Can bladder wall thickness predict videourodynamic findings in children with spina bifida?

（二分脊椎患児において膀胱壁厚はビデオウロダイナミクス検査所見を予測可能か）

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Abbreviations and Acronyms

BWT; bladder wall thickness

CIC; clean intermittent catheterization

DLPP; detrusor leak point pressure

DO; detrusor overactivity

dT; detrusor thickness

MCC; maximum cystometric capacity

MDP; maximum detrusor pressure

UDS; urodynamics

VUDS; videourodynamics

VUR; vesicoureteral reflux

INTRODUCTION

Urodynamic study is the gold standard to assess lower urinary tract function in children with spina bifida.[1] However, it cannot be performed frequently because of its invasiveness.

Ultrasound measurements of bladder wall thickness is currently thought to be potential noninvasive clinical tools for assessing the lower urinary tract.[2] However, there have been few reports regarding the associations between BWT and urodynamic data in spina bifida patients. In previous reports, when measuring BWT, bladder volume was not specifically defined and had a wide range.[3, 4] BWT is affected by bladder filling volume.[2] In addition, BWT is correlated to age in children with spina bifida.[3, 4] Therefore, whether BWT measured at specifically defined bladder volumes can be used to predict unfavorable findings on video urodynamic study in children with spina bifida was investigated. The association between BWT and age was also assessed.

MATERIALS AND METHODS

Consecutive spina bifida patients with clean intermittent catheterization who underwent VUDS between September 2012 and October 2013 were prospectively investigated. Patients were excluded if they

were not on CIC or had a status of symptomatic urinary tract infection, augmentation cystoplasty, catheterizable channel, vesicostomy or neurogenic bladder due to other anomalies. All measurements were performed by the first author (WJK).

Bladder Wall Thickness Measurement

Simultaneously with VUDS BWT measurements were performed by ultrasonography (Xario® SSA-660A) using a 6 MHz convex transducer. Measurements were obtained based on the maximally magnified image. Ventral BWT at a point between the median umbilical ligament and the start of the lateral walls was measured using the standardized method described by Müller et al.3, 5 BWT included the mucosa, submucosa, detrusor and adventitia of the bladder. Ventral BWT was measured at MCC. After MCC was defined bladder capacity was intentionally decreased to 50% MCC and 25% MCC, and ventral BWT was measured at each capacity. In addition, all patients underwent renal ultrasonography at MCC to evaluate dilatation of the renal collecting system.

Videourodynamic Evaluation

Standard fluid cystometry was done with patients in the supine position using a 6Fr to 9Fr double lumen urethral cystometry catheter and a rectal balloon catheter, filling at a rate of less than 10% of predicted bladder capacity per minute.1 VUR and bladder trabeculation were evaluated radiographically at MCC. Anticholinergic therapy was not discontinued before VUDS. MCC was defined as maximal tolerable cystometric capacity or capacity when leaking began. MDP was defined as maximum detrusor pressure during filling or at leak. DO was defined as involuntary detrusor contractions greater than 15 cm H_2O above baseline.6

Statistical Analysis

Spearman rank correlation coefficient was used to determine the association between BWT measured at MCC and each parameter, including age, maximum detrusor pressure and bladder compliance. Mann-Whitney test was used to analyze differences in bladder wall thickness measured at each percent MCC between patients with and without each unfavorable VUDS finding. High MDP (40 cm H_2O or greater), low bladder compliance (less than 10 ml/cm H_2O), DO, bladder trabeculation and vesicoureteral reflux were defined as unfavorable findings. A p value of less than 0.05 was considered significant. All statistical analyses were performed using JMP®, version 11.1.

RESULTS

A total of 23 males and 30 females with spina bifida (median age 7.8 years, range 0.8 to 21) underwent measurement of BWT at MCC. Patient characteristics are outlined in table 1. Hydronephrosis with caliectasis was seen on ultrasound at MCC in 12 patients. Three patients had low grade (I or II) and 7 had high grade VUR (III or greater). Mean ± SD MCC was 239 ± 99 ml (range 48 to 489). Mean ± SD BWT measured at MCC was 1.7 ± 0.5 mm (range 0.9 to 3.7). Age had a weak positive correlation with BWT measured at MCC (table 2). No correlation was found between BWT and UDS parameters.

BWT was measured at each percent MCC in 31 patients. Mean ± SD BWTs measured at MCC, 50% MCC and 25%MCC were 1.6 ± 0.4 mm, 2.0 ± 0.5 mm and 2.6_0.7mm, respectively. When comparing BWT measured at each percent MCC between patients with and without each unfavorable VUDS finding, no significant differences were found, except for bladder trabeculation (see figure). There was a significant difference in BWT measured at MCC between patients with and without bladder trabeculation (mean ± SD 1.8 ± 0.4mm vs 1.4 ± 0.3mm, p = 0.001). BWT measured at 50%MCC was significantly thicker in patients with vs without bladder trabeculation (mean ± SD 2.3 ± 0.5mm vs 1.8 ± 0.5mm, p = 0.012).

DISCUSSION

To our knowledge, 3 series have been published regarding the association between BWT and VUDS findings in children with spina bifida (table 3).3,4,7 Because of differences in methodology for measuring BWT, these reports have different results, with 2 studies concluding that BWT measurements are useful for predicting unfavorable findings on VUDS.4,7

Comparing patients with and without unfavorable UDS parameters, there were no significant differences in BWT measured at various bladder volumes, except for bladder trabeculation. BWT measured at more than 50% MCC was significantly increased in patients with bladder trabeculation. Age had a weak positive correlation with BWT.

Bladder volume has not specifically been defined when measuring BWT except in 1 report, and has varied widely. Tanaka et al did not specifically define bladder volume to measure BWT.4 Müller et al measured dT before CIC and excluded measurements assessed when bladder fullness was less than 10% of expected

bladder capacity (age ± 30 t 30 ml).3 Palmer et al found that expected bladder capacity was decreased in children with neurogenic bladder.8 Therefore, the estimated bladder capacity used in those children seems to have been inappropriate.

There has been only 1 known prior study assessing BWT measured at MCC. Sekerci et al performed ultrasonographic measurements of BWT simultaneously with VUDS.7 In our study bladder wall thickness was measured at MCC during VUDS to accurately determine bladder filling volume. However, it may be impractical to measure BWT at MCC by routine ultrasound. Thus, to determine which range of bladder volumes is appropriate, BWT was also measured at 25% MCC and 50% MCC. The figure shows that BWT decreased when it was measured at more bladder filling volumes. Hence, to minimize inter-subject variance, bladder filling volume must be strictly defined.

Müller et al reported that ventral and dorsal dT did not correlate with DLPP.3 In contrast to that series and our study, 2 previous reports concluded that dorsal BWT measurements were useful for predicting high DLPP. Tanaka et al reported that dorsal BWT was significantly correlated to DLPP and MDP.4 However, they did not specifically define bladder volume to measure BWT. Sekerci et al reported that the average of ventral and dorsal BWTs measured at MCC was significantly less in controls than in patients with DLPP 40 cm H_2O or greater and those with VUR.7 In the present study no significant differences in ventral BWT measured at each percent MCC were seen between patients with and without high detrusor leak point pressure and those with vesicoureteral reflux. We observed that some patients without increased ventral BWT had high MDP. This finding suggests that routine UDS cannot be skipped, even if the bladder wall is not terribly thick.

There has been only 1 published report on the association between BWT and bladder trabeculation in children with spina bifida. Müller et al observed that dT was not correlated with bladder trabeculation when comparing children with spina bifida to normal controls.3 We found that BWT measured at more than 50% MCC was significantly increased in patients with bladder trabeculation.

Shapiro et al reported that bladder specimens had significant interfascicular and pericellular infiltration of the smooth muscle by dense connective tissue in patients with spina bifida undergoing augmentation cystoplasty.9 It is often seen that patients with neurogenic bladder requiring augmentation cystoplasty have a

thickened bladder wall. Cystography detects a trabeculated bladder in such patients. The present results suggest that ultrasound measurements of BWT may be an alternative to radiographic evaluation.

There was a significant difference in the age of patients with (mean ± SD 7.1 ± 4.1 years) and without (11.5 ± 4.9 years, $p = 0.020$) low compliance. No significant difference was seen in the age of patients with and without other unfavorable VUDS findings. However, due to the small cohorts, further studies could not be done.

The positive correlation between age and BWT demonstrated in this study is consistent with previous reports.3,4 This trend is also seen in normal children.3,10 This correlation with age makes BWT assessment in children difficult. Further study by age group is needed in pediatric cohorts with spina bifida.

The present study had some limitations. A major limitation was the large age range. In this cohort it was difficult to evaluate the role of BWT at a specific age due to the limited number of patients. Also dorsal BWT could not be measured due to inadequate resolution and nonconstant thickness of the dorsal bladder wall. It has been reported that dorsal bladder wall thickness is correlated to high DLPP or VUR.4,7 Thus, further studies are warranted to evaluate the associations between dorsal BWT measured at various bladder volumes and VUDS findings.

Another limitation is that bladder volume was not measured by ultrasound, but by filling volume on VUDS. Hence, MCC was overestimated in patients with high grade VUR. Seven of 53 patients had grade III or greater VUR. Furthermore, the mucosal layer of bladder wall could be affected by infection.2 However, we did not evaluate the effect of infection on BWT. Finally, the effects of anticholinergics on BWT were not assessed, although anticholinergics can produce bladder wall changes.

CONCLUSIONS

Ventral BWT measured at various percent MCCs could not predict unfavorable VUDS findings except for bladder trabeculation in children with spina bifida. Ultrasound measurements of ventral BWT do not appear to be an alternative to UDS.

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Table 1. *Patient characteristics*

No. primary spinal pathology/total No. (%):	
Myelomeningocele	46/53 (87)
Lipoma of conus medullaris	7/53 (13)
No. complete urinary continence/total No. (%)*	17/45 (38)
No. antimuscarinic therapy/total No. (%)	47/53 (89)
Oxybutynin	39/47 (83)
Propiverine	7/47 (15)
Solifenacin	1/47 (2)
No. asymptomatic bacteriuria/total No. (%)	27/53 (51)
No. antibiotic prophylaxis/total No. (%)	10/53 (19)
No. ambulatory status/total No. (%)*	34/45 (76)

* Patients younger than 3 years were not evaluated.

Table 2. *Correlation of BWT measured at MCC with age, MDP and compliance*

Parameter	Spearman Rank Correlation Coefficient	p Value
Age	0.402	0.003
MDP	0.154	0.270
Bladder compliance	−0.162	0.247

Table 3. *Methodologies across studies*

References	No. Pts	Ultrasound Measurement	Bladder Vol at Measurement	Results/ Correlation
Müller et al[5]	66	Ventral + dorsal dT	Before CIC	No correlation
Tanaka et al[4]	57	Dorsal BWT	Not defined	MDP, DLPP, DO
Sekerci et al[7]	80	Ventral + dorsal BWT	MCC	DLPP, VUR
Current study	53	Ventral BWT	50% MCC, MCC	Trabeculation

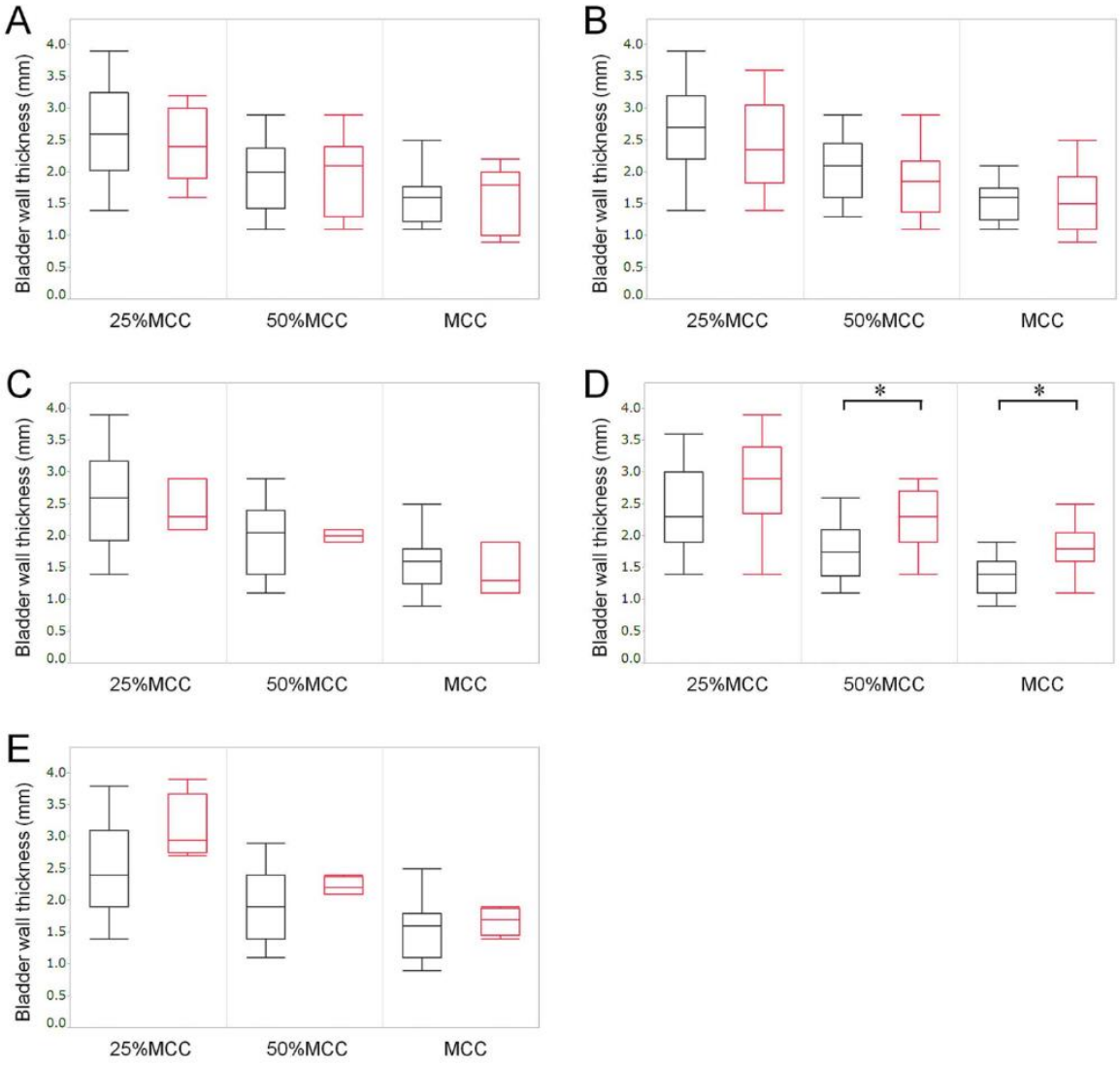

Figure. Comparison of bladder wall thickness measured at each percent MCC in patients with (red plot) and without (black plot) unfavorable VUDS findings. A, high MDP. B, low compliance. C, DO. D, bladder trabeculation. E, VUR. Asterisk indicates $p < 0.05$.

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