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Maximum Voided Volume Is a Better Clinical Parameter for Bladder Capacity Than Maximum Cystometric Capacity in Patients With Lower Urinary Tract Symptoms/Benign Prostatic Hyperplasia: A Prospective Cohort Study

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Purpose: Bladder capacity is an important parameter in the diagnosis of lower urinary tract dysfunction. We aimed to determine whether the maximum bladder capacity (MCC) measured during a urodynamic study was affected by involuntary detrusor contraction (IDC) in patients with Lower Urinary Tract Symptoms (LUTS)/Benign Prostatic Hyperplasia (BPH).
Methods: Between March 2020 and April 2021, we obtained maximum voided volume (MVV) from a 3-day frequency-volume chart, MCC during filling cystometry, and maximum anesthetic bladder capacity (MABC) during holmium laser enucleation of the prostate under spinal or general anesthesia in 139 men with LUTS/BPH aged >50 years. Patients were divided according to the presence of IDC during filling cystometry. We assumed that the MABC is close to the true value of the MCC, as it is measured under the condition of minimizing neural influence over the bladder.
Results: There was no difference in demographic and clinical characteristics between the non-IDC (n=20) and IDC groups (n=119) (mean age, 71.5±7.4) (P>0.05). The non-IDC group had greater bladder volume to feel the first sensation, first desire, and strong desire than the IDC group (P<0.001). In all patients, MABC and MVV were correlated (r=0.41, P<0.001); however, there was no correlation between MCC and MABC (r=0.19, P=0.02). There was no significant difference in MABC between the non-IDC and IDC groups (P=0.19), but MVV and MCC were significantly greater in the non-IDC group (P<0.001). There was no significant difference between MABC and MVV (MABC-MVV, P=0.54; MVV/MABC, P=0.07), but there was a significant difference between MABC and MCC between the non-IDC and IDC groups (MABC-MCC, P<0.001; MCC/MABC, P<0.001).
Conclusions: Maximum bladder capacity from a urodynamic study does not represent true bladder capacity because of involuntary contractions.

Keywords: Prostatic hyperplasia; Holmium; Urinary bladder; Overactive; Anesthetics; Urodynamics

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- **Research Ethics:** This study was approved by the Institutional Review Board (IRB) of Seoul National University Hospital (IRB No. H-2002-054-1100).
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INTRODUCTION

Lower urinary tract dysfunction (LUTD) is common not only in patients with neurogenic causes but also in patients with nonneurogenic diseases such as overactive bladder and benign prostatic hyperplasia (BPH) [1]. In particular, it is known that secondary bladder function changes frequently occur as part of a compensation mechanism according to an increase in bladder outlet resistance in BPH [2]. Accurately assessing bladder function in BPH/LUTD patients and understanding the pathophysiology of each disease is important in planning treatment. When bladder function changes, many changes occur in bladder function-related indicators such as bladder capacity, bladder sensation, detrusor activity, and bladder compliance [3].

Clinical indicators that can measure bladder capacity are divided into 3 major categories: (1) maximum voided volume (MVV), (2) maximum cystometric capacity (MCC), and (3) maximum anesthetic bladder capacity (MABC). MVV is defined as the highest voided volume recorded from the frequency-volume chart (FVC) measured continuously for 72 hours [4]. MCC is defined as the volume when micturition can no longer be delayed during filling cystometry in individuals with normal sensation [4,5]. MABC is defined as the volume in which the bladder can be filled under general or spinal anesthesia, and is known to be the closest to "anatomical bladder capacity" [4,5].

Concomitant urodynamic detrusor overactivity (DO) exists in many BPH patients with bladder outlet obstruction (BOO) [6]. In these patients, when terminal involuntary detrusor contraction (IDC) occurs early during filling cystometry, the problem of inaccurate bladder capacity measurement is frequently observed in clinical practice. We hypothesized that the bladder capacity measured during urodynamic studies would be affected by the occurrence of IDC. We aimed to compare the effects of IDC on bladder capacity by using various measurement methods in patients with lower urinary tract symptoms (LUTS) and BPH.

MATERIALS AND METHODS

This is a prospective study. Patients aged 50 years or older who consented to this study and underwent holmium laser enucleation of the prostate (HoLEP) with LUTS/BPH at Seoul National University Hospital between March 2020 and April 2021 were included. The exclusion criteria for this study were neurogenic bladder, urinary tract infection, patients who underwent surgery for voiding dysfunction, pelvic radiotherapy history, prostate cancer, bladder cancer, rectal cancer, and congenital genitourinary anomaly. However, patients who had minimal effects on lower urinary tract function, such as transient ischemic attack and mild spinal stenosis, were included [7]. This study was approved by the Institutional Review Board (IRB) of Seoul National University Hospital (IRB No. H-2002-054-1100).

On an outpatient basis, a physical examination including basic evaluation, history taking, and digital rectal exam was performed for all patients. Symptoms were assessed using the International Prostate Symptom Score (IPSS) and the Overactive Bladder Symptom Score (OABSS). Free uroflowmetry with postvoid residual volume measurements was performed. A FVC was recorded for 3 days and patients were instructed to bring it to the next outpatient clinic. Transrectal ultrasonography, filling cystometry, and pressure-flow study were performed in some patients with severe LUTS. To exclude prostate cancer, a blood prostate specific antigen test was performed.

Three basic parameters for bladder capacity were obtained: MVV, MCC, and MABC. MVV was obtained using FVC, which was recorded for 3 consecutive days. As an outpatient base, an experienced professional nurse distributed the FVC form to the patients and educated them about the recording method in detail. At the next outpatient clinic, FVC was collected, the records were analyzed according to the indicators, and the results were recorded [8]. MCC was the maximum capacity measured by filling cystometry, and MABC was the maximum bladder volume measured after anesthesia [4,5]. Among these values, MABC, which can minimize neurological interference, was determined as the true value of maximal bladder capacity. The urodynamic study was conducted in the same way as the previous test conducted by the same researcher [9]. Briefly, for Pabd (abdominal pressure) measurement, a 7.5F rectal catheter with a balloon was inserted into the rectum. To measure vesical pressure, a 6F dual lumen catheter was inserted into the urethra, and filling cystometry was performed in the standing position. The bladder filling rate was 50 mL/min, and the bladder was filled with normal saline. During filling, bladder sensations, such as first sensation of bladder filling, first desire to void, and strong desire to void, and bladder capacity were measured according to the definition of the International Continence Society (ICS) [4,5]. After filling cystometry, a pressure-flow study was performed.

MABC was measured under general or spinal anesthesia pri-

or to HoLEP surgery. Although spinal anesthesia was performed basically, the anesthesiologist decided whether to perform general anesthesia based on the patient's general condition. After the anesthesiologist confirmed that the neurologic reflex had disappeared, the patient was placed in the lithotomy position. A 26F resectoscope was inserted into the bladder through the urethra, and all the urine was drained. Normal saline was infused into the bladder for irrigation at a pressure of 60 cm H_2O. When the normal saline was no longer infused, the surgeon stopped the infusion and drained the bladder. The amount of normal saline drained was measured and recorded using an electronic balance [5].

In this study, subjective LUTS of patients were assessed using the OABSS and IPSS questionnaires. OAB was diagnosed when the score in Question 3 was 2 or more and the total score was 3 or more on the OABSS questionnaire administered before surgery [10]. All terms and criteria used in this study refer to ICS standards [4,5,11]. One research coordinator computerized all clinical data into a database, and 2 urologists (SJO and MHK) analyzed the above data. Patients with phasic or terminal DO observed on filling cystometry were classified into the IDC group. All data were divided into IDC and non-IDC groups, and we analyzed demographic, FVC, urodynamic study, and bladder capacity parameters such as MABC, MVV, and MCC.

The distribution of patient characteristics was compared using the Student t-test, Pearson chi-square test, or Fisher exact test. Continuous factors are expressed as means and standard deviations, and categorical factors are expressed as percentages. The Pearson correlation coefficient test was used to determine the relationship between the measured values (MVV, MCC, and MABC). All statistical comparisons were performed using IBM SPSS Statistics ver. 22.0 (IBM Co., Armonk, NY, USA). Statistical significance was set at P-value < 0.05.

RESULTS

From March 2020 to April 2021, 147 patients aged 50 years or older underwent HoLEP surgery at Seoul National University Hospital for LUTS/BPH. Eight patients met the exclusion criteria, and 139 patients were included in the analysis of the study results. The mean age of the patients was 71.5 ± 7.4 years. There was no significant difference in the demographic and clinical characteristics between the non-IDC and IDC groups (Table 1).

FVC analysis showed that the MVV during daytime in the

Table 1. Demographic and clinical characteristics of patients

Characteristic	Total (n = 139)	Non-IDC group (n = 20)	IDC group (n = 119)	P-value[a)]
Age (yr)	71.5 ± 7.4	70.5 ± 8.6	71.7 ± 7.2	0.483
Body mass index (kg/m^2)	24.4 ± 2.7	24.5 ± 1.2	24.4 ± 2.9	0.923
Comorbidity				
Diabetes mellitus	23 (16.5)	6 (30)	17 (14.3)	0.080
Hypertension	67 (48.2)	8 (40)	59 (49.6)	0.428
Mild neuropathy				0.432
Herniated intervertebral disc	11 (7.9)	3 (15)	8 (6.7)	
Transient ischemic attack	4 (2.8)	0 (0)	4 (3.3)	
Parkinson disease	1 (0.7)	0 (0)	1 (0.8)	
BPH medication				
Alpha-blocker	135 (97.1)	20 (100)	115 (96.6)	0.405
5-ARI	31 (22.3)	2 (10)	29 (24.4)	0.153
Onset duration (mo)	36.4 ± 26.5	33.4 ± 24.6	36.9 ± 26.8	0.584
Total prostate volume (mL)	71.8 ± 32.4	59.3 ± 30.2	74.0 ± 32.5	0.060
Transitional volume (mL)	43.7 ± 25.7	38.7 ± 23.6	44.7 ± 26.2	0.355
PSA (ng/mL)	5.2 ± 7.3	6.5 ± 9.2	5.0 ± 7.0	0.424

Values are presented as mean ± standard deviation or number (%).
IDC, involuntary detrusor contraction; BPH, benign prostatic hyperplasia; 5-ARI, 5-alpha reductase inhibitors; PSA, prostate specific antigen.
[a)]P-value between non-IDC group and IDC group.

non-IDC group was significantly greater than that in the IDC group (P = 0.019) (Table 2). However, there was no significant difference between the 2 groups in all other FVC indicators, including the MVV during night-time (P > 0.05). The results of

Table 2. Frequency-volume chart result according to IDC

Variable	Total (n = 139)	Non-IDC group (n = 20)	IDC group (n = 119)	P-value[a)]
24-Hour urine volume (mL)	1,571.5 ± 476.3	1,600.2 ± 399.0	1,567.8 ± 489.4	0.780
Nocturnal urine volume (mL)	538.4 ± 266.2	497.9 ± 201.2	545.2 ± 275.8	0.464
Nocturia index	1.8 ± 0.8	1.6 ± 0.6	1.9 ± 0.8	0.111
Nocturnal polyuria index	0.3 ± 0.2	0.3 ± 0.1	0.3 ± 0.1	0.529
Actual number of nightly voids	1.5 ± 1.6	1.2 ± 0.9	1.6 ± 1.0	0.169
Predicted number of nightly voids	1.9 ± 0.8	1.7 ± 0.6	1.9 ± 0.9	0.238
Nocturnal bladder capacity index	0.6 ± 0.4	0.6 ± 0.4	0.6 ± 0.4	0.859
Maximum voided volume during daytime (mL)	279.4 ± 106.4	331.0 ± 127.1	270.7 ± 100.5	0.019
Maximum voided volume during night-time (mL)	314.8 ± 102.0	346.7 ± 104.2	309.4 ± 101.1	0.131
24-Hour urinary frequency	8.0 ± 2.4	7.5 ± 2.3	8.0 ± 2.4	0.341
Daytime urinary frequency	6.4 ± 1.9	6.2 ± 2.0	6.4 ± 1.9	0.659
Night-time urinary frequency	1.5 ± 1.0	1.2 ± 0.9	1.6 ± 1.0	0.169
Average voided volume (mL)	208.2 ± 71.6	229.0 ± 68.0	204.7 ± 71.9	0.162
Average voided volume during daytime (mL)	167.2 ± 59.6	182.7 ± 53.3	164.3 ± 60.4	0.210
Average voided volume during night-time (mL)	182.7 ± 101.6	179.6 ± 87.2	183.2 ± 104.2	0.884

Values are presented as mean ± standard deviation.
IDC, involuntary detrusor contraction.
[a)]P-value between non-IDC group and IDC group.

Table 3. Urodynamic finding results according to IDC

Variable	Non-IDC group (n = 20)	IDC group (n = 119)	P-value
Free uroflowmetry			
Qmax (mL/sec)	11.2 ± 6.4	10.7 ± 5.3	0.720
PVR (mL)	94.3 ± 123.3	88.1 ± 90.7	0.789
Filling cystometry			
First sensation (mL)	253.8 ± 114.1	131.5 ± 74.5	< 0.001
First desire (mL)	258.8 ± 123.5	134.4 ± 77.3	< 0.001
Strong desire (mL)	389.6 ± 99.7	251.5 ± 142.6	0.001
MCC (mL)	430.4 ± 111.8	216.5 ± 136.0	< 0.001
Bladder compliance (mL/cm H_2O)	61.7 ± 41.4	71.1 ± 51.7	0.455
Pressure-flow study			
Qmax (mL/sec)	4.7 ± 2.7	7.6 ± 5.0	0.019
PdetQmax (cm H_2O)	54.2 ± 19.5	61.7 ± 24.9	0.212
Pdetmax (cm H_2O)	69.0 ± 19.6	72.7 ± 28.2	0.588
BOOI	45.2 ± 19.3	47.6 ± 26.1	0.707

Values are presented as mean ± standard deviation.
IDC, involuntary detrusor contraction; Qmax, Maximum flow rate; PVR, postvoid residual urine; MCC, maximum cystometric capacity; BOOI, bladder outlet obstruction index; PdetQmax, detrusor pressure at maximum flow rate; Pdetmax, maximum detrusor pressure.
Please define these abbreviations.

Table 4. Bladder volume indicators according to the presence of IDC

Variable	Non-IDC group (n=20)	IDC group (n=119)	P-value
MABC (mL)	622.2±141.5	573.1±157.7	0.195
MVV (mL)	386.2±132.6	323.5±102.3	0.017
MCC (mL)	430.4±111.8	216.5±136.0	<0.001
MABC-MCC (mL)	191.8±126.6	364.1±180.7	<0.001
MVV-MCC (mL)	-44.1±158.0	107.0±156.0	<0.001
MABC-MVV (mL)	236.0±207.9	257.1±131.6	0.547
MCC/MABC	0.7±0.1	0.3±0.2	<0.001
MVV/MABC	0.6±0.3	0.5±0.1	0.072
MCC/MVV	1.2±0.4	0.7±0.4	<0.001

Values are presented as mean±standard deviation.
IDC, involuntary detrusor contraction; MABC, maximum anesthetic bladder capacity; MVV, maximum voided volume; MCC, maximum cystometric capacity.

the urodynamic studies are shown in Table 3. During filling cystometry, bladder capacity at the first sensation of bladder filling, first desire to void, and strong desire to void in the IDC group were significantly smaller than those in the non-IDC group (P≤0.001). In the pressure-flow study, Qmax was 7.6±5.0 mL/sec in the IDC group, which was significantly higher than that in the non-IDC group (P=0.019).

MVV, MCC, and MABC indicators indicating maximum bladder capacity were compared between the non-IDC and IDC groups (Table 4). There was no statistical difference in MABC between the non-IDC and IDC groups (P=0.19), but MVV and MCC were significantly greater in the non-IDC group than in the IDC group (P<0.01). Comparison and analysis of the difference and ratio between the above indicators between the IDC and non-IDC groups revealed significant differences between the 2 groups in MABC-MCC (P<0.001), MVV-MCC (P<0.001), MCC/MABC (P<0.001), and MCC/MVV (P<0.001) indices. However, there were no differences in MABC-MVV (P=0.54) and MVV/MABC (P=0.07) between the 2 groups. As a result of performing correlation analysis on continuous variables, MABC, MCC, and MVV, the correlation between MABC and MVV (r=0.41, P<0.001) was greater than between MABC and MCC (r=0.19, P=0.021) (Supplementary Fig. 1).

DISCUSSION

Prostate tissue gradually proliferates from the age of 40, and it puts pressure on the urethra around the bladder outlet, causing LUTS and weakening or thinning of the urine stream [12]. When BOO occurs due to enlargement of the prostate, overactivity of the detrusor muscle may be accompanied [6]. This can be explained by neuroplasticity for BOO [13]. When BOO occurs due to prostate enlargement, detrusor smooth muscle blood flow is reduced and ischemic damage occurs [14]. This leads to apoptosis of smooth muscle cells and damage to the surrounding intrinsic nerve system. Neurons are more susceptible to ischemic damage than smooth muscles. When neuronal degeneration occurs, hypertrophy of smooth muscle cells of the prostate may occur [15]. Nerve growth factor is secreted for regrowth after nerve injury and recombines sodium and potassium channels in dorsal root ganglion neurons. This changes the membrane conductance and eventually lowers the activation threshold of the neuron to induce IDC [16].

This prospective study compared and analyzed clinical indicators (MVV, MCC, MABC) close to bladder capacity in BPH/LUTS patients. A 72-hour FVC and urodynamic study were used as representative evaluation methods for bladder capacity in BPH patients. However, it is not clear which of the 2 measures best represents the true value of bladder capacity, and which measure is more clinically meaningful. Yoon and Swift [17] studied 85 females with urinary incontinence and concluded that there was a strong correlation between MVV and MCC (r=0.473, P=0.006). On the other hand, Ertberg et al. [18], who compared bladder capacity in 60 female patients using cystometry, uroflowmetry, and 24-hour FVC, reported a poor correlation between the 3 measurements. Uluocak et al. [19] compared uroflowmetric capacity, MVV, and MCC in 84 children with idiopathic overactive bladder (32 males and 52 females). As a result of the age-adjusted comparison of the 3 variables, there was no significant difference between the measured values with uroflowmetric capacity of 165.44 mL, MCC 204.37 mL, and MVV 260.07 mL. Therefore, they recommended the use of MVV, a noninvasive method, to obtain bladder capacity in children. Therefore, they recommended the use of MVV, a noninvasive method, to obtain bladder capacity in children. Van Venrooij et al. [20] compared MVV and MCC in 160 males and claimed that the correlation between the 2 values was poor (r=0.35, P=0.01). Rubilotta et al. [21] compared uroflowmetry voided volume and MVV in 169 males and claimed that the correlation between the 2 values was also poor. Some previous studies have reported a correlation between MVV and MCC, but many studies have reported that the correlation be-

tween the 2 values is low.

On the other hand, there are reports that bladder volume decreases when IDC appears, but these reports are very limited. Romanzi et al. [22] prospectively conducted a urodynamic study of 132 patients and showed that bladder capacity in the presence of IDC was 80% of that in the absence of IDC. Van Venrooij et al.[20] previously reported, showed that the correlation between MVV and MCC in the presence of IDC ($r=0.27$, $P=0.01$) was worse than the correlation between MVV and MCC ($r=0.35$, $P=0.01$) in the absence of IDC. From the above studies, it can be seen that MCC does not accurately reflect the actual bladder volume in the presence of IDC. Since IDC is very commonly observed in patients with LUTS/BPH, the authors clearly thought that IDC would have a significant effect on bladder capacity. Among the patients included in this study, 85.6% had IDC of any type, including phasic and terminal IDC, and 58.2% had terminal IDC.

In patients with BPH/LUTS, DO may develop in response to BOO owing to neural influences [6]. Therefore, in this study, MABC measured by minimizing neural influence through anesthesia was regarded as the true value of bladder capacity, and MVV and MCC were comparatively analyzed. The patients were divided into IDC and non-IDC groups, and MVV and MCC were compared. The results of this study showed that both MCC and MVV were significantly higher in the non-IDC group than in the IDC group. But the difference in MABC values was not significant and MABC was larger than that of MCC and MVV in both groups. In addition, the MVV during daytime was significantly greater in the non-IDC group than in the IDC group, but there was no significant difference in the MVV during night-time between the 2 groups. This can be analyzed as a result of the fact that there is less neural influence during sleep than when awake. Based on these facts, it can be seen that MABC exhibits true bladder capacity regardless of IDC by minimizing the neural influence.

When the difference and ratio between MABC and the 2 measured values (MVV and MCC) were calculated, there was no significant difference between MABC and MVV, but there was a significant difference between MABC and MCC between the non-IDC and IDC groups (Table 4). In the filling cystometry, the measured indicators, such as first sensation of bladder filling, first desire to void, and strong desire to void, were greater in the non-IDC group than in the IDC group (Table 3). Through these results, bladder filling in an artificial environment other than natural bladder filling may cause DO due to fast bladder filling rate, low saline temperature, or transurethral catheter discomfort [20]. From the above results, MVV is a more accurate indicator for bladder capacity and MCC from the urodynamic study does not represent true bladder capacity because of the IDC. Therefore, it is reasonable to use a noninvasive 72-hour FVC rather than an invasive urodynamic study to obtain the bladder capacity of a patient.

In our study, MCC was found to be as inaccurate as bladder capacity when IDC occurred, and MVV was found to be a more accurate indicator of bladder capacity. To the best of the authors' knowledge, this study is the first to obtain MABC and compare it with MVV and MCC, and the first research result to describe MCC as an inaccurate indicator of terminal IDC.

This study had several limitations. First, the patients included in this study were unable to control their symptoms with BPH medication, and surgical treatment was planned. Therefore, there is a possibility of selection bias, as there were more patients in the IDC group than in the non-IDC group (non-IDC vs. IDC; 20 vs. 119). Second, since all the patients were males over 50 years of age, there may be limitations in generalizing our findings to children and females. Third, the total number of patients included in this study was 139, which is a disadvantage in that the number of sample groups was small. However, as a prospective cohort study, our study had the advantage of high data reliability. To overcome these limitations, large-scale prospective studies on various diseases are required in the future.

In conclusion, our study results showed that MCC from urodynamics does not represent the true bladder capacity because of IDC. MVV is an accurate indicator of bladder capacity in BPH patients with IDC.

SUPPLEMENTARY MATERIAL

Supplementary Fig. 1 can be fonud via https://doi.org/10.5213/inj.2244158.079

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AUTHOR CONTRIBUTION STATEMENT

· Conceptualization: *SJO, JS, HJK*
· Data curation: *MHK, SJO*
· Formal analysis: *MHK, SJO*

· Funding acquisition: *SJO, JS, HJK*
· Methodology: *MHK, SJO, JS, HJK*
· Project administration: *SJO, JS*
· Visualization: *MHK*
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