 scores for both urgency and urgency incontinence.

Keywords: Bladder wall thickness; Detrusor overactivity–with–detrusor underactivity; Detrusor underactivity; Urodynamic study

1. INTRODUCTION

The International Continence Society (ICS) defines "voiding dysfunction" as "abnormally slow or incomplete micturition, diagnosed by symptoms and urodynamic investigations."[1] Although voiding dysfunction bothers both male and female patients, the etiology of voiding dysfunction is quite different between the two genders because most symptoms in male patients are derived from benign prostatic obstruction.[2] Some previous reports have stated that the prevalence of voiding dysfunction in women varies from 10% to 60% in selected populations, determined according to various diagnostic criteria.[3] Voiding dysfunction has become one of the major reasons for female patients visiting urology offices. Voiding dysfunction in females might result from bladder outlet dysfunctions or innate bladder dysfunctions. Consequently, urodynamic studies can provide important information for the evaluation of lower urinary tract dysfunction.

Detrusor underactivity (DU) and detrusor overactivity–with–detrusor underactivity (DO-DU) are two diagnoses that have resulted from urodynamic studies of females. In addition to their similar symptoms (eg, slower urinary stream; incomplete bladder emptying), both DU and DO-DU are characterized in urodynamic studies by impaired detrusor contractility.[4] In 1987, Resnick et al were the first to propose DO-DU, and that it was, paradoxically, related to neurological hypersensitivity.[5,6] The presentation of DO-DU is, therefore, more complicated than DU.[6,7] The pathophysiology of the two diagnoses remains unclear and possibly multifactorial.[8] At present, it is hypothesized that the two diagnoses result from neurological dysfunction (eg, diabetic

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neuropathy) causing subsequent pathological changes to the bladder wall (eg, trabeculation, fibrosis, detrusor hypertrophy, or atrophy), with a decline in detrusor contractility in some cases.[8,9]

With this rationale, imaging studies (eg, bladder sonograms) of the bladder wall thickness (BWT) might be a possible indicator of any pathological changes to the bladder wall and might also be a possible predictor of the symptom severity as the bladder wall gets thicker or thinner. The relationship between detrusor overactivity (DO) and the BWT has been reported recently.[10,11] Furthermore, attempts have been made to correlate the BWT with cystometrical findings and other bladder diseases (eg, interstitial cystitis).[12,13] Although the measurement of BWT might not replace any contemporary diagnosing strategy as a direct diagnostic tool for DU or DO-DU, it can be a simple and noninvasive survey before performing invasive urodynamic studies while also being an alternative means of examination for those not amenable to urodynamic studies.

Because few literature reports discuss the correlation between sonographic images and females with DU and DO-DU, we were interested in the importance of BWT for these two diagnoses.[14] Our aim for this study was to investigate the difference in BWT between female patients with DU and DO-DU and to survey the correlations between the BWT and the clinical symptoms of female patients having these two diagnoses.

2. METHODS

Under the approval of the ethical committee of Taipei Veterans General Hospital (IRB No. 2018-07-031CC), all of the medical records of female patients who received a urodynamic study from 2011 to 2016 were reviewed retrospectively. Related parameters, including the maximal free flow rate, the detrusor pressure at maximal flow, and the urodynamic bladder capacity, were recorded for patient recruitment. All of the patients completed the three urological questionnaires—the International Prostate Symptom Score (IPSS), the Urogenital Distress Inventory (UDI-6), and the Overactive Bladder Symptom Score (OABSS)—before the urodynamic study.[15–17] The three questionnaires were given in their Mandarin versions. According to Uren et al and Gammie et al,[4,18] herein, we define DU by the following parameters: maximum free flow rate (Q_{max}) ≤ 15 cc/s; detrusor pressure at maximum flow ($P_{detQmax}$) ≤ 20 cmH_2O; bladder capacity > 150 cc. We define DO-DU as follows: Q_{max} ≤ 15 cc/s; $P_{detQmax}$ ≤ 20 cmH_2O; bladder capacity ≤ 150 cc.

BWTs were measured through transabdominal sonography in the Radiology Department of Taipei Veterans General Hospital. All of the ultrasound images recruited in this study were performed during the period in which the patients received the urodynamic study. Patients were scanned in supine position with a 3–5 MHz probe placed suprapubically. In the protocol of transabdominal sonography, patients were asked to drink water to maintain the bladder in a distended status—to provide a better view of the bladder and to prevent the BWT from varying through nondistention.[19–21] Although the capacity of the two diagnoses had already been defined by the urodynamic findings, we evaluated the volume of the urinary bladder (one of the major confounding factors for the accuracy of BWT measurements) under sonography through measurements of the three dimensions of the bladder. The length and width of bladder were obtained from the transverse view; the height was measured from the mid-sagittal view (Fig. 1A, B).[22] Several formulas can be used to estimate the bladder volume.[23] Here, assuming the bladder to be an ellipsoid, we applied the expression: 0.52 × bladder length (cm) × bladder width (cm) × bladder height (cm). To minimize inaccuracy, the first priority was measuring the width of the anterior wall—because the depth of the anterior wall from the abdominal wall is much less than that of the posterior wall. Therefore, the anterior wall was closer to the probe, improving the resolution and precision on the image (Fig. 1C).[20,24] The wall thickness was measured twice—once by a urologist and once by a radiologist—to minimize any bias.

SPSS Statistics 17.0 software was used for statistical analysis. The Mann–Whitney *U* test was applied to compare the BWTs between the two diagnostic groups of DU and DO-DU. Spearman's rank correlation coefficient was applied to correlate the BWTs with items from all three of the IPSS, UDI-6, and OABSS urology questionnaires. A value of p of less than 0.05 was considered to indicate statistical significance.

3. RESULTS

From 2011 to 2016, a total of 1301 female patients underwent urodynamic studies in our institute. After reviewing all of their urodynamic parameters, 48 patients met the criteria of female DU and 13 met the criteria of DO-DU. The mean age of these DU patients was 63.92 years old (SD = 11.80). Another 13 female patients were diagnosed with DO-DU, with a mean age of 55.37 years old (SD = 20.55). The mean ages of the patients in these two diagnostic groups were not significantly different (p = 0.449). Furthermore, there was also no significant difference in body mass index between the DU and DO-DU groups (DU: 23.96 ± 4.00; DO-DU: 22.69 ± 4.57; p = 0.436). Other underlying

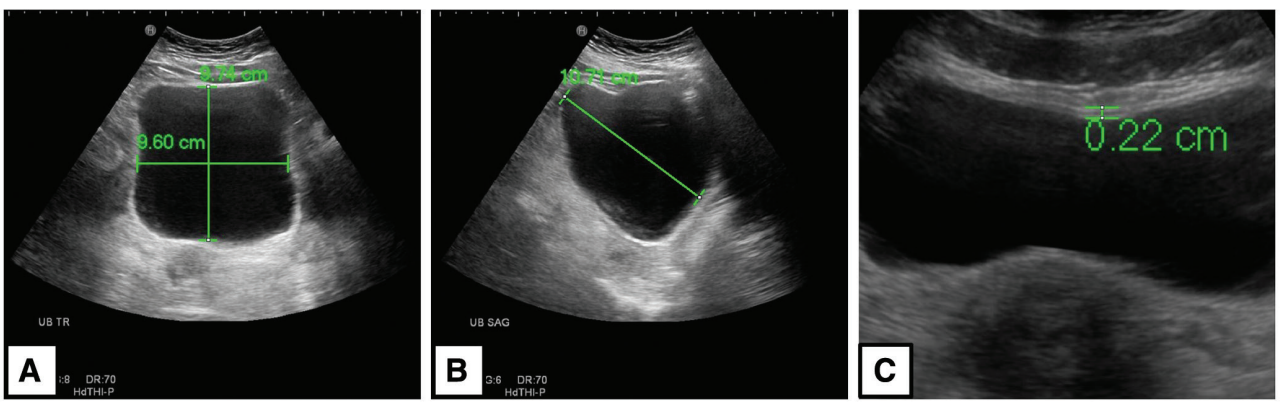

Fig. 1 Measurement of bladder volume and BWT under ultrasound. A, The length and width of the bladder were measured from the transverse view; the length was defined as the greatest antero-posterior measurement; the width was defined as the greatest transverse measurement. B, The height of bladder was measured from the mid-sagittal view; the height was defined as the greatest superior-inferior measurement. C, The bladder wall thickness was measured at the anterior bladder wall.

Table 1

Demography, bladder capacities (measured from transabdominal sonograms), and BWTs of DU and DO-DU patients

Patient Group (n)	DU (48)	DO-DU (13)	*p*
Mean age	63.92 ± 11.80	55.37 ± 20.55	0.449
Body mass index	23.96 ± 4.00	22.69 ± 4.57	0.436
Hypertension (N)	16	3	0.365
Diabetes mellitus (N)	6	1	0.534
Gynecological surgery (N)	5	1	0.622
Colorectal surgery (N)	1	1	0.384
Lumbar spine disease (N)	8	1	0.380
Bladder capacity (mL)[b]	171.76 ± 133.84	107.61 ± 89.36	0.084
BWT (mm)	3.42 ± 0.65	4.11 ± 0.53	0.001[a]

[a]$p < 0.05$ (two tails).

BWT = bladder wall thickness; DO-DU = detrusor overactivity–with–detrusor underactivity; DU = detrusor underactivity.

diseases that might have influenced the detrusor function (hypertension, diabetes mellitus, gynecological and colorectal surgery history, lumbar spine disease history) were also evaluated, but there were no differences in the disease distributions between the DU and DO-DU groups (Table 1).

Measured from the transabdominal sonograms, the mean calculated bladder volume of the DU patients was 171.76 ± 133.84 mL; for the DO-DU patients, it was 107.61 ± 89.36 mL. These values are consistent with the urodynamic definitions of DU (urodynamic capacity > 150 cc) and DO-DU (urodynamic capacity ≤ 150 cc). Although the capacities of the two diagnoses were different in terms of their urodynamic definitions, the measured volume while distended revealed no significant difference ($p = 0.084$). Before analysis, whether the bladder was distended or not was considered to be one of the major confounding factors that might have influenced the accuracy of wall thickness measurement. Because no significant difference in sonographic bladder volume was detected statistically between the two groups, no further adjustment to the BWT was applied according to the measured bladder volume. The mean measured BWT of the DO-DU patients (4.11 ± 0.53 mm) was significantly greater than that of the DU patients (3.42 ± 0.65 mm; $p = 0.001$; Table 1).

Table 2 reveals that 38 female DU patients and 9 female DO-DU patients completed the three questionnaires during the time of their urodynamic study. In the DU group, no correlation existed between the BWT and any of the items from the IPSS, UDI-6, and OABSS questionnaires. Thus, those symptoms might not be related to the BWT in the DU patients. In contrast, in the DO-DU group, high correlations existed between the BWT and three of the items in the UDI-6 questionnaire (urine leakage related to feeling of urgency: $r = 0.831$, $p = 0.006$; urine leakage related to physical activity, coughing, or sneezing: $r = 0.884$, $p = 0.002$; small amounts of urine leakage: $r = 0.809$, $p = 0.008$). A moderate correlation also appeared for the total score in UDI-6 ($r = 0.69$; $p = 0.04$). In addition, the BWT of the DO-DU patients was also correlated moderately with urgency incontinence in the OABSS questionnaire (how often do you leak urine, because you cannot defer the sudden desire to urinate: $r = 0.679$; $p = 0.044$). Nevertheless, no correlations existed between the BWT and the IPSS questionnaire items for the DO-DU patients. Thus, this study revealed correlations between some symptoms—especially urgency and urgency incontinence—and the BWT.

4. DISCUSSION

In this study, we initially defined the DU and DO-DU diagnostic groups in terms of various criteria related to cystometric capacity from urodynamic findings. Subsequently, we applied

Table 2

Correlation coefficients between BWT and items in IPSS, UDI-6, and OABSS questionnaires for female DU and DO-DU patients

	DU (38)		DO-DU (9)	
Patient group (*n*)	***r***	***p***	***r***	***p***
IPSS				
Incomplete emptying	–0.029	0.864	0.080	0.838
Frequency	0.036	0.831	0.196	0.613
Intermittency	–0.160	0.338	0.214	0.580
Urgency	–0.312	0.056	0.401	0.284
Weak stream	–0.075	0.654	0.436	0.241
Straining	0.106	0.525	0.241	0.532
Nocturia	0.176	0.290	0.078	0.841
Total score	–0.064	0.705	0.138	0.723
UDI-6				
Frequent urination	–0.287	0.085	0.190	0.624
Urine leakage related to feeling of urgency	–0.132	0.435	0.831[a]	0.006
Urine leakage related to physical activity, coughing, or sneezing	0.102	0.550	0.884[a]	0.002
Small amounts of urine leakage	0.220	0.190	0.809[a]	0.008
Difficulty emptying bladder	–0.181	0.283	0.141	0.717
Pain or discomfort in lower abdominal or genital area	0.112	0.508	0.036	0.927
Total score	–0.071	0.678	0.690[a]	0.040
OABSS				
How many times do you typically urinate from waking in the morning until sleeping at night?	–0.132	0.429	–0.093	0.812
How many times do you typically wake up to urinate from sleeping at night until waking in the morning?	0.212	0.201	–0.084	0.830
How often do you have a sudden desire to urinate, which is difficult to defer?	–0.088	0.599	0.348	0.358
How often do you leak urine, because you cannot defer the sudden desire to urinate?	–0.110	0.511	0.679[a]	0.044
Total score	–0.029	0.862	0.534	0.138

[a]$p < 0.05$ (two tails).

BWT = bladder wall thickness; DO-DU = detrusor overactivity–with–detrusor underactivity; DU = detrusor underactivity.

transabdominal ultrasonography to assess the bladder volume and BWT. To minimize the measuring bias and increase the accuracy and reproducibility of the sonographic exams, all measurements of BWT were performed by one urologist and one radiologist, with reference to the sonography measurement protocol proposed by Rachaneni et al.[25] All of the patients in our study were asked to distend their bladders during their sonographic examinations. Although there is a negative correlation between bladder volume and the BWT,[19] we found, interestingly, no statistically significant difference in the calculated bladder volume in each group when using our selected formula. Assuming that the bladder volumes were the same while performing the sonograms, interfering bias would have been relatively low during our measurements of the BWTs.

In a previous report, Hakenberg et al measured BWTs through transabdominal sonograms and demonstrated that the mean BWT of the normal healthy group was 3.35 mm with a normal distribution;[26] the BWT was 3.3 ± 1.1 mm in normal adult men and 3.0 ± 1.0 mm in normal adult women. In this current study, we found that the bladder walls of the DO-DU patients were significantly thicker than those of the DU patients. Indeed, the BWTs of the DU patients were closer to those of healthy specimens, whereas those of the DO-DU patient were much thicker than normal. Previous studies have found that, similar to male bladder outlet obstruction (BOO), greater BWTs appeared in female BOO patients with or without DO.[14,27] Yalla et al hypothesized that DO-DU is a consequence of DO, with resultant structural modification after frequent contractile activity.[6] This modification, including the gradual accumulation of collagen, interstitial fibrosis, and trabeculation, causes wall hypertrophy and malfunction of the detrusor muscle.

Furthermore, no such correlations existed between the BWT and the clinical manifestation observed in the DU group. In contrast, the BWT might be a possible predictor of the severity of the clinical manifestations in the DO-DU patients, especially for such symptoms as urgency or urgency incontinence. The distinct aspect of this study was to investigate the correlations between symptoms identified from the UDI-6, OABSS, and IPSS questionnaires and the BWT. To the best of our knowledge, no previous reports mention such correlations. The significant relationships that we note between the urge symptoms and the DO-DU wall thickness also indicate that the original neurological hyperfunction caused both the subjective clinical symptoms and the objective bladder wall thickening.

Measurement of only the detrusor muscle layer or the whole layer of the bladder wall with mucosa included remains unexplored for the DO-DU group. In a previous study, Oelke et al suggested that ultrasound measurements of the detrusor wall thickness could be better than uroflowmetry as a test for male BOO when using a high frequency (7.5 MHz) probe to differentiate the detrusor from other layers.[28] Another previous study revealed that only the detrusor wall thickness and bladder capacity needed to be applied to detect male DU.[29] In contrast, here we measured only the whole layer thickness of the urinary bladder as a means of detection, for two reasons: (i) because 3–5 MHz probes are widely used for transabdominal examinations and, therefore, the findings from our study would be more likely to apply; (ii) it avoids the necessity to differentiate the detrusor layer from other bladder wall layers when seeking a correlation to symptoms.

Nevertheless, this study has several limitations. First, only a small number of patients were recruited, excluding many other patients under strict criteria. Second, instead of studying a single institution, multicenter studies would be warranted in the future. Third, the definition of female DU and DO-DU remains obscure and uncertain. Greater consensus would be useful for future research—for example, when evaluating the treatment outcomes of DO-DU or DU patients in terms of BWT.

In conclusion, the BWT in female DO-DU patients is significantly thicker than that in female DU patients. Furthermore, the BWT of female DO-DU patients correlates with the severity of urgency and urgency incontinence. Further prospective studies, including cystoscopic surveillance or microscopic histology, are warranted to establish the relationship between the pathological changes in the bladder wall and clinical manifestations in female DU and DO-DU patients.

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