

Detrusor contraction power parameters (BCI and W_{\max}) rise with increasing bladder outlet obstruction grade in men with lower urinary tract symptoms: results from a urodynamic database analysis

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Received: 15 December 2013 / Accepted: 27 June 2014 / Published online: 10 July 2014
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Abstract

Purpose To investigate to what extent detrusor work during voiding is influenced by bladder outlet obstruction (BOO) in adult men with lower urinary tract symptoms (LUTS).

Materials and methods We reviewed data of patients with LUTS suggestive of benign prostatic hyperplasia who received computer-urodynamic investigations as part of their baseline clinical assessment. BOO was defined by the Schäfer classification and detrusor work during voiding was quantified by calculation of the bladder contractility index (BCI) and maximum Watt factor (W_{\max}) obtained by pressure-flow analysis.

Results A total of 786 men with medians of 64 years, IPSS 16 and prostate volume of 35 ml, were included in the study. A total of 462 patients (58.8 %) had BOO (Schäfer 2–6). Both detrusor contraction power parameters continuously increased with rising BOO grade. Median BCI increased from 73.3 in Schäfer 0 to 188.0 in Schäfer 6, whereas W_{\max} increased from 9.6 to 23.4 W/m² ($p < 0.001$). Results of BCI and W_{\max} correlated well ($p < 0.001$). With

increasing BOO grade, there was a significant decrease of voiding efficiency ($p < 0.001$).

Conclusions In adult male LUTS patients, detrusor contraction power parameters—BCI and W_{\max} —continuously increase with rising BOO grade. According to our results, it is impossible to determine a single threshold value for detrusor contraction power to diagnose detrusor underactivity in a group of LUTS patients with different BOO grades. The study is limited to men with non-neurogenic LUTS. Future studies should evaluate exact threshold values for BCI and W_{\max} in BOO subgroups to adequately define detrusor underactivity and investigate men with other bladder conditions.

Keywords Detrusor underactivity · Detrusor contractility · Bladder outlet obstruction · Lower urinary tract symptoms · Men · Urodynamics · Pathophysiology

Introduction

Voiding dysfunction in humans and animals may be caused by bladder outlet obstruction (BOO), detrusor underactivity (DU), dysfunctional voiding, or a combination of these conditions [1]. In experimental animals with BOO, bladder wall (smooth muscle cell) hypertrophy and increase of detrusor contraction power develop quickly after partial ligation of the urethra resulting in complete bladder emptying in the initial and compensated stages despite the presence of BOO [2, 3]. Bladder wall hypertrophy, diagnosed by ultrasound measurement of bladder or detrusor wall thickness, has been confirmed in adult men with BOO [4, 5]. It has been hypothesized that an increase of bladder/detrusor wall thickness (contractile elements) is responsible for increased detrusor contraction power in these men to

On behalf of the FORCE Research Group, Maastricht and Hannover.

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maintain voiding in the presence of BOO, similar to animal studies [5, 6].

In symptomatic men aged ≥ 50 , pressure-flow studies demonstrate BOO in approximately 60 % [7, 8], whereas DU, alone or in combination with BOO, is detected in up to 40 % [9]. With aging, voided volume and maximum urinary flow rate (Q_{\max}) continuously decrease and post-void residual (PVR) increases [10, 11]. The prevalence of BOO appears to be rather constant over different age groups [8, 10], while DU increases with aging [10] and approximately two-thirds of incontinent institutionalized elderly are affected [12]. Due to an increasing life expectancy of the Western societies, an increasing amount of patients with voiding dysfunction and especially DU are expected. Therefore, it appears important to adequately diagnose and differentiate the different types of bladder dysfunctions and to understand the relationship between BOO and DU.

Determination and quantification of BOO, DU, or dysfunctional voiding are currently only possible with pressure-flow analysis. Quantification of urethral resistance and determination of BOO are well established by using data derived from the pressure-flow plot and utilizing this information in a nomogram (e.g., ICS [13] or Schäfer nomogram [14]). In contrast, quantification of detrusor work during voiding is less verified [15]. The Watt factor [16], detrusor-adjusted mean PURR factor (DAMPF) [15, 17], and bladder contractility index (BCI) [18], a numerical expression of categorical DAMPF, have been suggested for quantifying detrusor contraction power [15]. It remains controversial which algorithm and threshold value should be used for the diagnosis of DU. Urodynamic experts have proposed a maximum Watt factor (W_{\max}) ≤ 7 – 10 W/m² or BCI < 100 [15, 18, 19] for the diagnosis of DU, but these threshold values have never been thoroughly investigated. Therefore, the aim of our study was to (1) evaluate the relationship between BOO and W_{\max} or BCI in a large sample of unselected men with LUTS, (2) compare these results with published data obtained from experimental animals, and (3) propose threshold values of W_{\max} and BCI for the diagnosis of DU.

Materials and methods

Patient selection

Unselected, treatment naïve men aged ≥ 40 with uncomplicated lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) who were evaluated in the Department of Urology of the Hannover Medical School in Germany between April 1993 and November 2003 were included in this study. In contrast,

men with upper or lower urinary tract complications suspicious of BOO (e.g., bladder stones, bladder diverticula, or urinary retention), men with LUTS after lower urinary tract or pelvic surgery, radiotherapy, neurological diseases, urinary tract infection, bladder cancer, urethral strictures, prostate cancer (PSA > 10 $\mu\text{g/l}$ or positive biopsies in cases of a PSA concentration between 4 and 10 $\mu\text{g/l}$ or palpable tumor), prostatitis, or distal ureteral stones were excluded from analysis. Furthermore, all men with drugs (α -blockers or antimuscarinics within the last 4 weeks or 5 α -reductase inhibitors within the last 6 months before urodynamic investigation) were also eliminated from the analyses.

Patient assessment

At the initial patient visit, a general and LUTS history as well as a blood sample for the measurement of PSA were taken, physical examination (including digito-rectal evaluation of the prostate) and ultrasound investigation of the kidneys, bladder and prostate were performed, the International Prostate Symptoms Score (IPSS) was completed (after 1995), and free uroflowmetry with a voided volume of at least 125 ml was carried out. Immediately afterward, measurement of PVR was taken using a 3.5 MHz ultrasound array.

One to three weeks after initial presentation, patients returned to the hospital, repeated uroflowmetry, and then underwent urodynamics. PVR was measured by bladder catheterization before the start of the first measurement. Computer-urodynamic investigation was performed by experienced investigators in line with the ICS-Good Urodynamic Practices standards [20]. A transurethral 6-F double-lumen catheter was placed in the bladder to measure the intravesical pressure and fill the bladder and a 10-F single-lumen catheter was inserted into the rectum to measure the intraabdominal pressure. During cystometry, the patient was positioned in the convenient sitting position and the bladder was filled with sterile physiological saline solution of 37 °C with a speed between 25 and 50 ml/min until the patient felt a strong desire to void. Afterward, the patient voided—according to his normal habit—in the sitting or standing position and pressure-flow measurement was taken. Cystometry and pressure-flow analysis were performed at least in duplicate.

Parameters for analyses

The free uroflowmetry measurement—after manual artifact correction—with the highest value for maximum urinary flow rate (Q_{\max}) was selected for analysis. The lowest amount of PVR determined by either ultrasound or catheterization was utilized. Voiding efficiency was calculated

by using the selected free uroflowmetry recording and applying the formula:

$$\text{Voiding efficiency} = (\text{voided volume}/(\text{voided volume} + \text{post-void residual})) \times 100 (\%)$$

As cystometry and pressure-flow recordings were carried out at least twice during one session, the recording with the lowest BOO grade was used for further analyses. Patients were divided into groups based on the Schäfer nomogram [14]. Accordingly, Schäfer grades 0 + 1 resemble unobstructed bladders, Schäfer grade 2 equivocal BOO, and Schäfer grades 3–6 different BOO grades, ranging from minor to severe. Patients with equivocal BOO were positioned in the BOO group because earlier results with ultrasound detrusor wall thickness measurements suggested that these patients have a significantly thicker detrusor compared to patients without BOO or healthy adult volunteers [5, 6].

Detrusor contraction power was determined and quantified by calculation of the bladder contractility index (BCI) by using the formula [18]:

$$\text{BCI} = P_{\text{detqmax}} + 5Q_{\text{max}}$$

(P_{detqmax} = detrusor pressure at maximum urinary flow rate; Q_{max} = maximum urinary flow rate) and maximum Watt factor (W_{max}) provided by the urodynamic machine was calculated, after elimination of measurement artifacts, on the basis of the formula [16]:

$$W = (P_{\text{det}} \cdot V_{\text{det}} + a \cdot V_{\text{det}} + b \cdot P_{\text{det}})/2\pi$$

$$[V_{\text{det}} = Q/2(3/(4\pi) \cdot (V_{\text{ves}} + V_{\text{t}}))^{-2/3}]$$

(W = detrusor contraction power; P_{det} = detrusor pressure; V_{det} = contraction speed; V = total bladder volume) Because both detrusor contraction power parameters (BCI and W_{max}) have not been thoroughly investigated or compared with each other, we used them as independent parameters without preference.

Statistical analyses

Median values and their 25 and 75 percentiles were calculated for patients' baseline and measurement parameters. Two measurement values were statistically compared by using the Mann–Whitney U test, and more than two measurement values were statistically compared by applying the Kruskal–Wallis test. For correlation analysis, Spearman's correlation coefficient was used. A p value ≤ 0.05 was considered significant. The Statistical Package for the Social Sciences (SPSS), version 18 (SPSS Inc, Chicago, IL, USA) was used to perform all statistical analyses.

Results

Patient characteristics

A total of 786 patients met the inclusion criteria and were evaluated. Median age of the patients was 64 years, median prostate volume 35 ml, and median IPSS 16. Based on the results of pressure-flow analysis, 324 men (41.2 %) had no signs of BOO (Schäfer 0 + 1), whereas 462 patients (58.8 %) had a variable degree of BOO (Schäfer 2–6). The patient characteristics and measurement results for all participants are shown in Table 1.

Differences between parameters in relation to BOO grades

Patient parameters and the statistical comparison of measurement values of patients with different BOO grades (Schäfer 0–6) are also presented in Table 1. BOO grades were unevenly distributed within the study population; either the absence of BOO or mild BOO was seen in a larger amount of patients than moderate or severe BOO. There was no statistical difference with regard to IPSS between the groups ($p = 0.059$). However, significant differences in age and prostate volume (both $p < 0.001$) were found when comparing different BOO grades.

We saw a continuous and significant decrease with increasing BOO grade when evaluating Q_{max} of free uroflowmetry ($p < 0.001$), voided volume of free uroflowmetry ($p < 0.001$), voiding efficiency ($p < 0.001$), and bladder capacity measured during cystometry ($p < 0.001$). In contrast, we observed a continuous and significant increase with rising BOO grade when evaluating PVR ($p = 0.011$), the presence of detrusor overactivity ($p < 0.001$), BCI ($p < 0.001$), and W_{max} ($p < 0.001$).

Detrusor contraction power parameters in relation to different BOO grades

Both detrusor contraction power parameters, BCI and W_{max} , showed a similar pattern characterized by a stepwise increase with rising BOO grade (Table 1; Fig. 1). Median BCI values ranged from 73.3 in Schäfer 0 to 188.0 in Schäfer 6, whereas W_{max} values increased from 9.6 W/m² in Schäfer 0 to 23.4 W/m² in Schäfer 6. All median BCI values for patients with Schäfer grades 0–2 were < 100 , whereas median $W_{\text{max}} < 7$ W/m² was not seen in any BOO grade.

The Kruskal–Wallis test showed significant differences of median BCI ($p < 0.001$) and W_{max} values ($p < 0.001$) within the entire group of patients. There was also a significant difference in median BCI or W_{max} values when patients without BOO (Schäfer 0 + 1) were compared with those having BOO in pressure-flow analysis (Schäfer

Table 1 Patient's characteristics and measurement results for all patients and for the individual BOO (Schäfer) classes; variables are presented as medians and 25–75 percentiles, unless otherwise indicated

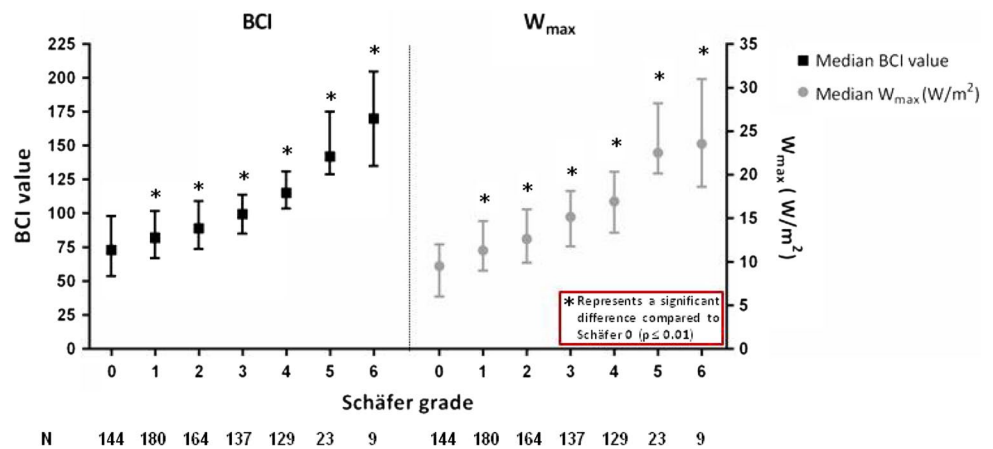
	Schäfer grade						<i>p</i> value*
	0 (<i>n</i> = 144)	1 (<i>n</i> = 180)	2 (<i>n</i> = 164)	3 (<i>n</i> = 137)	4 (<i>n</i> = 129)	5 (<i>n</i> = 23)	
All patients							
Age (years)	64 (57–69)	61 (56–67)	62 (56–69)	66 (60–71)	64 (58–69)	66 (62–72)	67 (63–75)
IPSS	16 (10–21)	15 (10–20)	15 (10–21)	16 (12–21)	18 (12–23)	17 (11–19)	23 (18–23)
Prostate volume (ml)	35 (26–48)	30 (24–40)	35 (25–46)	40 (30–57)	40 (31–52)	49 (36–71)	35 (20–45)
Free uroflowmetry							
Q_{\max} (ml/s)	10.8 (7.5–15.0)	13.5 (9.8–18.0)	10.7 (7.6–14.2)	9.7 (7.1–12.9)	8.2 (5.8–11.0)	7.0 (4.8–10.1)	8.7 (5.1–12.1)
Voided volume (ml)	228 (166–334)	287 (208–374)	242 (170–336)	197 (157–277)	192 (147–277)	146 (121–201)	211 (148–277)
PVR (ml)	65 (23–145)	50 (11–142)	58 (20–124)	70 (40–150)	80 (36–149)	60 (20–150)	101 (91–399)
Voiding efficiency (%)	79.3 (60.1–91.4)	86.9 (67.5–96.4)	79.4 (61.8–91.8)	77.3 (60.7–87.8)	73.7 (54.1–85.7)	65.1 (52.0–85.8)	58.5 (37.3–76.1)
Urodynamic investigation							
Bladder capacity (ml)	392 (286–542)	436 (330–592)	402 (285–556)	336 (275–446)	348 (246–460)	299 (220–406)	271 (155–451)
BOOI	35.0 (18.2–55.1)	20 (14–25)	37 (30–42)	51 (47–57)	75 (67–84)	102 (97–111)	149 (128–168)
Bladder contractility index	94.0 (74.1–114.2)	82 (67–102)	89 (74–109)	100 (85–114)	115 (103–131)	142 (129–175)	188 (157–201)
W_{\max} (W/m ²)	12.9 (9.8–17.2)	11.4 (9.0–14.7)	12.6 (9.9–16.0)	15.2 (11.8–18.1)	16.9 (13.3–20.3)	22.5 (20.1–28.2)	23.4 (16.1–29.5)

The *p* value refers to the Kruskal–Wallis test comparing patient parameters in the different Schäfer classes

IPSS international prostate symptom score, Q_{\max} maximum urinary flow rate, PVR post-void residual, BOOI bladder outlet obstruction index, W_{\max} maximum Watt factor

* Kruskal–Wallis test

Fig. 1 Bladder contractility index (BCI) and maximum Watt factor (W_{\max}) in relation to BOO (Schäfer) grades; variables are presented as median and 25–75 percentiles. Asterisk represents a significant difference compared to Schäfer 0 (Mann–Whitney U test; each $p < 0.01$). BCI Bladder Contractility Index, W_{\max} maximum Watt factor



2–6; $p < 0.001$). Moreover, median BCI or W_{\max} of Schäfer grade 0 was significantly lower compared to the median BCI or W_{\max} values of the other Schäfer grades (each $p < 0.01$; Fig. 1). Spearman's correlation showed a significant, moderate to strong correlation coefficient between both detrusor contraction power parameters (R^2 of 0.570; $p < 0.001$).

Discussion

Our study shows for the first time in patients with LUTS suggestive of BPH that the commonly used detrusor contraction power parameters BCI and W_{\max} continuously and significantly increase with rising BOO grade indicating that threshold values for the determination of DU have to be defined separately for the different BOO grades. Therefore, the commonly used threshold values for the definition of DU (BCI < 100 or $W_{\max} < 7$ W/m²) should be reconsidered. Moreover, our study demonstrates a continuous and significant decrease of voiding efficiency in men with increasing BOO grade and, for the first time as well, a significant correlation between BCI and W_{\max} .

Our results in a large group of unselected men, who were evaluated for LUTS suggestive of BPH during a 10-year period in one hospital with almost identical characteristics compared to those analyzed for health seeking behavior in Europe [21], show a strong correlation between BCI and W_{\max} and also a strong correlation between BOO and the two detrusor contraction power parameters. According to the literature, a BCI value < 100 indicates DU ('hypocontractility') in men [18], but this threshold value has never been validated and could refer to patients with BOO only. In order to make a comparison with our data, it would be useful to learn how the BCI threshold value of < 100 was determined in the original publication. Of particular interest would be to know whether this BCI threshold value was based on theoretical considerations or measurement

data. The same question accounts for the definition of the threshold value of W_{\max} [16]. Consequently, studies using a BCI (W_{\max}) threshold < 100 (< 7 W/m²) to define DU have to be used with caution, especially when applied for men or women without BOO [9]. If the BCI threshold value < 100 would be applied to our patient population, almost all men with Schäfer grades 0–2 and the majority of patients with Schäfer grade 3 would have been judged with the diagnosis of DU (Table 1; Fig. 1). Vice versa, all investigated men of our study population with Schäfer grades 4–6 have a BCI > 100 , and therefore, no patient would have had DU; these two considerations may be possible but seem unlikely.

Our study was able to confirm results obtained in experimental animals with artificial BOO; these studies showed a significant increase of detrusor contraction power and bladder weight during the initial and compensated stages during which bladder emptying remains complete [2]. Microscopic investigations of the bladder wall in these two stages revealed—besides fibroblast hyperplasia and deposition of collagen fibers—smooth muscle cell hypertrophy. Animal studies suggest that bladder emptying in the presence of BOO persists due to increasing detrusor contraction power as a result of structural changes of the bladder wall [2, 22]. Additionally, the results of our present study are in line with conclusions from previous studies showing a significant increase of bladder/detrusor wall thickness in symptomatic male patients with BOO [4, 5]; therefore, increased detrusor contraction power in patients seems to be generated by increased mass of smooth muscle cells of the bladder wall (detrusor) as well.

Our study is limited to the analysis of patients with compensated bladders, and hence, we cannot provide information about detrusor contraction power parameters in patients with decompensated bladders or urinary retention. Regardless of this selection bias, patients with increasing BOO grade show a continuous decrease of voiding efficiency which could be caused by BOO and/or DU and may

be the first sign of bladder decompensation. Therefore, it remains to be determined whether decreasing voiding efficiency will result in bladder decompensation and urinary retention, without necessarily having increased PVR values before.

Because the calculations of BCI and W_{\max} are partially dependent on Q_{\max} and abdominal straining during voiding would result in artificially increased BCI or W_{\max} values, it is possible that we have calculated too high median values in our sample of patients. Therefore, we have to exclude abdominal straining during voiding by asking patients not to strain during pressure-flow recordings. If straining was still present, manual correction of the pressure-flow plot should be done to determine the precise threshold values for DU of each BOO group in the future. However, the basic principle of increasing BCI or W_{\max} with rising Schäfer grade remains unaffected by potential straining during voiding because straining is likely to appear with similar frequency in all BOO groups. Additionally, it remains to be determined whether our results are only valid for maximum detrusor contraction power or also true for detrusor contraction duration, another component of DU [2, 17].

Future (longitudinal) studies should validate our results in an independent group of patients, compare our results with asymptomatic healthy men, determine—after correction for abdominal straining—the exact threshold values for the diagnosis of DU of different BOO grades, reproduce our results in women, evaluate whether differences exist for detrusor contraction duration, and correlate detrusor contraction power parameters with other (non-invasive) measurement data (e.g., detrusor wall thickness).

Conclusions

In patients with LUTS suggestive of BPH, both commonly used detrusor contraction power parameters—BCI and W_{\max} —continuously and significantly rise with increasing BOO grade. We could, for the first time, confirm data obtained from animal studies. According to our results, it is impossible to determine a single threshold value for BCI or W_{\max} for diagnosing DU in a group of patients with different BOO grades; therefore, future studies have to evaluate individual threshold values for BCI or W_{\max} for each BOO subgroup to adequately define DU.

Acknowledgments This study was supported by the Astellas European Foundation Grant 2012.

Conflict of interest M. Oelke and G. A. van Koevinge are consultants, speakers and trial participants of Astellas and have been rewarded with the Astellas European Foundation Grant in 2012. K.

L. J. Rademakers is employed from money provided by the Astellas European Foundation Grant.

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