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Postinjury Bladder Overdistension Deteriorates the Lower Urinary Tract's Storage Function in Patients with Spinal Cord Injury

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Keywords
Overdistension · Bladder · Spinal cord injury · Detrusor overactivity · Storage dysfunction

Abstract
Introduction: A recent article has reported that postinjury bladder overdistension (OD) deteriorates lower urinary tract function in the mouse spinal cord injury (SCI) model. However, there have been no reports examining the effect of postinjury bladder OD on lower urinary tract function in human SCI patients. ***Objective:*** The aim of the study was to investigate the effect of postinjury bladder OD during the acute bladder-areflexia phase on the subsequent lower urinary tract storage function in patients with SCI. ***Methods:*** Thirty-one patients with OD (OD group) and 19 patients without OD (non-OD group) during the acute bladder-areflexia phase were included in the study. All patients were confirmed to be completely paralyzed. Their lower urinary tract function was retrospectively evaluated through urodynamic studies 1, 3, and 5 years after injury. Qualiveen-30 questionnaire was used for the evaluation of quality of life. ***Results:*** No significant difference was observed in the maximum cystometric capacity between the OD and non-OD groups in their urodynamic evaluation; however, the maximum bladder pressure was significantly higher, and the bladder compliance was significantly lower in the OD group. The incidence of detrusor overactivity tended to be higher in the OD group, but no significant difference was observed. The use of anti-muscarinics was significantly higher in the OD group. No significant differences were observed in Qualiveen-30 scores between both groups. ***Conclusions:*** These results suggest that postinjury bladder OD during the acute phase deteriorates lower urinary tract storage function in patients with SCI during the later phase. Thus, it is assumed that a well-planned regular intermittent catheterization in the early spinal shock phase would be important for control of patients' subsequent storage function.

Introduction

Spinal cord injury (SCI) prevents voluntary control of voiding, which initially leads to areflexic bladder (spinal shock) and urinary retention. However, after a few months, detrusor overactivity (DO) appears, which causes urinary incontinence and affects quality of life (QoL). In addition, DO-induced high storage pressure is a risk factor for the progress of upper urinary tract dete-

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rioration and symptomatic urinary tract infection. To reduce DO, we usually administer medications, including anticholinergics or beta-3 agonists. In addition, other treatment strategies, including intradetrusor botulinum toxin A injection [1] or neuromodulation [2], are now available to overcome DO.

However, a few decades ago, we had no treatment strategies except for anti-muscarinics, and the treatment of anti-muscarinics-refractory patients was a severe problem. In 1980, Delaere et al. [3] tried bladder overdistension (OD) under epidural anesthesia in 53 patients with unstable bladder. Unfortunately, their results were discouraging because of the recurrence of DO and other complications, indicating that bladder OD is not effective once DO has occurred. Based on this study, we previously hypothesized that bladder OD in the period of spinal shock, when DO has not yet emerged, might be effective for patients with complete paralysis to reduce their subsequent DO and urinary incontinence. In 1984, we preliminarily reported favorable results [4]. However, the clinical effectiveness of this study was evaluated only by short-term subjective symptoms, and no objective long-term evaluation, including urodynamic study, was performed.

On the other hand, Wada et al. [5] recently reported that postinjury bladder OD deteriorates lower urinary tract function in the mouse SCI model. However, there have been no reports analyzing the effect of bladder OD on lower urinary tract function in human SCI patients. Although our data are very old and obtained about 20–30 years ago, we consider that a reexamination of the effect of bladder OD on subsequent lower urinary tract function could result in significant findings, and the results of analysis may give us some useful information. Therefore, in the present study, the urodynamic data for 5 years after bladder OD were retrospectively evaluated and compared with those of patients who received regular intermittent catheterization with less than 400 mL of capacity on each occasion.

Materials and Methods

Study Design and Patient Characteristics

We retrospectively reviewed the clinical data of SCI patients between January 1982 and December 2007 in a single institution. Patients who were hospitalized within 14 days after injury and evaluated with urodynamic studies for more than 5 years after injury were included. Finally, we included 31 patients (28 men and 3 women) managed with OD (OD group) and 19 patients (15 men and 4 women) managed without OD (non-OD group) and retrospectively evaluated their subsequent lower urinary tract storage function. The recruitment period was 1984–2004 in the OD group and 1982–2007 in the non-OD group. All patients had a confirmed complete paralysis with suprasacral SCI and were also supposed to undergo clean intermittent catheterization (CIC) in the future. Table 1 presents the demographic parameters of the patients, and there were no significant differences between these 2 groups. This study was conducted in accordance with the Declaration of Helsinki's (2013) ethical guidelines for clinical research and was approved by the Institutional Review Board at our institution.

Table 1. Demographic parameters

	OD (+)	OD (–)	*p* value
Patients, *n*	31	19	
Sex (male:female)	28:3	16:3	0.661
Age at injury, years	27 (22.5–36.0)	30 (21.5–37.5)	0.802
Duration of overdistention, days	21 (17.5–32.0)	–	
Injury levels (C/T/L)	2/22/7	3/11/5	0.443

OD, overdistension.

Bladder Overdistention and Follow-Up with Urodynamics

In the non-OD group, regular intermittent catheterization with <400 mL capacity on each occasion was performed 4–5 times per day. In the OD group, once the complete paralysis was confirmed at the first week after hospitalization, regular intermittent catheterization was discontinued and bladder OD was begun. In this group, intermittent catheterization was performed twice a day with 600–1000 mL volume of urine on each occasion. This management of these groups continued until self-catheterization was initiated. The median OD period was 21 days (Table 1). The selection of patients for the OD group or non-OD group depended on the doctor in charge of the patient. Between January 1982 and December 2007, our hospital had 2 leading urologists. One urologist managed patients with OD and the other managed patients without OD during the initial spinal shock phase.

Urodynamic assessments performed at 1, 3, and 5 years after injury were evaluated. The patient was in the supine position, and the bladder was filled with saline plus contrast media at a speed of 50 mL/min using an 8-French transurethral catheter for the measurement of bladder pressure. Urodynamic assessment parameters included maximum cystometric capacity, maximum bladder pressure (MBP), bladder compliance, and DO during the storage phase. The Qualiveen-30 questionnaire was used to evaluate the patients' QoL. We could not evaluate serum Cr or renal ultrasonography because some of the data were too old and could not be obtained.

Statistical Analysis

Data are expressed as median values (interquartile ranges, IQR). The differences in continuous variables between the OD and non-OD groups were evaluated using the Mann-Whitney's *U* test. The categorical variables between the OD and non-OD groups were assessed using Fisher's exact test. A p value of <0.05 was considered to be statistically significant. All statistical analyses were performed with EZR [6], which is a graphical user interface for *R*.

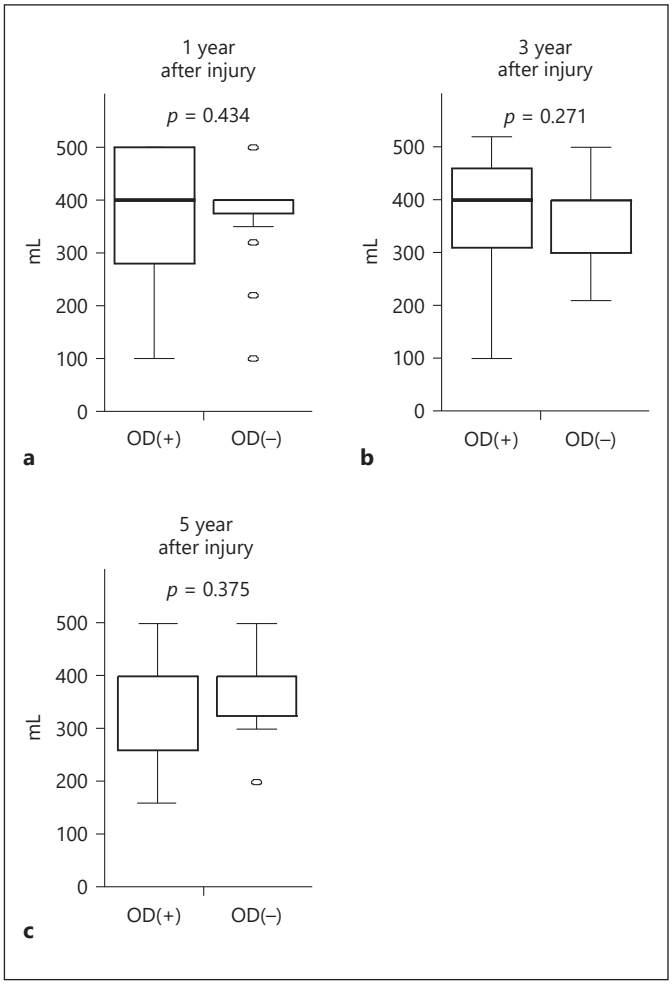

Fig. 1. Comparison of MCC between the OD and non-OD groups at 1 (**a**), 3 (**b**), and 5 years after SCI (**c**). The data are presented as median values (IQR). MCC, maximum cystometric capacity; OD, overdistension; SCI, spinal cord injury.

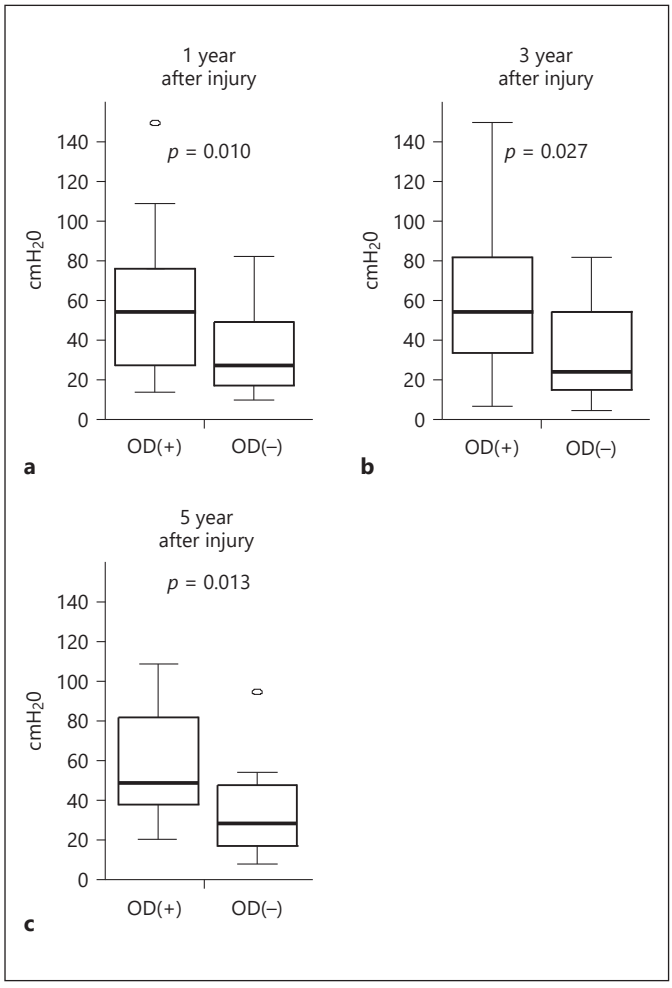

Fig. 2. Comparison of MBP between the OD and non-OD groups at 1 (**a**), 3 (**b**), and 5 years after SCI (**c**). The data are presented as median values (IQR). MBP, maximum bladder pressure; OD, overdistension; SCI, spinal cord injury.

Results

Urodynamic Parameters and QoL

At 5 years after injury, all patients had still been managed with CIC for their urinary management. Maximum cystometric capacity was not significantly different between the OD and non-OD groups at 1 (OD: 400 [280–500] mL, non-OD: 400 [388–400] mL, $p = 0.434$), 3 (OD: 400 [310–460] mL, non-OD: 400 [313–400] mL, $p = 0.271$), and 5 years (OD: 400 [263–400] mL, non-OD: 400 [338–400] mL, $p = 0.375$) after SCI (Fig. 1). However, MBP in the OD group was significantly higher than that in the non-OD group at 1 (OD: 54.4 [27.2–73.4] cmH_2O, non-OD: 27.2 [17.5–48.8] cmH_2O, $p = 0.010$), 3 (OD: 54.4 [34.0–81.6] cmH_2O, non-OD: 24.0 [16.4–50.3] cmH_2O, $p = 0.027$), and 5 years (OD: 48.8 [38.7–81.6] cmH_2O, non-OD: 28.6 [18.5–47.6] cmH_2O, $p = 0.013$) after SCI (Fig. 2). In addition, the bladder compliance was significantly lower in the OD group than in the non-OD group 3 years after SCI (OD: 11.0 [5.9–14.7] mL/cmH_2O, non-OD: 20.0 [11.9–47.5] mL/cmH_2O, $p = 0.013$, Fig. 3). No significant differences were observed in Qualiveen-30 scores between these 2 groups (data not shown) (Fig. 3).

Incidence of DO and Prescription of Anticholinergics

The incidence of DO tended to be higher in the OD group than that in the non-OD group, but no significant difference was observed (Table 2). The use of anticholinergics was significantly higher in the OD group than in

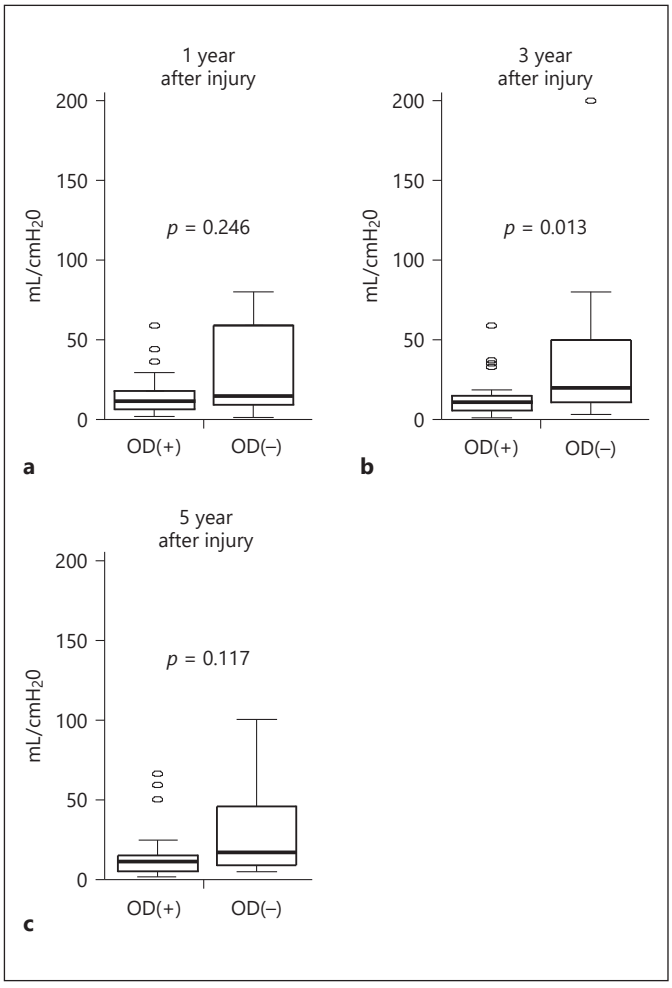

Fig. 3. Comparison of bladder compliance between the OD and non-OD groups at 1 (**a**), 3 (**b**), and 5 years after SCI (**c**). The data are presented as median values (IQR). OD, overdistension; SCI, spinal cord injury.

the non-OD group at 1 ($p = 0.029$), 3 ($p = 0.013$), and 5 years ($p = 0.013$) after SCI (Table 3).

Discussion

The present study demonstrates that the lower urinary tract storage function had deteriorated significantly more in the OD group than in the non-OD group, which suggests that initial postinjury bladder management with regular intermittent catheterization is important to maintain a better urinary tract storage function. How to control the storage function is crucial to providing patients with SCI who undergo CIC with better QoL for their urinary management; therefore, many attempts have been made to maintain a better storage function for them. Sievert et al. [7] reported that early sacral neuromodulation preserves bladder compliance and prevents the emergence of DO in patients with complete suprasacral SCI. Animal studies have also demonstrated that early medications, intradetrusor botulinum toxin A, and neuromodulation can modify the long-term bladder function after SCI [8–10]. In 1984, we hypothesized that bladder OD in the period of spinal shock may prevent the recovery of DO and urinary incontinence and reported preliminary favorable results [4]. However, the clinical effectiveness of this study was evaluated only with short-term subjective symptoms. Therefore, in the present study, we evaluated the long-term objective findings, including the urodynamic data at 1, 3, and 5 years after bladder OD (OD group), and compared this with patients who received regular intermittent catheterization with less than 400 mL of capacity on each occasion (non-OD group). Unfortunately, as shown in the results section, the obtained results were contrary to our hypothesis and demonstrated that bladder OD in the period of spinal shock worsens lower urinary tract storage function and increases the use of anticholinergics. These results indicate that the concept of early bladder distension after SCI to improve the bladder function in the future has failed and even showed worse results than beginning with regular CIC immediately.

Table 2. Comparison of the incidence of DO between the OD and non-OD groups at 1, 3, and 5 years after SCI

	OD (+)	OD (–)	*p* value
1 year after injury	50% (14/28)	25% (4/16)	0.125
3 years after injury	52% (13/25)	33% (6/18)	0.351
5 years after injury	55% (12/22)	33% (4/12)	0.297

OD, overdistension; DO, detrusor overactivity; SCI, spinal cord injury.

Table 3. Comparison of the use rate of anticholinergics between the OD and non-OD group at 1, 3, and 5 years after SCI

	OD (+)	OD (–)	*p* value
1 year after injury	62% (18/29)	25% (4/16)	0.029
3 years after injury	56% (14/25)	17% (3/18)	0.013
5 years after injury	64% (14/22)	17% (2/12)	0.013

OD, overdistension; SCI, spinal cord injury.

The mechanisms of the emergence of DO after SCI have been investigated extensively and the hyperexcitability of bladder afferent pathways has been proposed as a pathophysiological basis of neurogenic DO [11, 12]. Bladder OD is considered to stimulate increased levels of neurotrophins, including nerve growth factor in the bladder wall [13], and they are taken up by afferent nerve endings and transported to dorsal root ganglion cells where they mediate the expression of genes, leading to modulation of ion channels and increased excitability of neurons [11, 14]. Adenosine triphosphate receptors and transient receptor potential channels are involved in sensitization of C fiber bladder afferent pathways after SCI [11]. Recently, Wada et al. [5] demonstrated that frequent bladder emptying can prevent bladder hypertrophy through avoiding bladder OD and reduce the expression level of nerve growth factor in the bladder of an SCI mouse model, which results in the improvement of lower urinary tract dysfunction. Yokoyama et al. [15] also reported that intermittent catheterization was performed less frequently in patients with worsening bladder compliance. Taken together, it is now generally accepted that bladder OD is one of the risk factors for the emergence of DO after SCI. Although the results obtained in this study were contrary to our hypothesis, our results are reasonable against the recent evidence and provide us with an important suggestion that the urinary management with regular intermittent catheterization in the acute phase of SCI is important to maintain lower urinary tract storage function in a better condition after SCI.

There are some limitations to the present study. First, this was a retrospective study. Second, the number of patients was small, which may be the reason why no significant differences in comparisons of some of the parameters were observed. Despite these limitations, we believe that the results of the present study are significant because this is the first report to examine the influence of bladder OD during the initial spinal shock phase on subsequent lower urinary tract storage function in human patients with SCI.

Conclusion

These results suggest that postinjury bladder OD worsens lower urinary tract storage function after SCI, as shown by an increase in MBP and a decrease in bladder compliance. Thus, it is assumed that a well-planned initial management strategy guaranteeing low bladder filling volumes would be important for the control of lower urinary tract dysfunction in patients with SCI.

Acknowledgement

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Statement of Ethics

The study protocol complied with the Declaration of Helsinki and was approved by the ethics committee of Spinal Injuries Center, Fukuoka, Japan.

Disclosure Statement

The authors have no conflict of interest to declare.

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The authors have not received any funding for this study.

Author Contributions

All authors contributed equally to data collection and preparation of the manuscript.

References

1 Cruz F, Herschorn S, Aliotta P, Brin M, Thompson C, Lam W, et al. Efficacy and safety of onabotulinumtoxinA in patients with urinary incontinence due to neurogenic detrusor overactivity: a randomised, double-blind, placebo-controlled trial. Eur Urol. 2011;60(4):742–50.

2 Kessler TM, La Framboise D, Trelle S, Fowler CJ, Kiss G, Pannek J, et al. Sacral neuromodulation for neurogenic lower urinary tract dysfunction: systematic review and meta-analysis. Eur Urol. 2010;58(6):865–74.

3 Delaere KP, Debruyne FM, Michiels HG, Moonen WA. Prolonged bladder distension in the management of the unstable bladder. J Urol. 1980;124(3):334–7.

4 Iwatsubo E, Komine S, Yamashita H, Imamura A, Akatsu T. Over-distension therapy of the bladder in paraplegic patients using self-catheterisation: a preliminary study. Paraplegia 1984;22(4):210–5.

5 Wada N, Shimizu T, Takai S, Shimizu N, Kanai AJ, Tyagi P, et al. Post-injury bladder management strategy influences lower urinary tract dysfunction in the mouse model of spinal cord injury. Neurourol Urodyn. 2017;36(5):1301–5.

6 Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant. 2013;48(3):452–8.

7 Sievert KD, Amend B, Gakis G, Toomey P, Badke A, Kaps HP, et al. Early sacral neuromodulation prevents urinary incontinence after complete spinal cord injury. Ann Neurol. 2010;67(1):74–84.
8 Lee KK, Lee MY, Han DY, Jung HJ, Joo MC. Effects of bladder function by early tamsulosin treatment in a spinal cord injury rat model. Ann Rehabil Med. 2014;38(4):433–42.
9 Li P, Liao L, Chen G, Zhang F, Tian Y. Early low-frequency stimulation of the pudendal nerve can inhibit detrusor overactivity and delay progress of bladder fibrosis in dogs with spinal cord injuries. Spinal Cord. 2013;51(9):668–72.
10 Temeltas G, Tikiz C, Dagci T, Tuglu I, Yavasoglu A. The effects of botulinum-A toxin on bladder function and histology in spinal cord injured rats: is there any difference between early and late application? J Urol. 2005;174(6):2393–6.
11 de Groat WC, Yoshimura N. Plasticity in reflex pathways to the lower urinary tract following spinal cord injury. Exp Neurol. 2012;235(1):123–32.
12 Takahashi R, Yoshizawa T, Yunoki T, Tyagi P, Naito S, de Groat WC, et al. Hyperexcitability of bladder afferent neurons associated with reduction of Kv1.4 α-subunit in rats with spinal cord injury. J Urol. 2013;190(6):2296–304.
13 Vizzard MA. Changes in urinary bladder neurotrophic factor mRNA and NGF protein following urinary bladder dysfunction. Exp Neurol. 2000;161(1):273–84.
14 Vizzard MA. Neurochemical plasticity and the role of neurotrophic factors in bladder reflex pathways after spinal cord injury. Prog Brain Res. 2006;152:97–115.
15 Yokoyama O, Hasegawa T, Ishiura Y, Ohkawa M, Sugiyama Y, Izumida S. Morphological and functional factors predicting bladder deterioration after spinal cord injury. J Urol. 1996;155(1):271–4.