Tzu Chi Medical Journal 24 (2012) 121–126

Contents lists available at SciVerse ScienceDirect

Tzu Chi Medical Journal

journal homepage: www.tzuchimedjnl.com

Original Article

Do baseline urodynamic parameters affect the treatment outcome after intravesical 100 U onabotulinumtoxinA injection in patients with idiopathic detrusor overactivity?

Qian-Shen Ke [a], Yih-Chou Chen [b], Hann-Chorng Kuo [a,*]

[a] Department of Urology, Buddhist Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan
[b] Department of Urology, Hualien General Hospital, Hualien, Taiwan

ARTICLE INFO

Article history:
Received 13 October 2011
Received in revised form
26 December 2011
Accepted 27 December 2011

Keywords:
Detrusor overactivity
OnabotulinumtoxinA
Overactive bladder
Treatment outcome
Urodynamics

ABSTRACT

Objectives: Intravesical injection of onabotulinumtoxinA (BoNT-A) provides effective treatment for idiopathic detrusor overactivity (IDO). However, not all patients have successful long-term therapeutic effects. This study investigated the effects of baseline urodynamic parameters on the therapeutic outcome, after injecting 100 U BoNT-A in patients with IDO.

Materials and Methods: A total of 174 patients who received a first single intravesical BoNT-A 100 U injection for refractory IDO were included. A successful outcome was defined as an improvement of at least two points on a patient perception of bladder condition scale, which was scored from 0 to 6. The short-term (3 months) and long-term (up to 24 months) success rates were analyzed according to baseline urodynamic parameters, including cystometric bladder capacity, maximum flow rate, postvoid residual, voiding efficiency, and detrusor overactivity (DO) subtypes. BoNT-A- related adverse events were also reported.

Results: A successful outcome was reported by 138 (79.3%) patients at 3 months. The baseline urodynamic parameters did not affect the success rates, except that patients with phasic DO had a significantly higher success rate at 3 months than patients with terminal DO. Patients with a baseline postvoid residual (PVR) > 100 mL, had higher rates of acute urinary retention and need to strain to void. However, long-term success rates up to 24 months showed no significant differences between patients with different urodynamic parameters.

Conclusions: Except for patients with phasic DO, the baseline urodynamic parameters did not affect the treatment outcome of intravesical injection of 100 U BoNT-A for IDO. However, acute urinary retention and difficult urination occurred more often in patients with a baseline PVR of > 100 mL.

1. Introduction

Intravesical injection of onabotulinumtoxinA (BoNT-A) has recently been accepted as an alternative treatment for patients with overactive bladder (OAB) and detrusor overactivity (DO), refractory to antimuscarinic therapy [1,2]. BoNT-A injection provides an alternative for non-surgical augmentation of the dysfunctional bladder. About 50–80% of OAB patients, with or without DO, regain urinary continence or have improved urinary control [3–5]. Studies in which the dose of BoNT-A was decreased from 300 U to 100 U in the treatment of OAB, found similar therapeutic effects [5–8]. Recent studies revealed a dose of 100 U BoNT-A had acceptable therapeutic effects and adverse events (AE) [8,9].

The response duration of BoNT-A injection in patients with DO is closely related to the dose. In one study, detrusor injection of 200 U BoNT-A yielded a response duration of 12–15 months [10], whereas the therapeutic duration of 100 U BoNT-A was 6–9 months in other studies [11,12]. However, the incidence of AEs is also closely related to the dose of BoNT-A. Doses > 150 U BoNT-A contributed minimal additional or clinically relevant improvements in symptoms, but carried higher rates of AE compared with 100 U. Dose dependent changes in the postvoid residual (PVR) were observed and the use of clean intermittent catheterization (CIC) was also dose- dependent [9].

Conflict of interest: none.

* Corresponding author. Department of Urology, Buddhist Tzu Chi General Hospital, 707, Section 3, Chung-Yang Road, Hualien, Taiwan. Tel.: +886 3 8561825x2117; fax: +886 3 8560794.
E-mail address: hck@tzuchi.com.tw (H.-C. Kuo).

1016-3190/$ – see front matter
doi:10.1016/j.tcmj.2012.02.002

Patients with DO might have different urodynamic characteristics. Because parasympathetic activity is silent during the storage phase, a basal release of acetylcholine from non-neuronal (urothelial) as well as neuronal sources has been demonstrated in isolated human detrusor muscle. It is suggested that this release, which is increased by stretching the muscle and in the aging bladder, contributes to DO and OAB by eventually increasing bladder afferent activity during storage [13]. Detrusor contractions which occur during that phase might be due to increased purinergic activity, or sensor afferent input. Decreased levels of sensory receptors, including purinergic receptors $P2X_3$ and/or transient receptor potential vanilloid receptors subfamily 1 ($TRPV_1$), may contribute to the clinical effect of BoNT-A in DO [14]. Patients with DO might have adequate or inadequate detrusor contractility [15]. The PVR and voiding efficiency (VE) might have significant changes after intravesical BoNT-A injection, causing a large PVR, difficult urination, acute urinary retention (AUR) or urinary tract infection (UTI) [16]. In other words, the baseline urodynamic characteristics might affect the treatment outcome and the occurrence of AEs. The long-term therapeutic effect might also be affected by baseline urodynamic parameters.

This study analyzed the therapeutic outcome and AEs after intravesical injection of 100 U BoNT-A in patients with idiopathic DO (IDO). The influence of baseline urodynamic parameters on therapeutic outcome was also investigated. The results may provide evidence for us to choose candidates for intravesical BoNT-A injection and enable urologists to handle the patients when intravesical BoNT-A injection is planned in the treatment of patients with IDO.

2. Materials and methods

A total of 174 patients, who had received clinical trials of intravesical BoNT-A 100 U injection for refractory DO and urinary incontinence, were included in this study from 2005 to 2010 [4,8,11,17]. The inclusion criteria were: urodynamic DO with or without urinary incontinence refractory to previous anti-muscarinics for more than 3 months and no UTI, stress urinary incontinence, bladder outlet obstruction (BOO) or neurogenic bladder at enrollment.

Before patients were screened for intravesical BoNT-A injection, videourodynamic study was routinely used for the diagnosis of DO and to identify the presence of BOO or intrinsic sphincter deficiency. Patients with a baseline PVR $>$ 150 mL were excluded from the clinical trials. The cystometric bladder capacity (CBC), voiding detrusor pressure (Pdet), maximum flow rate (Qmax), and PVR were recorded. DO was classified as phasic or terminal DO, depending on whether the uninhibited detrusor contractions occurred during the filling phase, or on reaching bladder capacity, respectively [18]. All terminology used in this study were in accordance with the recommendations of the International Continence Society. Videourodynamic study was performed at baseline and every 3 months after intravesical BoNT-A injection.

All patients received 100 U BoNT-A using different methods of intravesical injection, including detrusor or suburothelial injections in the bladder body, bladder base and trigone injections [8,11,17]. All studies were approved by the Institutional Review Board and Ethics committee of Tzu Chi General Hospital. All patients were informed about the advantages and possible AEs and written informed consent was obtained from all patients before BoNT-A injection.

One hundred units of BoNT-A (BOTOX, Allergan Inc., Irvine, CA, USA) were reconstituted to 10–20 mL with normal saline for detrusor and suburothelial injections, and to 10 mL with normal saline for bladder base and trigone injections. Detrusor injections were performed by injecting BoNT-A solution into 20–40 sites about 1 mm in depth, in the lateral wall, posterior wall and dome of the bladder, using a 23 gauge needle in a rigid cystoscopic injection instrument (22 Fr, Richard-Wolf, Knittlingen, Germany). The injection sites were equally distributed in the bladder body. Suburothelial injections were performed using a procedure identical to that for detrusor injection, except that the needle was inserted just into the suburothelial space and a ballooning formation was noted during injection. Bladder base injections were performed by injecting BoNT-A solution into 10 sites in the suburothelial space with two injections in a row near the bladder neck and three injections in a second row anterior, and five injections posterior, to the interureteric ridge, about 1 cm from the ureteral orifices.

All procedures were performed transurethrally under intravenous general anesthesia in the operating room. Anticoagulants were discontinued 1 week before BoNT-A treatment. The bladder volume was kept at 100–150 mL, and blood vessels were avoided during injections. An indwelling 14 Fr Foley catheter was placed overnight and patients were discharged the next morning. Oral broad spectrum prophylactic antibiotics (cephalosporin 500 mg tid) were given for 3 days.

Patients were requested to make regular follow-up visits until their voiding condition returned to baseline. Uroflowmetry for Qmax, voided volume and PVR were performed at each visit. The functional bladder capacity (FBC) was obtained from the maximum voided volume recorded in a voiding diary or uroflowmetry. The VE was calculated as the percentage of voided volume of the bladder capacity measured during urodynamic study or uroflowmetry.

All patients were closely monitored at 1–2 weeks, 1 month, 3 months and every 3 months thereafter, until the response to BoNT-A had disappeared. Patients who failed treatment, were not followed up after 6 months. The occurrence of urgency episodes and urgency incontinence were verified using a 3-day voiding diary. All patients were requested to grade the treatment outcome at 3 months after BoNT-A injection (primary end-point), based on the patient perception of bladder condition (PPBC, scored from 0 to 6), the therapeutic effects and bothersome AE [19]. An improvement in the PPBC score of ≥ 2 was considered a successful outcome; otherwise, the treatment was considered to have failed. The period between the treatment date and the visit that patients reported disappearance of the therapeutic effect, was defined as the therapeutic duration.

Any AE considered possibly related to the BoNT-A treatment was recorded. These AEs included AUR, hematuria and general weakness in the early post-treatment period, and large PVR, straining to void, and UTI during the follow-up period. The success rate at 3 months and the urodynamic changes were analyzed between patients with different baseline urodynamic parameters. Kaplan-Meier survival curves were used to analyze the cumulative success rates over time, between subgroups with different baseline urodynamic parameters. A p value < 0.05 was considered statistically significant.

3. Results

A total of 174 patients were studied, including 85 women and 89 men, aged 18–94 years old, with a median age of 67 years. Forty-one of the 79 men $\geq$ 50 years old had previously undergone transurethral resection of the prostate. Bladder body injections were given to 129 patients, and bladder base/trigonal injections were used in 45 patients. There was no significant difference in the mean age of each baseline variable subgroup.

At 3 months, a successful result was reported by 138 (79.3%) patients. The success rate at 3 months was not significantly different between any of the baseline urodynamic variable subgroups.

Table 1
The changes of urodynamic variables at baseline and 3 months after intravesical BoNT-A 100 U injection in patients with detrusor overactivity and different baseline cystometric bladder capacity.

UDS variables	*n*	Baseline	3 mo	Changes	*p*#
Qmax					
CBC < 250 mL	85	11.0 ± 6.04	11.3 ± 5.78	0.33 ± 4.74	0.136
CBC ≥ 250 mL	89	14.0 ± 13.1	13.1 ± 6.71	−0.89 ± 5.23	
FBC					
CBC < 250 mL	85	137 ± 45.6	174.1 ± 84.2	37.2 ± 78.1*	0.000
CBC ≥ 250 mL	89	291 ± 106.6	245.8 ± 118.5	−45.4 ± 108.1*	
PVR					
CBC < 250 mL	85	22.4 ± 35.0	88.4 ± 78.8	66.1 ± 76.6*	0.323
CBC ≥ 250 mL	89	43.8 ± 51.6	124.9 ± 115.1	81.1 ± 112.3*	
Pdet					
CBC < 250 mL	85	26.6 ± 15.8	23.6 ± 14.6	−3.07 ± 13.1	0.872
CBC ≥ 250 mL	89	25.6 ± 13.0	22.9 ± 12.2	−2.76 ± 8.15*	
CBC					
CBC < 250 mL	85	157 ± 49.8	258.8 ± 106.9	101.7 ± 99.3*	0.000
CBC ≥ 250 mL	89	349 ± 81.7	370.3 ± 134.5	21.8 ± 143.9	

# *p* value for the changes of data between groups; * *p* value < 0.05 between baseline and 3 months within groups.
CBC = cystometric bladder capacity; FBC = functional bladder capacity; Pdet = detrusor pressure; PVR = postvoid residual; Qmax = maximum flow rate; UDS = urodynamic study.

Table 3
The changes of urodynamic variables at baseline and 3 months after intravesical BoNT-A 100 U injection in patients with detrusor overactivity and different baseline PVR.

UDS variables	*n*	Baseline	3 mo	Changes	*p*#
Qmax					
PVR < 100 mL	144	13.1 ± 6.13	12.7 ± 6.59	-0.35 ± 5.03	0.820
PVR ≥ 100 mL	30	10.2 ± 5.3	10.1 ± 5.49	-0.11 ± 5.08	
FBC					
PVR < 100 mL	144	227.2 ± 114.7	222.2 ± 111.2	4.98 ± 105.9	0.699
PVR ≥ 100 mL	30	179.6 ± 101.8	166.2 ± 89.4	-13.4 ± 93.4	
PVR					
PVR < 100 mL	144	14.2 ± 19.5	94.2 ± 91.1	80.1 ± 89.5*	0.191
PVR ≥ 100 mL	30	119.4 ± 23.6	173.4 ± 121.7	54.1 ± 130.9*	
Pdet					
PVR < 100 mL	144	26.3 ± 14.3	23.6 ± 13.3	−2.65 ± 11.1*	0.534
PVR ≥ 100 mL	30	25.1 ± 14.6	20.9 ± 13.3	−4.24 ± 8.17*	
CBC					
PVR < 100 mL	144	239.7 ± 113.8	311.6 ± 131.4	71.9 ± 121.2*	0.014
PVR ≥ 100 mL	30	339.1 ± 100.8	343.9 ± 144.7	4.79 ± 158.1	

# *p* value for the changes of data between groups; * *p* value < 0.05 between baseline and 3 months within groups.
CBC = cystometric bladder capacity; FBC = functional bladder capacity; Pdet = detrusor pressure; PVR = postvoid residual; Qmax = maximum flow rate; UDS = urodynamic study.

During the follow-up period, AUR occurred in 12 (6.9%) patients, a large PVR ≥ 150 mL developed in 81 (46.6%) patients and 73 (42%) patients needed to strain to void. Gross hematuria occurred in 17 (9.8%) patients, UTI developed in 27 (15.5%) patients and general weakness was noted in 6 (3.4%) patients.

Tables 1–5 show the changes in CBC, Qmax, FBC, PVR, and Pdet from baseline to 3 months after BoNT-A injection, in patient subgroups with different baseline urodynamic variables. In patients with a baseline CBC < 250 mL, the FBC and CBC at 3 months increased significantly compared with those with a baseline CBC ≥ 250 mL. Patients with baseline Qmax < 10 mL/s had significant increases in the Qmax and FBC at 3 months, compared with those with baseline Qmax ≥ 10 mL/s. Patients with a baseline PVR < 100 mL had a significant increase of CBC at 3 months, compared with those with a baseline PVR ≥ 100 mL. However, patients with baseline VE < 70% or ≥ 70%, and those with phasic or terminal DO, did not differ in any urodynamic change after BoNT-A injection.

Table 6 shows the success rates at 3 months and the occurrence of AE between patient subgroups with different baseline urodynamic parameters. The only significant urodynamic factor was a baseline PVR ≥ 100 mL, which resulted in a higher rate of AUR, and more patients needing to strain to void.

Fig. 1 shows the cumulative success rates between subgroups with different baseline urodynamic variables. There were no significant differences in the cumulative success rates between any patient subgroup with: CBC ≥ 250 mL or CBC < 250 mL, Qmax ≥ 10 mL/s or Qmax <10 mL/s, PVR ≥ 100 mL or PVR < 100 mL, VE ≥ 70% or VE < 70%, and those with phasic or terminal DO.

Table 2
The changes of urodynamic variables at baseline and 3 months after intravesical BoNT-A 100 U injection in patients with detrusor overactivity and different baseline Qmax.

UDS variables	*n*	Baseline	3 mo	Changes	*p* #
Qmax					
Qmax < 10 mL/s	64	6.81 ± 2.03	8.01 ± 3.87	1.20 ± 4.14*	0.006
Qmax ≥ 10 mL/s	110	15.6 ± 5.24	14.5 ± 6.46	−1.11 ± 5.28*	
FBC					
Qmax < 10 mL/s	64	146 ± 82.7	166 ± 93.6	19.6 ± 98.7	0.023
Qmax ≥ 10 mL/s	110	256 ± 110	236 ± 110	−20.1 ± 104	
PVR					
Qmax < 10 mL/s	64	46.7 ± 52.6	110 ± 113	63.5 ± 111*	0.293
Qmax ≥ 10 mL/s	110	25.6 ± 39.0	106 ± 92.8	80.0 ± 87.0*	
Pdet					
Qmax < 10 mL/s	64	26.8 ± 16.4	24.6 ± 14.9	−2.23 ± 14.0	0.633
Qmax ≥ 10 mL/s	110	25.8 ± 13.4	22.6 ± 12.6	−3.19 ± 8.99*	
CBC					
Qmax < 10 mL/s	64	205 ± 103	271 ± 123	66.0 ± 117	0.666
Qmax ≥ 10 mL/s	110	285 ± 116	342 ± 134	56.4 ± 138*	

# *p* value for the changes of data between groups; * *p* value < 0.05 between baseline and 3 months within groups.
CBC = cystometric bladder capacity; FBC = functional bladder capacity; Pdet = detrusor pressure; PVR = postvoid residual; Qmax = maximum flow rate; UDS = urodynamic study.

Table 4
The changes of urodynamic variables at baseline and 3 months after intravesical BoNT-A 100 U injection in patients with detrusor overactivity and different baseline voiding efficiency.

UDS variables	*n*	Baseline	3 mo	Changes	*p*#
Qmax					
VE < 70%	27	8.27 ± 4.43	9.20 ± 4.87	0.93 ± 4.81	0.214
VE ≥ 70%	147	13.3 ± 6.03	12.8 ± 6.58	−0.52 ± 5.05	
FBC					
VE < 70%	27	119.2 ± 48.8	141.4 ± 80.4	22.2 ± 82.9	0.161
VE ≥ 70%	147	235 ± 113	224 ± 109.5	−11.3 ± 106.1	
PVR					
VE < 70%	27	115.4 ± 35.0	172.6 ± 125	57.2 ± 134*	0.339
VE ≥ 70%	147	18.0 ± 27.0	95.0 ± 90.8	77.0 ± 88.4*	
Pdet					
VE < 70%	27	25.9 ± 16.1	22.5 ± 14.7	−3.33 ± 9.08	0.869
VE ≥ 70%	147	26.1 ± 14.2	23.3 ± 13.2	−2.85 ± 10.9*	
CBC					
VE < 70%	27	290 ± 110	328 ± 142	38.5 ± 162	0.413
VE ≥ 70%	147	252 ± 118	316 ± 133	63.2 ± 125*	

# *p* value for the changes of data between groups; * *p* value < 0.05 between baseline and 3 months within groups.
CBC = cystometric bladder capacity; FBC = functional bladder capacity; Pdet = detrusor pressure; PVR = postvoid residual; Qmax = maximum flow rate; UDS = urodynamic study.

Table 5
The changes of urodynamic variables at baseline and 3 months after intravesical BoNT-A 100 U injection in patients with different types of baseline detrusor overactivity.

UDS variables	*n*	Baseline	3 mo	Changes	*p*#
Qmax					
Phasic DO	100	12.9 ± 6.22	12.2 ± 6.46	-0.65 ± 4.62	0.325
Terminal DO	74	12.2 ± 5.90	12.3 ± 6.53	0.16 ± 5.52	
FBC					
Phasic DO	100	214 ± 117	210 ± 106	-3.64 ± 108	0.691
Terminal DO	74	225 ± 109	214 ± 115	-10.4 ± 98.6	
PVR					
Phasic DO	100	32.7 ± 49.6	104 ± 106	71.7 ± 101*	0.568
Terminal DO	74	34.2 ± 39.1	115 ± 96.0	80.6 ± 94.5*	
Pdet					
Phasic DO	100	24.0 ± 12.4	21.4 ± 12.4	-2.68 ± 9.99*	0.787
Terminal DO	74	28.8 ± 16.2	25.6 ± 14.2	-3.19 ± 11.6*	
CBC					
Phasic DO	100	254 ± 125	308 ± 126	54.2 ± 141*	0.549
Terminal DO	74	263 ± 107	330 ± 144	67.0 ± 117*	

# *p* value for the changes of data between groups; * *p* value < 0.05 between baseline and 3 months within groups.
CBC = cystometric bladder capacity; DO = detrusor overactivity; FBC = functional bladder capacity; Pdet = detrusor pressure; PVR = postvoid residual; Qmax = maximum flow rate; UDS = urodynamic study.

4. Discussion

This study found that baseline urodynamic parameters do not generally affect the long term therapeutic outcome and occurrence of AEs after 100 U BoNT-A injection in patients with IDO. However, patients with phasic DO had a higher success rate than those with terminal DO at 3 months. Although a baseline PVR $\geq$ 100 mL may yield a higher rate of AUR and straining to void, the long-term success rate was not inferior to that in patients with a PVR $<$ 100 mL.

In the past decade, intravesical BoNT-A injection has been shown to be an effective therapeutic alternative for IDO refractory to antimuscarinics. Urinary frequency and episodes of incontinence improve after BoNT-A injection [20]. Although clinical trials have provided evidence for the efficacy of BoNT-A in patients with OAB, the incidence of AEs remains high, and also seems to have been underreported. Increased doses of BoNT-A do not add additional benefits, but do increase the incidence of AEs, especially a large PVR and AUR needing CIC [9].

Although numerous studies have explored the underlying pathophysiology of DO, the actual mechanism of development of DO is not fully understood. Urothelial dysfunction, myogenic hyperactivity, neuromuscular junction dysfunction and a central nervous system (CNS) inhibitory deficit, might contribute to the occurrence of DO [21–24]. There is also no useful biomarker to identify the pathophysiology of DO [25]. Most urologists diagnose and treat DO based on urodynamic study and assess the treatment outcome by increases in bladder capacity or symptomatic improvement. Clinical parameters, such as bladder capacity, voided volume and PVR, in part, might reflect the underlying pathophysiology of DO [26].

DO might occur during the storage phase or at bladder capacity, which results in phasic or terminal detrusor contractions, respectively. Parasympathetic activity during the bladder storage phase is supposed to be silent, therefore, any detrusor contractions occurring during the storage phase are likely to be mediated by sensory afferent fibers other than parasympathetic cholinergic fibers [13,14]. Two signaling pathways can be identified in bladder afferent mechanisms. The urothelial pathway is a functional unit consisting of the urothelium, interstitial cells and afferent nerves in the lamina propria. Signaling occurs via muscle-mucosal mechanoreceptors, mucosal mechanoreceptors and chemoreceptors. The myogenic pathway is activated via in-series mechanoreceptors responding to distention, and via spontaneous contractile activity in units of myocytes generating afferent noise [27]. Phasic DO during the storage phase might be mainly due to increased sensory input from urothelial dysfunction, and therefore, the bladder also shows oversensitivity and a small capacity [28]. Terminal DO might involve increased muscarinic receptor expression or lack of an inhibitory effect from the CNS [24]. These different types of DO might have different responses to intravesical BoNT-A injection. The results of this study revealed that the success rate at 3 months was lower in patients with terminal DO, suggesting that the lack of CNS inhibition might play an important role in the failed treatment in these patients.

In this study, patients with a small baseline CBC ($<$ 250 mL) had a significantly greater increment of FBC and CBC after BoNT-A injection than those with a CBC $\geq$ 250 mL at baseline. The PVR changes between these 2 groups were not different, therefore, the differences in CBC and FBC changes between groups are likely to result from a true bladder capacity increase after BoNT-A injection. Although the actual mechanism has not been elucidated, we speculate that the pathophysiology might be different between DO patients with a small and large CBC.

In clinical practice, DO is often associated with bladder oversensitivity [28]. Urothelial dysfunction has been considered to be responsible for DO in patients with a small CBC [29]. On the other

Table 6
Correlation of success rate and the incidence of adverse events with baseline urodynamic variables.

	n	Success rate	AUR	Large PVR	Straining to void	Hematuria	UTI	General weakness
CBC $<$ 250 mL	85	65 (77.4%)	5 (6.0%)	35 (41.7%)	30 (35.7%)	9 (10.7%)	15 (18%)	3 (3.65%)
CBC $\geq$ 250 mL	89	72 (80.9%)	7 (7.9%)	45 (50.6%)	42 (47.2%)	8 (9.0%)	12 (14%)	3 (3.4%)
p		0.351	0.424	0.154	0.084	0.449	0.280	0.631
Qmax $<$ 10 mL/s	64	52 (82.5%)	6 (9.5%)	31 (49.2%)	24 (38.1%)	4 (6.3%)	6 (9.5%)	3 (4.8%)
Qmax $\geq$ 10 mL/s	110	85 (77.3%)	6 (5.5%)	49 (44.5%)	48 (43.6%)	13 (11.8%)	21 (19%)	3 (2.7%)
p		0.268	0.238	0.332	0.291	0.186	0.071	0.381
PVR $<$100 mL	144	113 (79%)	6 (4.2%)	63 (43.8%)	55 (38.2%)	15 (10.4%)	22 (15%)	3 (2.1%)
PVR $\geq$100 mL	30	25 (83.3%)	6 (20%)	18 (60%)	18 (60%)	2 (6.7%)	5 (17%)	3 (10%)
p		0.374	0.007	0.078	0.023	0.409	0.517	0.065
VE $<$ 70%	27	22 (81.5%)	3 (11%)	16 (59.3%)	14 (51.9%)	1 (3.7%)	5 (18.5%)	3 (11%)
VE $\geq$ 70%	147	115 (79%)	9 (6.2%)	64 (43.8%)	58 (39.7%)	16 (11%)	22 (15%)	3 (2.1%)
p		0.490	0.282	0.103	0.168	0.217	0.417	0.049
Phasic DO	100	84 (84%)	5 (5%)	48 (48%)	41 (41%)	6 (6%)	19 (19%)	3 (3%)
Terminal DO	74	54 (73%)	7 (9.5%)	33 (46%)	32 (43.2%)	11 (14.9%)	8 (10.8%)	3 (4.1)
p		0.050	0.198	0.386	0.443	0.046	0.102	0.509

AUR = acute urinary retention; CBC = cystometric bladder capacity; DO = detrusor overactivity; Pdet = detrusor pressure; PVR = postvoid residual; Qmax = maximum flow rate; UTI = urinary tract infection; VE = voiding efficiency.

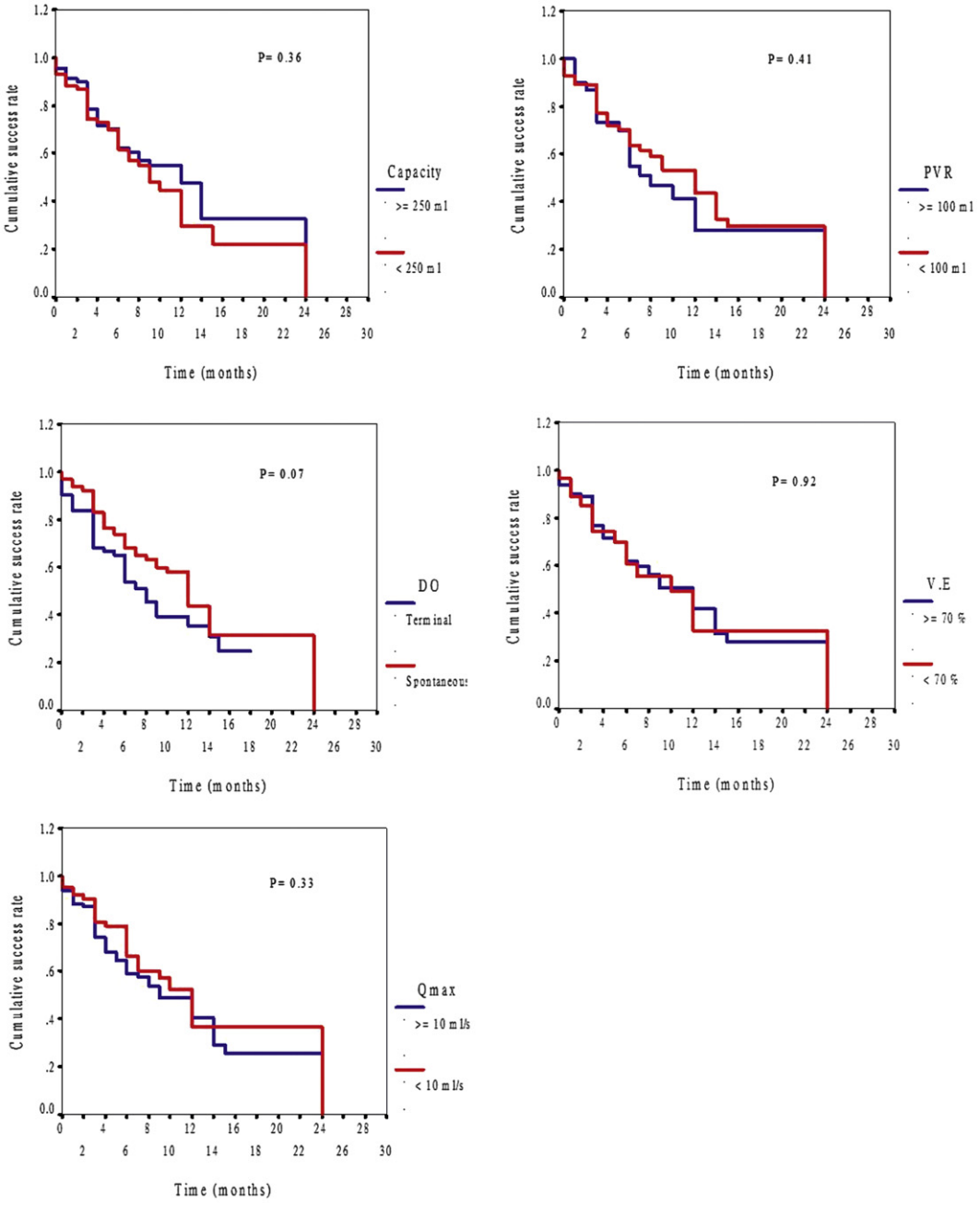

Fig. 1. Kaplan-Meier survival curves for the cumulative success rates of different patient subgroups with varying baseline urodynamic parameters. The treatment outcome was assessed using the patient perception of bladder condition (PPBC), with an improvement of the PPBC score from baseline of ≥ 2 considered to be a successful outcome. There was no significant difference in the success rate in all comparisons.

hand, DO in patients with a large CBC possibly results from inhibitory deficiency from CNS control. Therefore, the effects on CBC and FBC after BoNT-A injection are different. Our previous study also showed that improvement of urgency severity is significantly associated with a higher success rate at 3 months and longer therapeutic duration after intravesical BoNT-A injection for IDO, suggesting that effective urothelial sensory nerve desensitization is important in the mechanism of action of BoNT-A on DO [30].

Another interesting finding is that patients with a baseline PVR $<$ 100 mL had a significantly greater increment in CBC after BoNT-A injection than with those with a baseline PVR $>$100 mL. A higher baseline PVR may result in a greater risk of AUR and the need to strain to void. Although the CBC increased, the PVR also increased significantly after BoNT-A injection, resulting in a smaller FBC in patients with a baseline PVR $>$ 100 mL. A large PVR reflects lower detrusor contractility, which might be a consequence of aging, bladder ischemia, myogenic effect or partial denervation [31]. Whether these factors influence the action of BoNT-A deserves further investigation, and might provide pharmacological perspectives in the treatment of DO [32].

In conclusion, except for patients with phasic DO, the baseline urodynamic parameters did not affect the treatment outcome after intravesical injection of 100 U BoNT-A for IDO. AUR and difficult urination occurred significantly more often in patients with a baseline PVR $\geq$ 100 mL. However, the occurrence of a large PVR

after treatment did not affect the success rate at 3 months or long-term follow-up.

References

[1] Kuo HC. Urodynamic evidence of effectiveness of botulinum A toxin injection in treatment of detrusor overactivity refractory to anticholinergic agents. Urology 2004;63:868–72.

[2] Kessler TM, Danuser H, Schumacher M, Studer VE, Burkhard FC. Botulinum A toxin injections into the detrusor: an effective treatment in idiopathic and neurogenic detrusor overactivity? Neurourol Urodyn 2005;24:231–6.

[3] Werner M, Schmid DM, Schussler B. Efficacy of botulinum-A toxin in the treatment of detrusor overactivity incontinence: a prospective non-randomized study. Am J Obstet Gynecol 2005;192:1735–40.

[4] Kuo HC. Clinical effects of suburothelial injection of botulinum A toxin in patients with non-neurogenic detrusor overactivity refractory to anticholinergics. Urology 2005;66:94–8.

[5] Schulte-Baukloh H, Weiss C, Stolze T, Sturzebecher B, Knispel HH. Botulinum-A toxin for treatment of overactive bladder without detrusor overactivity: urodynamic outcome and patient satisfaction. Urology 2005;66:82–7.

[6] Rajkumar GN, Small DR, Mustafa AW, Conn G. A prospective study to evaluate the safety, tolerability, efficacy and durability of response of intravesical injection of botulinum toxin type A into detrusor muscle in patients with refractory idiopathic detrusor overactivity. BJU Int 2005;96:848–52.

[7] Schmid DM, Sauermann P, Werner M, Schuessler B, Blick N, Muentener M, et al. Experience with 100 cases treated with botulinum-a toxin injections in the detrusor muscle for idiopathic overactive. J Urol 2006;176:177–85.

[8] Kuo HC. Will suburothelial injection of a small dose of botulinum A toxin have similar therapeutic effects and less adverse events for refractory detrusor overactivity? Urology 2006;68:993–7.

[9] Dmochowski R, Chapple C, Nitti VW, Chancellor M, Thompson C, Daniell G, et al. Efficacy and safety of onabotulinumtoxinA for idiopathic overactive bladder: a double-blind, placebo controlled, randomized, dose ranging trial. J Urol 2010;184:2416–22.

[10] Sahai A, Khan MS, Dasgupta P. Efficacy of botulinum toxin-A for treating idiopathic detrusor overactivity: results from a single center, randomized, double-blind, placebo controlled trial. J Urol 2007;177:2231–6.

[11] Kuo HC. Comparison of effectiveness of detrusor, suburothelial and bladder base injections of botulinum toxin A for idiopathic detrusor overactivity. J Urol 2007;178:1359–63.

[12] Jeffery S, Fynes M, Lee F, Wang K, Williams L, Morley R. Efficacy and complications of intradetrusor injection with botulinum toxin A in patients with refractory idiopathic detrusor overactivity. BJU Int 2007;100:1302–6.

[13] Andersson KE, Yoshida M. Antimuscarinics and the overactive detrusor – which is the main mechanism of action? Eur Urol 2003;43:1–5.

[14] Apostolidis A, Popat R, Yiangou Y, Cockayne D, Ford AP, Davis JB, et al. Decreased sensory receptors P2X3 and TRPV1 in suburothelial nerve fibers following intradetrusor injections of botulinum toxin for human detrusor overactivity. J Urol 2005;174:977–82.

[15] Griffiths DJ, McCracken PN, Harrison GM, Gormley EA, Moore KN. Urge incontinence and impaired detrusor contractility in the elderly. Neurourol Urodyn 2006;25:356–60.

[16] Kuo HC, Liao CH, Chung SD. Adverse events of intravesical botulinum toxin a injections for idiopathic detrusor overactivity: risk factors and influence on treatment outcome. Eur Urol 2010;58:919–26.

[17] Kuo HC. Bladder base/trigone injection is safe and as effective as bladder body injection of onabotulinumtoxinA for idiopathic detrusor overactivity refractory to antimuscarinics. Neurourol Urodyn 2011;30:242–8.

[18] Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. Neurourol Urodyn 2002;21:167–78.

[19] Coyne KS, Matza LS, Kopp Z, Abrams P. The validation of the patient perception of bladder condition (PPBC): a single-item global measure for patients with overactive bladder. Eur Urol 2006;49:1079–86.

[20] Anger JT, Weinberg A, Suttorp MJ, Litwin MS, Shekelle PG. Outcome of intravesical botulinum toxin for idiopathic overactive bladder syndrome: A systemic review of the literature. J Urol 2010;183:2258–64.

[21] Birder L. Role of the urothelium in bladder function. Scand J Urol Nephrol Suppl 2004;215:48–53.

[22] Brady CM, Apostolidis AN, Harper M, Yiangou Y, Beckett A, Jacques TS, et al. Parallel changes in bladder suburothelial vanilloid receptor TRPV1 (VR1) and pan-neuronal marker PGP9.5 immunoreactivity in patients with neurogenic detrusor overactivity after intravesical resiniferatoxin treatment. BJU Int 2004;93:770–6.

[23] Brady C, Apostolidis A, Yiangou Y, Baecker PA, Ford AP, Freeman A, et al. P2X3-immunoreactive nerve fibers in neurogenic detrusor overactivity and the effect of intravesical resiniferatoxin (RTX). Eur Urol 2004;46:247–53.

[24] Andersson KE. Mechanisms of Disease: central nervous system involvement in overactive bladder syndrome. Nat Clin Pract Urol 2004;1:103–8.

[25] Kuo HC, Liu HT, Chancellor MB. Can urinary nerve growth factor be a biomarker for overactive bladder? Rev Urol 2010;12:e69–77.

[26] Romanzi LJ, Groutz A, Heritz DM, Blaivas JG. Involuntary detrusor contractions: correlation of urodynamic data to clinical categories. Neurourol Urodyn 2001;20:249–57.

[27] Kanai A, Andersson KE. Bladder afferent signaling: recent findings. J Urol 2010;183:1288–95.

[28] Yamaguchi O. Antimuscarinics and overactive bladder: other mechanism of action. Neurourol Urodyn 2010;29:112–5.

[29] Apostolidis A, Dasgupta P, Fowler CJ. Proposed mechanism for the efficacy of injected botulinum toxin in the treatment of human detrusor overactivity. Eur Urol 2006;49:644–50.

[30] Kuo HC. Reduction of urgency severity is associated with long-term therapeutic effect after intravesical onabotulinumtoxinA injection for idiopathic detrusor overactivity. Neurourol Urodyn 2011;30:1497–502.

[31] van Koeveringe GA, Vahabi B, Andersson KE, Kirschner-Herrmans R, Oelke M. Detrusor underactivity: a plea for new approaches to a common bladder dysfunction. Neurourol Urodyn 2011;30:723–8.

[32] Andersson KE, Hedlund P. Pharmacologic perspective on the physiology of the lower urinary tract. Urology 2002;60:13–20.