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Original Article

Relationship between detrusor wall thickness and lower urinary tract dysfunctions in patients with spinal cord injuries

Hong-Jun Zhu[1,2], Wei-Xin Yang[2], Da-Wei Zhang[2], Yun-Qiang Zan[2], Chuan-Dao Liu[2], Jin-Fa Feng[2], Jian-An Li[1]

[1]*Department of Rehabilitation, The First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China;* [2]*Department of Rehabilitation, The First Affiliated Hospital of Soochow University, Suzhou 215006, China*

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Abstract: The aim of this study was to measure the detrusor wall thickness (DWT) by ultrasound in patients with spinal cord injury (SCI)-based neurogenic lower urinary tract dysfunction (NLUTD) in order to assess the potential role of DWT in the prediction of functional renal impairment risk. An 8-13 MHz linear array ultrasound probe was used to measure the DWT of the anterior bladder wall in 48 adult patients with SCI-NLUTD (the patient group) and 41 normal adult subjects (the control group). The critical DWT values of moderate-to-high-risk patients (detrusor leak-point pressure (DLPP ≥40 cmH_2O) and low-risk patients (detrusor leak-point pressure <40 cmH_2O) were also studied in the patient group. The patient group exhibited a significant decrease in DWT when bladder capacity (BC) was <250 mL ($P<0.05$). Under conditions of maximum BC, the patient group exhibited a significantly increased DWT (0.97±0.31) mm as compared to the control group ($P<0.05$). A correlation was detected between DWT and DLPP in the patient group ($r = 0.77$, $P<0.01$), such that a DWT ≥0.87 mm could be used as the critical value to predict the risk of functional renal impairment (sensitivity 89.5%, specificity 58.6%) at maximum BC. Patients with SCI exhibited significantly increased DWT, which was positively correlated with DLPP. Additionally, DWT could be used to predict the risk of functional renal impairment in patients with SCI-based NLUTD.

Keywords: Detrusor wall thickness, ultrasound, spinal cord injury, neurogenic lower urinary tract dysfunction

Introduction

Neurogenic lower urinary tract dysfunction (NLUTD), a common complication of spinal cord injury (SCI), may manifest as urinary incontinence or urinary retention. These conditions can easily lead to increased intravesical pressure, renal damage and potentially endanger the lives of patients. The standard methods for treating NLUTD include emptying the bladder, reducing the intravesical pressure, and preventing renal damage [1]. Traditionally, an urodynamic diagnosis has been considered as the gold standard for lower urinary tract dysfunction (LUTD); however, it is an invasive, time-consuming, laborious, and costly examination method and may cause urinary tract infections. Therefore, it may not be re-performed in the short-term and has not been easily accepted by patients.

Recently, the development of ultrasound technology has provided a new, non-invasive, non-radioactive, low-cost, practical urological examination method [2]. In fact, the International Continence Society had noted that the ultrasound examination was an ideal way to diagnose LUTD [3]. Furthermore, study results have shown that ultrasound images of the bladder wall may be used to determine LUTD [4, 5]. In 1994, Schoor et al. [6] was the first to use ultrasound to accurately measure bladder wall thickness (BWT) and detrusor wall thickness (DWT) in rabbits [6]. In 2009, Berges et al. [7] applied this technology to the diagnosis of prostatic hyperplasia attributable to lower urinary tract obstruction. Based on further research, the ultrasound determination of BWT or DWT was considered as an ideal, non-invasive method for the assessment of LUTD [8, 9]. The bladder wall layer includes the mucosal layer, detrusor,

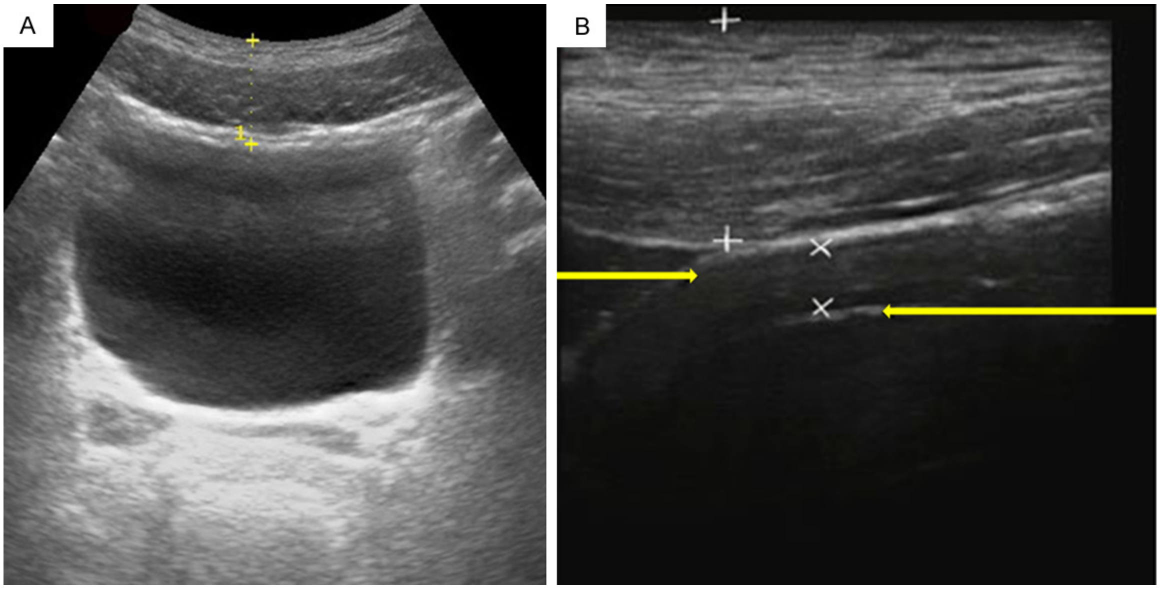

Figure 1. A: Distance determination between bladder wall and abdominal wall. The low-frequency ultrasound probe was used to detect the distance between the bladder wall and abdominal wall, i.e., the distance between two "+". B: DWT determination. The high-frequency linear array probe was used to measure DWT, namely the hypoechoic area (black band) between two "+" was the abdominal wall, the low signal area between the two "X" was detrusor, the hyperechoic area (white band) between the two "→" was the serosa and mucosa of bladder wall.

Table 1. DWT of the patient group at different BC ($\bar{x}\pm s$)

	50 ml	100 ml	150 ml	200 ml	250 ml	300 ml	400 ml	500 ml
DWT (mm)	2.92±0.62*	2.32±0.62*	1.90±0.53*	1.54±0.46*	1.25±0.38*	1.08±0.37*	0.96±0.35*	0.93±0.33*

*: P<0.05, compared with other groups.

and externa, and thus the thickness of bladder wall is greater than that of detrusor wall. The aim of the current study was to observe changes in DWT in patients with SCI using ultrasound. Additionally, the relationships among DWT, bladder capacity (BC), and LUTD types in patients with SCI were explored in order to assess the role of DWT in predicting functional renal impairment risks in patients with SCI-based NLUTD.

Materials and methods

General information

Patients with SCI combined with LUTD (N = 48) were selected and designated as the patient group. Diagnoses were confirmed for all patients by urodynamic studies. The inclusion criteria were as follows: (1) the spinal cord injury caused by trauma; (2) obvious lower urinary tract dysfunction; (3) without obvious craniocerebral trauma; (4) clear consciousness and stable vital signs. All members of the patient group were male, aged 25-68 years old, and had disease duration of 15-216 days. The neurological plate classification of patients with SCI according to American Spinal Injury Association (ASIA) Classification was as follows: 18 cases of cervical cord injury, 23 cases of thoracic cord injury, 5 cases of lumbar cord injury, and 2 cases of sacral cord injury. Treatment methods used for patients with SCI included 43 cases of intrasurgical fixation and 5 cases of conservative treatment. Of the 48 cases, 31 underwent catheterization, and the remaining 17 underwent interval cleaning and intermittent catheterization. In addition, 41 normal adult subjects were designated as the control group. All members of the control group were male and were aged 20-40 years. Before enrollment, the control group underwent urodynamic study to ensure a maximum urine flow rate of >15 mL/s, and a residual urine amount of <10 mL. Any patient or control subject with

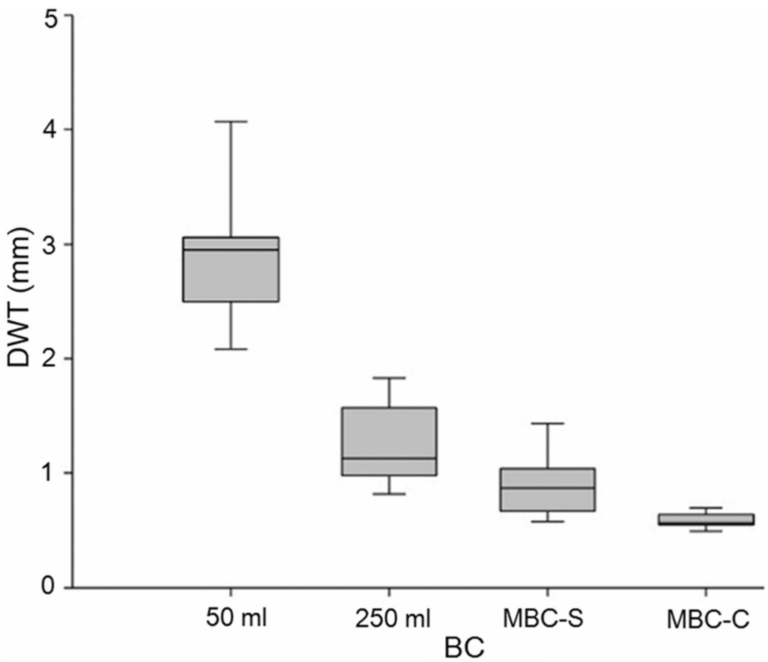

Figure 2. Impacts of BC to DWT. Comparison of DWT and its variability at different BC. "50 ml, 250 ml, MBC-S" represented the "50 ml, 250 ml and maximum bladder capacity" of the test group, MBC-C represented the maximum bladder capacity of the control group.

urinary tract infections, pelvic fractures, prior urinary tract surgeries, or a history of diabetes was excluded. This study was conducted in accordance with the declaration of Helsinki, and was conducted with approval from the Ethics Committee of Nanjing Medical University. Written informed consent was obtained from all participants.

Urodynamic examination

Patients with SCI were placed in the supine position for urodynamic measurements with the urodynamic instrument (Laborie Delphis B type, Canada). One 8 French (F) triple lumen catheter (diameter 2.7 mm) was transurethrally inserted to detect bladder pressure, and 18F balloon catheter was inserted through the anus to measure abdominal pressure. The upper edge plane of the pubic symphysis was set as the zero point, and 4 mL of liquid was added to the rectal catheter balloon. The self-adhesive electrodes were applied 0.5 cm away from the perianus, and the electrical signal of the external anal sphincter was recorded to replace that of the external urethral sphincter. After emptying the bladder, saline (37°C) was pumped in at a rate of 50 mL/min. Before and during the intravesical perfusion, patients were asked to cough. If the changes in bladder and abdominal pressure were consistent during the cough, this indicated that the position of the piezometer was correct and that the catheters were smooth. Furthermore, it also indicated the contractions of the detrusor and the external urethral sphincter, maximum BC, bladder compliance, and DLPP were all recorded under effective and reliable conditions. After the filling bladder pressure measurement was complete, the bladder was emptied and reperfused with 150 mL saline. The 8F transurethral triple-lumen catheter was then re-inserted. The perfusion speed was 2 mL/min, and the catheter was drawn at a speed of 2 cm/min. Additionally, the maximum urethral pressure was recorded. According to the results of the urodynamic examination and clinical findings, NLUTD was divided into the following types: detrusor-external urethral sphincter dyssynergia (A type); detrusor could contract/external urethral sphincter could not (B type); detrusor could not contract/external urethral sphincter could (C type); both detrusor and external urethral sphincter could not contract (D type) [10]. The patients were also divided into high-risk (DLPP ≥40 cmH_2O) and low-risk (DLPP <40 cmH_2O) groups.

Determination of BC and DWT

During the urodynamic examination, the bladder DWT was measured when the perfusion amount reached 50, 100, 150, 200, 250, 300, 400, and 500 mL. If the patient's maximum BC was <500 mL, the maximum BC was then set as the measurement endpoint. After emptying the bladder, the control group drank 500-1000 mL, and DWT was measured when subjects experienced a strong urge to micturate. The bladder was then emptied, and the amount of urine produced was recorded immediately to determine the maximum BC. When measuring DWT, all subjects were placed in the supine

Table 2. LUTD classification of the patient group

LUTD classification	Cervical cord injury	Thoracic cord injury	Lumbar cord injury	Sacral cord injury	Sum (cases)
A type	10	15	0	0	25
B type	0	0	1	0	1
C type	8	8	3	0	19
D type	0	0	1	2	3

position with the ultrasound probe (Sonosite M-Turbo-ICTx type, USA) placed slightly above the pubic symphysis. The probe direction was adjusted to ensure that it was perpendicular to the bladder wall being measured. The 3.5-5.0 MHz probe was initially used to measure the distance from the anterior bladder wall to the abdominal wall (**Figure 1A**), and then an 8-13 MHz linear array probe was used to distinguish the abdominal wall and the bladder wall. The B ultrasound images would reflect the peribladder tissues, bladder wall mucosa, and submucosa as high-level echoes (white), and the detrusor reflected as a low-level echo (black). Thus, the bladder wall intima, detrusor, and extema could be distinguished. When the bladder wall intima and extema exhibited thin, smooth, and continuous high signals, the image was frozen and a "zoom" fig window was opened to enlarge the ultrasound image by 5-fold in order to identify and measure the DWT (**Figure 1B**). Three different anterior bladder wall sites were selected for the DWT measurement, with the average set as the final value.

Statistical analysis

All statistical analyses were performed using SPSS13.0 software. Non-parametric tests were used to compare the DWT of different groups at different BCs. The DWT of the 2 groups at maximum BC, as well as the DWT of different types of LUTD, were also compared. The Pearson correlation coefficient was used to analyze the correlations between DWT, bladder compliance, maximum urethral pressure, and detrusor leak point pressure. The receiver operating characteristic curves were then used to generate and identify the DWT critical values of high- and low-risk patients.

Results

Impacts of BC on DWT

As BC increased, the patient group exhibited a gradual reduction in DWT, although the amplitude differed based on the amount of liquid added. When the BC was gradually increased from 50 to 250 mL, the DWT decreased by 57.1% ($P<0.05$); however, when the BC was gradually increased from 250 mL to maximum BC, the DWT was only reduced by 27.9% ($P<0.05$). There was significant difference in DWT among different BCs (**Table 1**). The results also showed that DWT exhibited minimal variability at maximum BC, such that the mean DWT of the patient and control groups were 0.91±0.31 mm and 0.59±0.08 mm, respectively ($P<0.05$; **Figure 2**).

LUTD types and DWT

The incidence of LUTD within the patient group with A type had the highest incidence (52.1%), followed by C type (39.6%), while the incidence rates of B and D types were as low as 2.1% and 6.2%, respectively. The specific classification results are shown in **Table 2**. The patients with different LUTD types also had different DWT measurements. At maximum BC, the DWT of the A type patients was 1.10±0.34 mm and that of the C type patients was 0.81±0.19 mm, both of which were increased as compared to the control group by 86.4% and 37.3%, respectively ($P<0.05$ for both). Furthermore, the increment of A type was much more obvious than that associated with the C type ($P<0.05$; **Figure 3**).

Correlation analysis

The correlation analysis showed that DWT was not significantly correlated with the maximum urethral pressure ($r = -0.08$, $P>0.05$), but it was negatively correlated with bladder compliance ($r = -0.51$, $P<0.01$) and positively correlated with DLLP ($r = 0.77$, $P<0.01$). According the criteria of DLLP ≥40 cmH_2O, a total of 19 cases were classified as high-risk patients, including 17 A type cases and 2 C type cases. The receiver operating characteristic curve analysis showed that the area under the curve was 0.928 (**Figure 4**). At a sensitivity of 89.5% and a

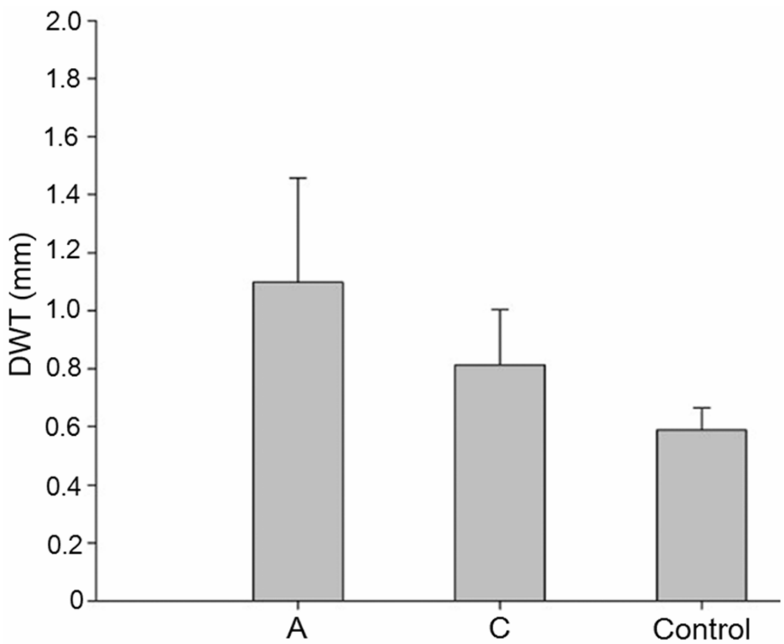

Figure 3. DWT comparison of different NLUTD-type patients. When at MBC, the DWT comparison among the A, C-type LUTD and normal control bladder revealed that DWT of A- and C-type were significantly increased than the control group (P<0.05), and that of A-type was much more significant than C-type (P<0.05).

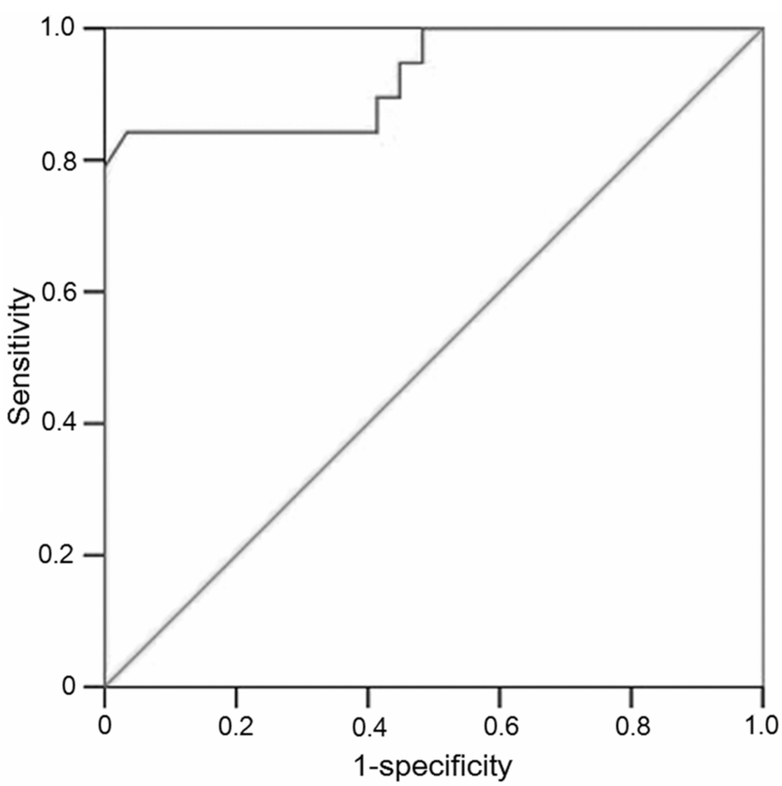

Figure 4. ROC curve analysis. ROC curve analysis showed that the area under the curve was 0.928. When the sensitivity was 89.5% and the specificity was 58.6%, DWT was 0.87 mm, and could be used as the critical value to identify the high and low-risk.

specificity of 58.6%, DWT was 0.87 mm. Using this DWT as the critical value for identifying high- and low-risk patients, the current study would include 29 high-risk patients, including 18 A type cases and 11 C type cases. Among all patients, 2 cases who were urodynamically diagnosed as high-risk were misdiagnosed because of a DWT <0.87 mm, and 12 patients who were urodynamically diagnosed as low-risk were misdiagnosed as high-risk because of a DWT ≥0.87 mm.

Discussion

The observed refunctionalization and neurological remodeling of the lower urinary tract after SCI [11], expressed as changes in the bladder wall structures and physicochemical properties [12], may be reflected by changes in DWT. Our results indicated that the DWT of patients with SCI was significantly greater than that of normal adults at maximum BC, and the DWT of A type patients exhibited more significant increases than other patient types. This finding may be related to the increased bladder outlet resistance and bladder workload, which in turn provoked the hypertrophy of detrusor muscle. The DWT of patients with bladder outlet obstructions was increased significantly [13], and a DWT >2.9 mm should be used as the diagnostic standard of bladder outlet obstruction [14]. Additionally, Kessler advocated for replacing the urinary pressure flow rate examination with the DWT-ultrasound examination [14]. Therefore, the determination of DWT could be used to assess the degree of lower urinary tract obstruction [9]. The DWT measured was lower than the criteria proposed by Kessler and may have been attributable to differences in subjects. The subjects did not have nerve damage, while the patients exhibited different types of lower urinary tract obstruction characteristics as compared to those with non-NLUT obstruction [15]. The former exhibited a dynamic increase in resistance, while the latter exhibited a more static increase in resistance [15]. The DWT of C type was also significantly increased, which may be due to the often overfilled bladders of these patients. Thus, the bladder wall suffered from long-term and high-load mechanical traction. Mechanical traction stimulation can induce the remodeling of the smooth muscle of the bladder and increase the elasticity of the bladder wall [16], while persistent bladder filling can lead to detrusor hypertrophy [17]. However, the C type patients had no detrusor contraction, and this may have caused the detrusor hypertrophy to be less obvious as that seen in A type cases. The results support the assertion that a DWT ultrasound determination could be used to identify post-SCI A and C type LUTD. Similar to Ukimura et al. [18]. The compliance of the bladder wall often changes after SCI, and we found that the DWT was negatively correlated with bladder wall compliance. After SCI, the reduction of bladder wall compliance has been associated with increases in detrusor collagen and reductions in elastin [12]. Indeed, the risk of urine refluxing back to the upper urinary tract would be significantly increased in cases where DLPP ≥40 cmH_2O. Therefore, the experimental group was divided into the high- and low-risk groups according to their DLPP. Results showed that DWT was positively correlated with DLPP [19]. Herein, the critical value for identifying high- and low-risk patients (DWT = 0.87 mm) had relatively high sensitivity (89.5%). The sensitivity less than 90% may be due to that the increase of detrusor leak-point pressure is ahead of DWT change which is a gradual process. The possible reason for relatively low specificity is more patients with C type NLUTD where the detrusor leak-point pressure is reduced. Furthermore, the 10 high-risk patients misdiagnosed were of the C type and usually had significantly sustained bladder over-filling (BC>600 mL), resulting in a significant increase in DWT. Collectively, we speculated that the patients with sustained bladder over-filling could not be identified as high- or low-risk patients using DWT as an indicator.

Currently, 2 indicators are used to reflect bladder wall thickness: bladder wall thickness and detrusor wall thickness. We chose to measure DWT as opposed to BWT because: 1) LUT obstruction-derived bladder wall thickness was mainly caused by detrusor wall thickness; 2) the mucosal layer and externa of the bladder wall were susceptible to inflammation and many other factors; and 3) the high signals of peribladder adipose tissues in the ultrasound imaging were sometimes difficult to distinguish from those of the bladder wall externa, thus resulting in larger errors in the complete bladder wall thickness measurement. Currently, bladder wall thickness measurement methods include trans-lower abdominal wall measurement, trans-rectum measurement, and trans-vaginal measurement. Performance of the latter 2 methods may cause some degree of patient discomfort. Conversely, performance of the first method is regarded as simple and painless, which is why it was chosen for the study. Under the same degree of bladder filling, the thicknesses of different parts of the bladder wall showed no significant differences [20]. We chose to measure the anterior bladder wall, as it is close to the abdominal wall and can be easily distinguished under ultrasound. Additionally, the close proximity of the anterior bladder wall to the posterior abdominal wall was not considered to be problematic. In fact, we found that when the pressure from the ultrasound probe onto the anterior abdominal wall increased, the DWT was reduced. If the pressure from the probe onto the abdominal wall was strictly controlled, the DWT measurement of the anterior bladder wall would not be affected. The ultrasound resolution was frequency-dependent such that the higher the frequency, the better the ultrasound resolution. The resolution associated with the 7.5 MHz ultrasound was <0.13 mm, and the resolution of the 3.5 MHz ultrasound was only 0.3 mm [21]. Therefore, we used an 8-13 MHz linear array probe to measure DWT in order to distinguish small differences. Results from the current study demonstrated that the 8-13 MHz linear array probe could clearly distinguish the anterior bladder wall when it was 2-5 cm away from the anterior abdominal wall.

Studies have shown that the bladder wall thickness is related to the bladder capacity. When the BC was between 0-50 mL, bladder wall thickness showed no significant changes [22], which is why we set 50 mL as the starting point of the BC measurement. With increasing BC, the bladder wall thickness of healthy people and patients with prostatic hyperplasia was slightly but significantly decreased [23]. When the BC was increased from 50 to 250 mL, the DWT of patients with SCI exhibited a large amplitude reduction, and when the BC was increased from 250 mL to maximum BC, the DWT exhibited a small amplitude reduction, similar to the DWT changes observed in healthy people [21]. Data also showed that when the BC was increased from 250 mL to maximum BC, significant differences remained, although the DWT was only slightly changed. Conversely, when the BC of healthy people was >250 mL, no significant changes were observed [21]. These inconsistent findings may be attributable to differences in the frequencies of the ultrasonic probes. The 8-13 MHz frequency linear array probe used delivered higher frequencies than probes in other studies. This allowed for greater clarity in distinguishing the detrusor from the peribladder tissues and mucous membranes and contributed to the enhanced accuracy of measurements. An additional reason for the disparate findings between studies may have been the morphological changes of the bladder wall caused by SCI [23], which may have led to variation in DWT measurements that were inconsistent with normal values. Furthermore, results showed that increased BC was associated with decreased DWT variability in patients with SCI, and at maximum BC, the DWT variability was minimal, similar to the results of Pannek et al. [19] Therefore, this result suggested that it would be much more appropriate to study DWT at maximum BC.

The maximum urethral pressure represents the pressure at external urethral sphincter. It will change the process between urine storage and voiding. This study only observes the maximum urethral pressure in urine storage period, which may be the reason why the maximum urethral pressure is not significantly correlated with DWT. Moreover, the change of detrusor wall after spinal cord injury is a gradual process, so the duration of spinal cord injury may affect DWT. Herein, the acute-phase and chronic-phase cases are less. It needs to further collect more acute-phase and chronic-phase cases to investigate the relationship between spinal cord injury and DWT.

Conclusions

The detrusor wall thickness of patients with SCI was significantly increased and positively correlated with detrusor leak-point pressure. Detrusor wall thickness could be used to assess the risk of kidney damage in post-SCI-NLUTD patients.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Jian-An Li, Department of Rehabilitation, The First Affiliated Hospital of Nanjing Medical University, No. 300 Guangzhou Road, Nanjing 210029, China. Tel: +86 025 8331 8752; E-mail: jiananlicn@163.com

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