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·Original Article·

Cross-sectional and longitudinal studies on interaction between bladder compliance and outflow obstruction in men with benign prostatic hyperplasia

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Abstract

Aim: To explore the interaction between bladder compliance (BC) and bladder outflow obstruction (BOO) in men with benign prostatic hyperplasia (BPH) using cross-sectional and longitudinal studies. **Methods:** A total of 181 men with BPH were recruited, and 100 of them were followed for one year. Cystometry was performed in a standing or a sitting position with 30 mL/min infusion. BC was manually corrected and defined. Obstruction coefficient (OCO), linear passive urethral resistance relation and international continence society (ICS) nomogram were used to diagnose BOO. The obstructed parameters were compared between the reduced BC group and the non-reduced group. BC was compared between the first investigation at the beginning of study and the second investigation at the end of study during the one-year follow-up period. **Results:** The group with reduced BC had increased OCO and linear passive urethral resistance relation. BC was significantly lower in the obstructed group (55.7 mL/cm water) than that in unobstructed and equivocal one (74.9 mL/cm water, $P < 0.01$). BC gradually reduced with the increased obstructed grade. There was a significantly weak negative correlation between BC and OCO ($r = -0.132$, $P < 0.01$). Over the one-year follow-up period in the longitudinal study, BC for all men changed from 54.4 to 48.8 mL/cm water ($P > 0.05$), and BC for the group with BOO fell from 58.4 ± 70.1 to 46.5 ± 38.7 mL/cm water ($P > 0.05$). **Conclusion:** In men with BPH, a significant systematic decrease occurred in BC in the obstructed group and a significant systematic increase with urethral resistance occurred in the low BC group. A longitudinal study of the tendency of BC reduction in a group with BOO is necessary in the future. *(Asian J Androl 2007 Jan; 9: 51–56)*

Keywords: benign prostatic hyperplasia; bladder compliance; bladder outflow obstruction

1 Introduction

According to the new definition from the International Continence Society (ICS), lower urinary tract symptoms (LUTS) are divided into three groups: storage, voiding and post-micturition symptoms. Storage symptoms include daytime frequency, nocturia, urgency and urinary incontinence. Voiding symptoms include slow stream, splitting or spraying of the urine stream, intermittent stream, hesitancy and straining [1]. Benign prostatic hyperplasia (BPH) is a disease that has its etiology

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in the abnormal growth of the adult human prostate gland that accompanies the aging process in men [2]. The presentation of LUTS suggestive of BPH, however, is related largely to degenerative changes in the bladder that occur as a result of the increasing urethral resistance and bladder outlet obstruction (BOO) caused by the growing prostate gland. Bladder dysfunction includes instability, impaired contractility and low bladder compliance (BC). These pathophysiologic elements are all common in elderly men, might be present alone or in all possible combinations, each giving rise to specific complaints [3–5]. Previous studies analyzed the roles of BOO, detrusor instability (DI) and impaired detrusor contractility (IDC) in LUTS. However, the change of BC in men with LUTS suggestive of BPH has not received much attention, especially the longitudinal change of BC in these patients [4–9]. Therefore, the present study aims to investigate the interaction of BC with urethral resistance and BOO in elderly men with LUTS using a cross-sectional study and longitudinal observation.

2 Materials and methods

A cross-sectional study including 181 men aged 43–86 years (mean: 65.3 years) with BPH was performed. Additionally, 100 of 181 men were followed up for 1 year. For each patient, cystometry was carried out in a standing or a sitting position with a 30-mL/min infusion rate using the Dantec Menuet urodynamic system (Dantec Company, Copenhagen, Denmark). Methods, definitions and units comforted to the standards proposed by the ICS, except where specifically noted. A total of 582 cystometric traces were reviewed and underwent quality control. The exclusive criteria for the traces included in the studies were that: (i) initial detrusor pressure (P_{det}) was negative; and (ii) the difference between initial P_{det} and P_{det} at filling end was zero. According to the criteria, a total of 571 traces entered into a cross-sectional study, and 170 traces from 85 men with nature history of LUTS participated in a longitudinal observation. For each trace, BC was manually corrected and defined (Figure 1). BC was calculated using the following method. The cystometric curve during filling consisted of two components of different steepness, and the flat part was considered to correspond to BC. Bladder capacity was defined as the volume at which the slope of the flat part of the cystometric curve (the tonus limb) crossed the slope of the ascending part of the curve (the terminal limb).

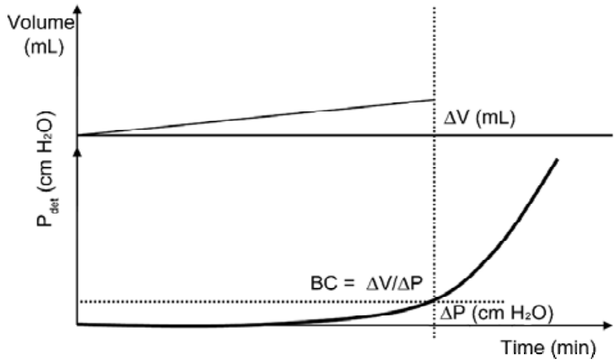

Figure 1. Diagram of definition and calculation for bladder compliance (BC) in cystometry.

The calculation of BC was made by dividing the bladder capacity by the change of pressure corresponding to this capacity (Figure 1). During filling, DI was recognized. In the presence of involuntary detrusor contractions, the point on the baseline of P_{det} tracing before contraction was used to calculate BC. Therefore, interferences of bladder overdistention and DI with compliance calculation were ruled out; and influence of bladder volume on compliance calculation was reduced.

Three methods were used to assess for BOO. The obstruction coefficient (OCO), developed by Schaefer *et al.* [11], was used to quantitatively evaluate urethral resistance, following the formula: $OCO = P_{det}.Q_{max}/(40 + 2Q_{max})$. Linear passive urethral resistance relation (L-PURR) according to Schaefer nomogram was used to grade BOO; and ICS nomogram was used to classify and diagnose BOO [11, 12].

In the cross-sectional study, the interaction between BC and BOO was explored in two ways. First, 40 mL/cm water was considered the normal value for BC [7], and the obstructed parameters in the reduced BC group were compared with those in the non-reduced group. Second, OCO = 1 was considered a cut-off value for distinguishing BOO, and BC of the low urethral resistance group was compared with that of the high resistance group. BC was compared in the classifications for BOO in the ICS nomogram and among the grades for BOO in the Schaefer nomogram. A correlation analysis between BC and OCO was performed.

In the one-year follow-up study, the natural history of BOO and BC was described, and the longitudinal change of BC was observed in the obstructed and the unobstructed groups as well as among the groups with the different L-PURR grades after one year. The changes of OCO and BC were assessed at intervals over the one-year follow-up period.

Statistical analyses were performed with the Wilcoxon rank sum test for the measurement data and the ranked data, and with the χ^2 test for the frequencies. Data was assessed by nonlinear regression with the Newton–Raphson test. The level of significance (two-tailed) was set at $P < 0.05$.

3 Results

According to our definition, the BC of 274 of 571 measurements (48%) fell, and the BC of 297 (52%) did not fall. The reduced BC group underwent increased OCO and L-PURR as well as more frequent obstruction in the ICS nomogram (Table 1). Of the 571 measurements, 426 (74.6%) were classified into the obstructed group, and 145 (25.4%) were classified into equivocal and unobstructed group. BC was significantly lower in the obstructed group (55.7 mL/cm water) than that in the others (74.9 mL/cm water, $P < 0.01$, Table 2). According to the Schaefer nomogram, the percentages of unobstructed (0–I), mild obstructed (II–III) and obstructed (IV–VI) were 5.4, 45.4 and 49.2%, respectively; the values of BC in these groups were 76.7, 70.7 and 51.7 mL/cm water, respectively. This suggests that BC gradually reduced with the increased obstructed grade (Table 2). The correlation analyses showed that there was a statistically significant weak negative correction between BC and OCO ($r = -0.132$, $P < 0.01$) or between BC and L-PURR ($r = -0.135$, $P < 0.01$).

In the group with BC < 40 mL/cm water, the percentages of DI were higher than that in group with BC ≥ 40 mL/cm water (Table 1). BC in the group with DI (40.1 ± 35.9 mL/cm water) was lower than that in the group with stable detrusor (71.3 ± 62.7 mL/cm water). This suggests that DI interfered with the assessment for BC. Furthermore, the association between BC and BOO in the group with stable detrusor was assessed. In 376 measurements with stable detrusor, 36.7% of traces showed BC < 40 mL/cm water, and 63.3% of traces showed BC ≥ 40 mL/cm water. The results also indicated that OCO, L-PURR and percentage of obstruction in the group with BC < 40 mL/cm water were significantly higher than those in the group with BC ≥ 40 mL/cm water (Table 3).

In the longitudinal study, a change of BC from 54.4 mL/cm water to 48.8 mL/cm water ($P > 0.05$, Table 4) was observed in 85 pairs of traces at the one-year follow-up. These pairs of traces were divided into an obstructed group and an unobstructed group: the BC of the obstructed group changed from 58.4 to 46.5 mL/cm water ($P > 0.05$, Table 4) whereas a significant increase in BC was observed in the unobstructed group ($P < 0.05$,

Table 1. Comparison of urethral resistance, obstructed grade and classification between BC < 40 mL/cm water group and BC ≥ 40 mL/cm water group (mean ± SD and number). BC, bladder compliance; BOO, bladder outlet obstruction; L-PURR, linear passive urethral resistance; OCO, obstruction coefficient.

	BC < 40 (*n* = 274)	BC ≥ 40 (*n* = 297)	*P*-value
BOO (*n*, %)	228 (83.2)	198 (66.7)	< 0.01
L-PURR	3.7 ± 1.2	3.2 ± 1.2	< 0.001
OCO	1.56 ± 0.72	1.31 ± 0.54	< 0.001
Unstable detrusor (*n*, %)	136 (49.6)	59 (19.9)	< 0.01

Table 2. Comparison of BC between obstructed and unobstructed groups and among different obstructed grades (mean ± SD). BC, bladder compliance; ICS, international continence society; L-PURR, linear passive urethral resistance; OCO, obstruction coefficient. [c]$P < 0.01$, compared with OCO < 1 group.

	n (%)	BC (mL/cm water)
OCO > 1	426 (74.6)	55.7 ± 53.1[c]
OCO < 1	145 (25.4)	74.9 ± 65.2
ICS nomogram		
Obstructed	426 (74.6)	55.7 ± 53.1
Equivocal	115 (20.1)	74.4 ± 68.2
Unobstructed	30 (5.3)	76.9 ± 53.0
L-PURR in Schaefer nomogram		
0–I	31 (5.4)	76.7 ± 45.1
II	95 (16.6)	70.0 ± 60.6
III	164 (28.7)	67.2 ± 62.1
IV–VI	281 (49.2)	51.7 ± 52.4

Table 3. The association between BC and BOO in stable detrusor group (mean ± SD and number). BC, bladder compliance; BOO, bladder outlet obstruction; L-PURR, linear passive urethral resistance; OCO, obstruction coefficient.

	BC < 40 mL/cm water (*n* = 138)	BC ≥ 40 mL/cm water (*n* = 238)	*P*-value
OCO	1.48 ± 0.55	1.27 ± 0.53	< 0.001
BOO (*n*, %)	114 (82.6)	152 (63.9)	< 0.01
L-PURR	3.68 ± 1.17	3.11 ± 1.23	< 0.001

Table 4. Longitudinal studies on BC change in the one-year follow-up period in 85 men with LUTS resulting from BPH (mean ± SD). BC, bladder compliance; L-PURR, linear passive urethral resistance. [b]$P < 0.05$, compared with the second BC.

	n	First BC (mL/cm water)	Second BC (mL/cm water)	*P*-value
Obstructed group	71	58.4 ± 70.1	46.5 ± 38.7	0.212
L-PURR grade:				
III	25	53.9 ± 37.3	53.2 ± 43.1	0.954
IV	24	45.2 ± 50.1	44.1 ± 43.9	0.933
V–VI	22	78.1 ± 106.7	41.6 ± 25.7	0.132
Unobstructed group	14	34.0 ± 24.7[b]	60.5 ± 39.0	0.043
Total	85	54.4 ± 65.3	48.8 ± 38.8	0.498

Table 4). After one year, the patients with BOO underwent a slight change in urethral resistance (ΔOCO = 0.01 ± 0.34), and a change of BC (ΔBC = –11.9 ± 76.5 mL/cm water). These results suggest that BC showed a possible tendency of reduction with the aggravation of BOO during the longitudinal one-year observation period.

4 Discussion

In the past, most urodynamic studies in men with LUTS as a result of BPH focused on identifying lower urinary tract dysfunction (LUTD), including BOO, DI, IDC and abnormal BC. BC is an important and sophisticated biomechanical parameter of the bladder during the filling phase. Although several studies on BC have been carried out in animal models of BOO [3, 13], the research in human is limited. BC is a parameter worthy of much attention in men with LUTS resulting from BPH. A few published papers have contributed to the discussion of the abnormality of BC to LUTS suggestive of BPH. Madersbacher *et al.* [8] presented a direct investigation into the interaction of BC with BOO in men with BPH. However, their study was cross-sectional without a longitudinal observation, and the interferences of DI and bladder overdistention as a result of a problematic BC calculation were not ruled out. Moreover, different filling rates from 30 to 50 mL/min were used in the study by Madersbacher *et al.* [8]. These factors can influence the accuracy of BC measurements. Both the 2001 publication [14] and the 2002 [15] publication from Boon's group only mentioned that a significantly low BC is an exceptional finding and, therefore, was not suited for a further analysis. Rule *et al.* [9] discussed a longitudinal decrease of BC after observing longitudinal changes of post-void residual and voided volume in men.

The purpose of the present study was to explore the interaction between BC and BOO in men with LUTS resulting from BPH by studying cross-sectional and longitudinal samples. To investigate the association between BC and BOO under clinical conditions, an exact calculation for BC and a precise assessment for urethral resistance were a prerequisite. BC was defined using the ICS as the change of volume per unit change of pressure during filling [1]. According to this definition, several factors, such as bladder volume or size, bladder shape, detrusor instability, bladder distention and bladder filling rate, could influence the determination of BC [14, 16]. In particular, different bladder sizes and shapes introduced considerable problems into the calculation of BC and the comparison in clinical research. In the present study, we could not normalize the bladder volume, and could not get rid of the impact of the bladder volume and shape on BC calculation under clinical conditions; but we could rule out some artifacts caused by DI, bladder overdistention and fast bladder filling using the appropriate definition for the filling-end point and a fixed low filling rate. In the present study, continuous quantitative and semi-quantitative indexes as well as a nomogram were used to assess urethral resistance and BOO, respectively.

The cross-sectional study demonstrated that there was a statistically significant weak negative correlation between urethral resistance (OCO) and BC. There was a high urethral resistance or more obstruction in the group with low BC, and there was a low BC in the group with high urethral resistance. This suggests that BC showed a systematic reduction with the increase of urethral resistance or obstruction.

The present study was descriptive and observational in nature. The longitudinal study indicated that BC had a possible tendency of reduction with the aggravation of BOO and the development of LUTS resulting from BPH in the one-year follow-up. This suggested that BOO contributed to the development of decreased BC. Slight changes of urethral resistance and BC suggest that the development of BOO and the alterations of BC in human beings is a slow and long progressive process. The longitudinal changes of obstruction and BC in the one-year follow-up period were not statistically significant; therefore, a longer follow-up period is encouraged in further studies. There were major differences [3, 13] between the clinical studies in human beings and those in animal experiments. A longer longitudinal observation on the interaction between BC and BOO is necessary in the future [17].

Obstructed bladder dysfunction secondary to BPH is a slow, progressive disease that is strongly associated with human aging. However, there are some age-dependent alterations in detrusor function. The pathophysiologic changes in aging detrusor include DI, IDC, detrusor hyperactivity with impaired contractility in older men and women [18, 19], and reduced BC in rats [20]. In the present study, after 1 year BC in the non-obstructed group increased and was higher than that in the obstructed group. A possible explanation could be that the aging detrusor underwent an aging-related change including increased BC or IDC in human beings, but not in rats. Therefore, the complications of interactions among aging detrusor, BOO and BC made it difficult to assess the change of BC in men with LUTS resulting from BPH. In future longitudinal research, multivariate analysis should be performed for the assessment of the impact of age to clarify the contribution of each factor to BC in patients with LUTS.

Although some studies suggest that low BC after obstruction is the result of the change in the passive properties of the bladder wall rather than the active ones [4], several clinical and animal studies show that the active properties of the bladder wall related to the neuromuscular aspect are involved in the change of BC after obstruction [16]. Animal and clinical studies demonstrate that overdistention and increased wall tension of the bladder caused by BOO could result in nerve degeneration with the supersensitivity of the detrusor to acetylcholine. This denervation supersensitivity could cause DI. Our results are in accord with those of published papers, suggesting that BC was lower in the group with an unstable detrusor than in the group with a stable detrusor. However, Yokoyama *et al.* [16] found that BC increased after prostatic urethral anesthesia. This finding suggests that easy irritability of the anatomically altered prostatic urethra is considered an important factor affecting BC through the spinal reflex arc. The above-mentioned evidence suggests that neuromuscular aspects play an important role in the development of low BC after obstruction.

Even through a systematic reduction of BC in the obstructed group and a possible tendency of BC reduction with the aggravation of obstruction, the reverse change in individuals was possible as a result of the complex alterations of detrusor in structure and function after obstruction. In particular, a patient with LUTS resulting from BPH could undergo a long interval from occurrence of obstruction to the development of LUTS. During this one-year interval, there were many factors that could affect the changes of BC. Some of them had been studied, but others had not been researched well, for example, aging-related alterations in detrusor and the compensation of detrusor function. At present, the studies focused on interactions among BOO, BC and aging detrusor and on the changes of BC and the mechanism of changes after obstruction in elderly men with LUTS resulting BPH are still lacking. A clinical longitudinal long-term study on the age-dependent changes of BC is necessary.

In conclusion, in a cross-sectional study, a statistically significant weak negative correction between BC and urethral resistance was demonstrated. A statistically significant systematic reduction of BC in the obstructed group, a statistically significant systematic increase of urethral resistance in the low BC group, and a statistically significant weak negative correction between BC and urethral resistance were observed. In a longitudinal study, a possible tendency of BC reduction with the aggravation of BOO was observed in one-year follow-up period. A statistically significant increase of BC in the non-obstructed group was shown one-year follow-up period. We conclude that BOO contributes to the development of decreased BC but aging can impact on detrusor function, and there are complex interactions among BC, BOO and aging detrusor in elderly men with LUTS resulting from BPH.

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