J Pediatr Res 2021;8(2):110-5
DOI: 10.4274/jpr.galenos.2020.26918

Original Article

Long-term Outcome of Infants with Spina Bifida Through Assessment of the Prognostic Value of Hostile Bladder Parameters

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ABSTRACT

Aim: In 2016, the Centers for Disease Control and Prevention (CDC) published a management algorithm for spina bifida (SB) cases from birth and started collecting data prospectively. They designated risk factors from urodynamic studies as end filling pressure or detrusor leak point pressure (DLPP) ≥40 cmH2O or neurogenic detrusor overactivity (NDO) with detrusor sphincter dyssynergia (DSD), and named this type of bladder dysfunction as "hostile bladder" (HB). They recommended the immediate start of clean intermittent catheterization and anticholinergics in these patients. Having similar concerns on this patient population, we designed a retrospective study to identify and reveal long-term outcomes of SB patients with HB.

Materials and Methods: All urodynamic studies and hospital records of SB patients admitted and followed between 1994-2014 were reviewed retrospectively. The demographic data, the presence of DLPP, DSD and NDO in the first urodynamic examination, bladder compliance, first and last radiologic and scintigraphic imagings, surgical interventions were evaluated. Upper tract damage was defined as new scars in DMSA scans.

Results: A total of 58 patients were included in the study. The mean follow-up was 12.17±5.17 years. The presence of a scar in the first scintigraphy (p=0.01) and the presence of hydronephrosis in the first and last ultrasonography (p=0.03) were found to be independent risk factors for new scar development. When DLPP values were evaluated with ROC analysis, 50cmH2O was observed as a significant threshold value with 73% sensitivity and 60% specificity.

Conclusion: Our study confirmed the detrimental effects of high pressure and detrusor-sphincter dyssynergia; however, hostile bladder parameters were not sufficient to distinguish high-risk group patients. The presence of scars in the first scintigraphic evaluation, DLPP above 50cmH2O, and the presence of hydronephrosis in the first ultrasound were found to be risk factors for renal deterioration. More frequent monitoring and detailed evaluation may be necessary for patients with these risk factors.

Keywords: Spina Bifida, Hostile Bladder, Neurophatic Bladder, Detrusor Leak Point Pressure, Neurogenic Detrusor Overactivity

Introduction

Spina bifida (SB) is a condition that may result in chronic kidney disease secondary to bladder dysfunction. Despite a worldwide varying incidence, 1-6 cases are seen in every 1000 live births (1). Several studies reported better results with pro-active management strategies. (2,3). Different urodynamic parameters or scoring systems were suggested to detect patients who are at risk of upper urinary tract damage (4–6). In 2016, the Centers for Disease Control and Prevention (CDC) published a management algorithm for SB

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Received: *07.10.2020* **Accepted:** *20.10.2020*

cases from birth and started collecting data prospectively (7). They designated risk factors from urodynamic studies as end filling pressure or detrusor leak point pressure (DLPP) 40 cmH2O or greater, or neurogenic detrusor overactivity (NDO) with detrusor sphincter dyssynergia (DSD), and named this type of bladder dysfunction as "hostile bladder". They recommended the immediate start of clean intermittent catheterization (CIC) and anticholinergics in these patients. Having similar concerns on this patient population in our region, we designed a retrospective study in an aim to identify and reveal long-term outcomes of SB patients with "hostile bladders".

Material and Method

All urodynamic studies and hospital records of SB patients admitted and followed between 1994 and 2014 were reviewed retrospectively to identify patients with "hostile" bladders according to the above-mentioned criteria. Patients with the first admission after infancy, those who did not comply with the SB follow-up protocol of our department, and patients followed for less than five years were excluded from the study.

Urodynamic tests (pressure-flow study) were performed according to our protocol in all cases with a double-lumen 6 Fr urodynamic catheter using Dyno (AYMEDÒ İstanbul, Turkey). Pelvic floor activity was evaluated with a total of 3 electromyography electrodes, 2 of them placed on the perianal skin (right and left to the anus), and one for reference on the thigh. Intraabdominal pressure was measured using an 8 Fr rectal balloon catheter. At least two fillings were done for each case. The lowest leakage pressure was described as DLPP. DSD was defined as involuntary pelvic floor activation during voiding. The involuntary phasic or terminal detrusor contractions during filling were described as neurogenic detrusor overactivity (NDO). The demographic data of the cases, the presence of DLPP, DSD and NDO in the first urodynamic examination, bladder compliance, first and last dimercaptosuccinic acid (DMSA) scans, first and last voiding cystourethrograms (VCUG), surgical interventions, first and last kidney ultrasound, and the medications they received were evaluated. All patients were followed according to the standardized program of our department (table 1). Urodynamic and clinical data, along with the above-defined hostile bladder parameters, were evaluated for predicting upper tract damage. Upper tract damage was defined as new scars in DMSA scans. Statistical analysis was done with IBM SPSS 21 program. Kolmogorov-Smirnov test was used to evaluate the distribution, Pearson Chi-square, Mann - Whitney U, Kruskal Wallis, regression analysis, and Reciever Operator Characteristics Curve (ROC) tests were used for analysis where appropriate. Institutional Ethical Approval was obtained for the retrospective patient chart review (20-8T/26).

Results

The flow-chart describes patient selection for the study (figure). A total of 58 patients (33 boys and 25 girls) with "hostile" bladder were included in the study. The mean follow-up was 12.17 ± 5.17 years. Hydronephrosis was present in the first ultrasonography (US) in eight cases. It resolved in five cases and was present in a total of 5 cases with two new-onset ones. Renal scars were observed initially in the first DMSA scan of 10 cases. Nine patients developed new scars at the last DMSA, making a total of 19 cases with renal parenchymal scars.

The mean DLPP value at the first urodynamic study was 54.88 ± 30.43 cmH2O. Of 58 patients, DSD was present in 48 (82.7%) in the first and 49 (84.5%) in the last urodynamic study. NDO was present in 38 cases (65.5%) in the first and last urodynamics (with nine new-onset in the last and nine other dissolved after the first).

The presence of a scar in the first scintigraphy (p = 0.01) and the presence of hydronephrosis in the first and last ultrasonography (p=0.03) were found to be independent risk factors for new scar development. When 40 cmH2O was accepted as a threshold value, no significant relation was found between DLPP and new scar development (p = 0.05). When DLPP values were evaluated with ROC analysis for new scar development, 50 cmH2O was observed as a significant threshold value with 73% sensitivity and 60% specificity. A significant correlation was found between this threshold of DLPP and the development of a new scar (p= 0.03).

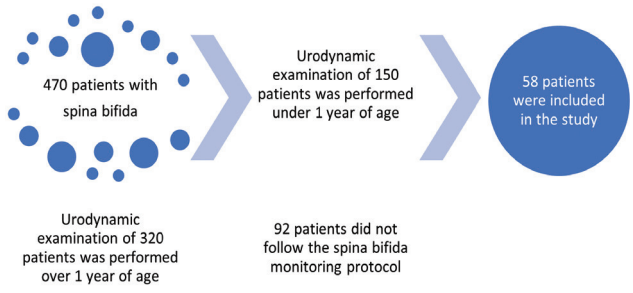

Figure 1. Patient admission flow chart

Table 1. Urological Follow-up Protocol in Spina Bifida Patients

Age	UA & UC	Urinary US	UD	Scintigraphy	VCUG
Preoperative	X	X			
Postoperative 1 week	X	X			
6 week	X	X	X		
6 months	X	X	X	X	X
1 year	X	X	X	(X)	
1.5 year	X				(X)
2 year	X	X	X	X	
3 year	X	(X)	(X)		(X)
4 year	X	X	X		
5 year	X	(X)	(X)		(X)
6 year	X	X	X		
7 year	X	(X)	(X)		(X)
8 year	X	X	X		
9 year	X	(X)	(X)		
10 year	X	X	X		(X)

X: These are mandatory examinations.
(X): In patients without infection, reflux and urodynamic examination within normal limits, these examinations are optional depending on the clinical situation.
CIC: CIC training is given to families of all newborn patients. If there is no hydronephrosis and if there is no residual urine in the urodynamic examination at Week 6, CIC is discontinued.
Anticholinergic therapy is started in patients with the following features:
- NDO
- DSD
- DLPP>40 cmH2O
- Low compliance

Prophylactic antibiotic is started (amoxicillin or trimethoprim-sulfamethoxazole, depending on the age) in patients with the following features:
- 3-6 months after initiation of CIC
- VUR
- Recurrent UTI

UA & UC: Urinalysis and urine culture
US: Ultrasound
UD: Urodynamics
VCUG: Voiding cystourethrogram
CIC: Clean intermittent catheterization
NDO: Neurogenic detrusor overactivity
DSD: Detrusor-sphincter dyssynergia
DLPP: Detrusor leak point pressure
VUR: Vesicoureteral reflux
UTI: Urinary tract infection

Table 2. Patient characteristics according to the presence of new-onset scar in the last DMSA

New-onset scar in the last DMSA	First urodynamic DLPP value (mean)	HN presence in the first RBUS	Scar presence in the first DMSA	DSD Presence in the first UD	NDO presence in the first UD	DLPP>50 cmH2O in the first UD
Positive	65.40±40.03*	6**	9**	15*	11*	11**
Negative	51.21±25.88	2	1	33	27	17

*p>0.05
**p<0.05
DMSA: Dimertcapto Succinic Acid Scintigraphy
DLPP: Detrusor leak point pressure
RBUS: Renal bladder ultrasound
DSD: Detrusor sphincter dyssynergia
UD: Urodynamics
NDO: Neurogenic detrusor overactivity

Kidney failure was observed in only one case. Bladder augmentation was performed in 7 (12.1%) of the cases. All patients who underwent augmentation cystoplasty had NDO (p:0,041). There was no relation to other variables, such as the presence of vesicoureteral reflux or DSD. The mean DLPP values (63.86 ± 24.98 cm H2O) in the first urodynamic studies of the patients who required bladder augmentation were higher than in other cases (53.65 ± 31.12 cm H2O), but it was not significant (p=0.41).

Discussion

The necessity of urological follow-up is not questioned for patients with SB, but the frequency and design of follow-up are not well-defined and standardized. Close monitoring and pro-active patient management are shown to reduce the upper urinary tract damage and bladder surgery (2,3). The follow-up protocol of our department involves outpatient visits every 6 months until the age of 2, followed by annual visits even in the uneventful cases. Long-term follow-up of all cases is recommended due to the risk of tethered cord and its urological consequences (8)However, our study revealed that only a small part of the patients was compliant with this protocol, and only a small group of the patients we followed could be included in the study (flow-chart). Many factors, such as mobility restrictions of the patients, and socioeconomic problems, may hinder attending the outpatient visits regularly. Identifying patients at risk and arranging follow-up intervals according to these risk factors may provide better adaptation of families to protocols and decrease the burden on centers caring for these patients.

ICCS classifies detrusor anomalies in the voiding phase as overactive and underactive [8]. In the voiding phase, the inability of the urethral sphincter to relax due to neuropathic reasons has been defined as detrusor sphincter dyssynergia. By the addition of cases with no sphincter activity, basically, four types of neuropathic bladder-sphincter disorders are revealed (9,10). Various studies were conducted showing the possible negative effects of high detrusor pressure on kidney function. Steinhardt et al. showed that in patients with SB, the glomerular filtration rate decreased when the bladder filling pressure was 35-40 cm H2O (11). Austin et al. highlighted that DLPP over 40 cmH2O is a high value that can cause upper urinary system damage (12). The cases with overactive bladder and detrusor sphincter dyssynergia would be the most vulnerable patients who have higher bladder pressure (13). For these reasons, DLPP over 40 cmH2O, DSD, and high-pressure overactivity are defined as urodynamic "hostile bladder" parameters by CDC (7).

There are different studies to determine the threshold DLPP value that causes urinary tract damage. The threshold value that generally indicates the hostility of the bladder has been determined as 40-50 cm H2O (11,12). Intravesical pressure reaching high values during the filling phase will likely affect the upper urinary tract. Determining this threshold may help to guide the treatment. Although this threshold value appeared as 50 cm H2O in our study, it could be safer to accept a lower threshold value as different results were found in different studies, and some of these were as low as 20 cmH2O. (14). Prospective large series are needed for finding the answer to this question.

Tanaka et al. found the renal scar rate in the first scintigraphic examination of children with SB as 7.5% (4). This rate seems to be lower than in our study. This may be due to unintentional sampling bias in our study as patients with more problems tend to comply better with longer follow-up periods.

Vesicoureteral reflux studies revealed the existing renal scar as a risk factor for developing new scars (15,16). Our study showed similar results with having a scar in the first scan as an independent risk factor for new scar development.

Hydronephrosis was observed in 8 (13.7%) of our cases; six of these were high grade. Tanaka et al. detected hydronephrosis in 44.1% of cases with SB, and 3.7% had high-grade hydronephrosis in the initial US examinations. This rate is quite high compared to the rate in our study. In our series, 6 of 8 cases with hydronephrosis in the first US developed new scars ($p < 0.05$). A high degree of HN was present in 5 of these six cases. High-grade HN was found to be a significant risk factor in terms of new scar development. Due to the sequelae dilatations observed in some patients, hydronephrosis in SB patients can sometimes be considered insignificant. Our study emphasizes the importance of high-grade hydronephrosis as a warning sign for further evaluation to prevent kidney damage.

Bladder augmentation is performed in cases with high bladder pressure, low capacity, incontinence, and upper tract damage despite appropriate management. (17). The rate of patients undergoing bladder augmentation in pre-treated patients varies between 5-17%, while in untreated cases, this rate can rise to 41% (3,17–19). In our study, the bladder augmentation rate was 12.1%, similar to these, and similar to that of American Spina Bifida Centers (12.7%) (19). In a study by Corona et al., VUR and a DLPP of 40 cm H2O and above at the end of the filling phase were defined as

the factors that increase the need for bladder augmentation (20). In studies conducted by different researchers, VUR incidence in patients with SB was between 27-34% (6,21). The VUR incidence in our study was similar to other studies, as 24.1%. The mean first DLPP of patients who underwent augmentation cystoplasty was higher than the patients who did not require; however, the difference was not significant. The presence of NDO in the first urodynamic examination emerged as an independent risk factor for the need for augmentation.

Study Limitations

The most important limitation of our study is its retrospective nature. Also, the lack of compliance with the protocol caused many patients to be excluded from the study. This is mostly secondary to being a tertiary center with patients referred from other provinces and centers, to re-evaluate their management.

Conclusion

Loss of low-pressure reservoir function of the bladder in cases with SB can cause upper urinary tract damage. Therefore, the hostile bladder was defined by CDC to predict patients at risk for kidney damage. Our study confirmed the detrimental effects of high pressure and detrusor-sphincter dyssynergia; however, hostile bladder parameters were not sufficient to distinguish high-risk group patients. The presence of scars in the first scintigraphic evaluation, DLPP above 50 cm H2O, and the presence of hydronephrosis in the first ultrasound were found to be risk factors for renal deterioration. More frequent monitoring and detailed evaluation may be necessary for patients with these risk factors. Prospective studies are required to design better management strategies individualized for each patient.

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