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Voiding Dysfunction

Transitional Zone Index and Intravesical Prostatic Protrusion in Benign Prostatic Hyperplasia Patients: Correlations according to Treatment Received and Other Clinical Data

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Purpose: The aim of this research was to assess the value of the transitional zone index (TZI) and intravesical prostatic protrusion (IPP) from transrectal ultrasonography in evaluating the severity and progression of disease by analyzing the relationship between the 2 parameters and symptoms, clinical history, and urodynamics in benign prostatic hyperplasia (BPH) patients undergoing different treatment.

Materials and Methods: A total of 203 patients receiving medication and 162 patients who underwent transurethral resection of the prostate because of BPH were enrolled in this retrospective analysis. The clinical history and subjective and objective examination results of all patients were recorded and compared after being classified by TZI and IPP level. Linear regression was used to find correlations between IPP, TZI, and urodynamics.

Results: The 2 parameters were found to differ significantly between patients receiving medication and patients undergoing surgical therapy ($p < 0.05$). PSA, maximum flow rate (Qmax), detrusor pressure at Qmax (PdetQmax), and the bladder outlet obstruction index (BOOI) differed according to various TZI levels ($p < 0.05$). In addition, the voiding symptom score, Qmax, and BOOI of subgroups with various IPP levels were also significantly different ($p < 0.05$). Both TZI and IPP had significant effects on Qmax, BOOI, and PdetQmax ($p < 0.05$) and the incidence of acute urinary retention ($p=0.000$).

Conclusions: The results demonstrated that both TZI and IPP had favorable value for assessing severity and progression in patients with BPH. Further studies are needed to confirm whether the two parameters have predictive value in the efficacy of BPH treatment and could be considered as factors in the selection of therapy.

Key Words: *Benign prostatic hyperplasia; Medication; Transurethral resection of the prostate; Ultrasonography; Urodynamics*

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INTRODUCTION

Benign prostatic hyperplasia (BPH) is found in over half of 60-year-old men and in almost all 80-year-old men who develop bladder outlet obstruction (BOO) and lower urinary tract symptoms (LUTS) [1]. BOO is the initial pathophysiological change caused by an enlarged adenoma and is followed by detrusor overactivity (DO) or underactivity (DUA). The degree of BOO is an important factor that can reflect the severity of disease and that can aid in choosing a treatment method as well as in measuring the outcome of the treatment. It has been shown that one third of male patients with LUTS do not have definite BOO and that 5 to 35% of the patients with LUTS and undefined BOO do not have favorable symptom recovery after transurethral resection of the prostate (TURP) [2-7]. Relevant examinations ranging from serum prostate-specific antigen (PSA) to urodynamics can all reflect different aspects of the se-

verity of BPH. Urodynamics is the only method, however, that can quantify the degree of BOO and the status of detrusor contractility. Therefore, guidelines from the International Scientific Committee and the American Urological Association on the management of BPH both recommend the use of urodynamics to evaluate BPH patients considered as candidates for invasive therapy [8]. However, the routine use of preoperative urodynamics is still a controversial point in published articles because of the invasiveness and high costs of the method [9]. In this research, we attempted to determine whether other parameters could be used to measure the severity of BOO through less-invasive or noninvasive examinations by analyzing correlations among parameters from clinical history, symptoms, ultrasonography, and urodynamics.

MATERIALS AND METHODS

This retrospective analysis was conducted on patients with BPH who had received either medication or surgical treatment at this hospital between May 2010 and June 2011. The therapeutic decision for TURP was based on both clinical assessment and the patient's desire. All patients were evaluated with the International Prostate Symptom Score (IPSS, including the total score; subtotal score of storage symptoms comprising the summation of nocturia, urgency, and an increased frequency score; and subtotal score of voiding symptoms comprising the summation of hesitancy, intermittency, and weak stream score) and quality of life (QoL) questionnaires in addition to undergoing basic clinical evaluations (medical history, physical examination, urinalysis, and renal function assessment) before treatment. Free flowmetry measurement was performed for all patients with the result being adopted when the voiding volume was more than 150 ml. Urodynamics was performed only for patients needing surgery by use of a multichannel system (UDS64-III, Laborie Co., Quebec, Canada). First, water-Filling cystometry was done with the patients in the supine position with the use of a transurethral 12 Fr double-lumen catheter and the simultaneous monitoring of rectal pressure. Filling was performed at a rate of 50 ml/min with normal saline and was stopped if the patient had a strong desire to void. Pressure flow study (PFS) was then performed by asking the patients to void in an upright position with a suprapubically placed 6 Fr cystostomy tube to monitor the bladder pressure. Maximum urinary flow (Qmax) and pressure of the detrusor at Qmax (PdetQmax) were recorded. The bladder outlet obstruction index (BOOI, by "PdetQmax-2Qmax") and the bladder contractility index (by "PdetQmax+5Qmax") were then calculated by use of equations from the ICS [10]. Total prostate volume (TPV), transitional zone volume (TZV), intravesical prostatic protrusion (IPP), and post-voiding residual (PVR) were measured by transrectal ultrasonography (TRUS) with the transitional zone index (TZI, by "TZV/TPV") being calculated for all patients. The exclusion criteria for enrolled subjects were 1) BOOI less than 20 or Qmax more than 20 ml/s, 2) disease with BOO other than BPH, 3) history of prostatic or urethral surgery, 4) diagnosed carcinoma of the prostate or bladder, 5) known bladder stones or neurogenic bladder dysfunction, and 6) not having taken standard medication involving both alpha-adrenergic blockers and 5-alpha-reductase inhibitors for over 6 months.

The relevant clinical data of the subjects were recorded and classified by degree of IPP (<10 mm, 10 to 20 mm, and >20 mm) and TZI value (<0.5, 0.5 to 0.7, and >0.7). All quantitative variables were tested for the type of distribution by use of the one-sample Kolmogorov-Smirnov test. Univariate analyses including one-way analysis of variance and Kruskal-Wallis test were used for variables with normal or skewed distributions, respectively, to assess the differences between patients receiving drug therapy and those undergoing surgical therapy and between patients with different degrees of IPP and TZI values. The χ^2-test was used for categorical variables to identify whether there were different incidences of acute urinary retention (AUR) influenced by different IPP or TZI grade. Finally, bivariate correlation and multiple regression analysis were used to assess correlations between parameters from TRUS and PFS. All analyses were performed by using the routines of the IBM SPSS ver. 19.0 (IBM Co., New York, NY, USA), and statistical significance was defined as a p-value less than 0.05. The research attained ethical approval from the ethics committee of Xin Hua Hospital, and all subjects gave written informed consent.

RESULTS

A total of 365 patients were enrolled in the research study, with 203 patients receiving medication and the remainder having undergone TURP. The clinical data of all subjects were classified according to therapy and degree of IPP and TZI and are listed in Tables 1 and 2. Univariate analyses showed significant differences in the total, storage, and voiding scores of the IPSS; QoL score; TPV; TZV; TZI; IPP; and Qmax between the therapy groups ($p<0.05$). Baseline total prostate-specific antigen, TPV, TZV, IPP, Qmax, PdetQmax, and BOOI classified by different degrees of TZI were also found to be significantly different ($p<0.05$). Differences were also found in the voiding symptom score, TPV, TZV, TZI, Qmax, and BOOI classified by degree of IPP ($p<0.05$). IPP (p=0.000) and TZI (p=0.000) both had statistically significant effects on the cause of AUR (Table 2) by χ^2-test. The bivariate correlation analysis of parameters from symptom score, TRUS, and urodynamics showed significant correlations between TZI and Qmax (r=-0.887, p=0.001), PdetQmax (r=0.725, p=0.028), and BOOI (r=0.508, p=0.029) and between IPP and voiding symptom score (r=0.353, p=0.033), Qmax (r=-0.852, p=0.014), and BOOI (r=0.469, p=0.042). Multiple regression analysis in the subjects who underwent TURP showed that both TZI and IPP had significant correlations with Qmax and BOOI, whereas TZI had a significant correlation with PdetQmax

TABLE 1. Comparisons of baseline characteristics in patients between different methods of therapy

Characteristic	Overall (n=365)	Medication (n=203)	Surgery (n=162)	p-value
Age (yr)	66.8±9.4	63.7±5.8	73.3±4.2	0.066[a]
T-PSA (ng/ml)	5.1 (0.32-23.9)	4.0 (0.32-9.8)	5.3 (1.4-18.7)	0.146[b]
Total IPSS	12.2±7.1	9.3±5.5	18.6±4.1	0.021[a]
Storage IPSS	6.9±3.3	6.5±3.4	7.2±7.0	0.053[a]
Voiding IPSS	5.8±3.9	3.0±1.8	8.1±4.2	0.007[a]
QOL score	3.6±2.6	2.5±1.2	4.1±8.4	0.029[a]
TPV (g)	43.0±11.7	36.8±14.5	50.6±27.3	0.012[a]
TZV (g)	26.6±19.0	21.5±18.2	35.4±22.7	0.008[a]
TZI	0.51±0.8	0.33±0.2	0.62±0.4	0.005[a]
IPP (mm)	14.6±8.3	11.2±5.9	17.1±12.0	0.011[a]
PVR (ml)	56.5±40.8	30.2±21.7	81.0±54.4	0.000[a]
Qmax (ml/s)	10.1±4.8	12.4±6.9	6.9±3.0	0.027[a]
PdetQmax (cm H2O)	73.0±40.9	69.4±27.8	83.2±35.5	0.011[a]
BOOI	53.5±28.2	43.1±18.4	78.7±36.3	0.024[a]
BCI	120.1±36.6	118.4±23.9	126.2±25.0	0.070[a]
Presence of AUR history	65 (17.8)	21 (10.3)	44 (27.2)	0.000[c]

Values are presented as mean±SD, median (range) or number (%).
T-PSA, total prostate-specific antigen; IPSS, International Prostate Symptom Score; QOL, quality of life; TPV, total prostate volume; TZV, transitional zone volume; TZI, transitional zone index; IPP, intravesical prostatic protrusion; PRV, postvoiding residual volume; Qmax, maximum urinary flow; PdetQmax, pressure of detrusor at Qmax; BOOI, bladder outlet obstruction index; BCI, bladder contractility index; AUR, acute urinary retention.
[a]: Student's t-test, [b]: Mann-Whitney U test, [c]: Fisher's exact test.

TABLE 2. Comparisons of baseline characteristics in patients according to TZI and IPP

Characteristic	TZI				IPP			
All patients	<0.5 (n=133)	0.5-0.7 (n=108)	>0.7 (n=124)	p-value	<10 mm (n=110)	10-20 mm (n=157)	>20 mm (n=98)	p-value
Age (yr)	61.3±7.1	63.0±9.27	64.00±8.32	0.291[a]	58.6±6.3	63.6±4.9	61.2±7.9	0.240[a]
T-PSA (ng/ml)	3.5 (0.3-13.3)	4.3 (2.0-23.9)	7.4 (6.1-14.1)	0.048[b]	4.4 (0.3-17.1)	3.1 (0.8-10.3)	5.9 (4.8-23.9)	0.072[b]
Total IPSS	11.6±5.9	10.8±8.2	14.2±7.5	0.158[a]	12.1±7.3	15.9±6.5	14.8±9.0	0.103[a]
Storage IPSS	6.4±3.7	6.1±4.0	7.2±4.62	0.084[a]	5.1±2.2	7.0±4.4	6.8±3.1	0.119[a]
Voiding IPSS	4.2±5.8	6.1±4.5	6.6±3.2	0.055[a]	2.8±3.3	5.5±4.2	8.9±5.4	0.008[a]
QOL score	3.1±1.1	2.8±1.3	3.9±1.4	0.106[a]	3.7±1.6	4.2±1.4	4.7±1.0	0.379[a]
TPV (g)	29.9±24.1	43.8±26.5	70.4±58.9	0.029[a]	32.8±29.7	58.0±30.9	81.7±45.3	0.015[a]
TZV (g)	17.7±10.2	23.4±18.8	41.9±30.6	0.014[a]	26.6±21.0	31.3±26.9	55.6±38.5	0.022[a]
TZI	NS	NS	NS	NS	0.53±0.27	0.62±0.19	0.78±0.11	0.036[a]
IPP (mm)	13.3±5.2	17.0±3.1	20.5±8.4	0.035[a]	NS	NS	NS	NS
PVR (ml)	48.0±34.1	51.2±49.6	50.7±48.7	0.214[a]	51.0±54.1	46.2±37.6	61.2±50.7	0.066[a]
Qmax (ml/s)	12.3±4.2	9.6±3.7	6.1±5.9	0.017[a]	11.0±7.3	8.8±5.2	6.3±4.4	0.032[a]
AUR history	11 (8.2)	25 (23.2)	53 (42.7)	0.000[c]	18 (16.4)	41 (26.1)	40 (40.8)	0.000[c]
Surgical patients	<0.5 (n=71)	0.5-0.7 (n=48)	>0.7 (n=43)		<10 mm (n=64)	10-20 mm (n=51)	>20 mm (n=47)	
PdetQmax (cm H2O)	65.2±39.0	74.6±30.1	83.8±45.8	0.022[a]	77.4±29.8	75.1±39.2	78.6±34.2	0.078[a]
BOOI	50.9±22.8	60.4±28.5	72.3±25.1	0.028[a]	53.6±31.7	58.8±37.0	64.9±34.4	0.041[a]
BCI	126.1±33.8	129.8±35.4	118.7±28.0	0.164[a]	125.6±20.9	123.7±33.2	118.1±21.4	0.356[a]

Values are presented as mean±SD, median (range) or number (%).
TZI, transitional zone index; IPP, intravesical prostatic protrusion; T-PSA, total prostate-specific antigen; IPSS, International Prostate Symptom Score; QOL, quality of life; TPV, total prostate volume; TZV, transitional zone volume; IPP, intravesical prostatic protrusion; PRV, postvoiding residual volume; Qmax, maximum urinary flow; AUR, acute urinary retention; PdetQmax, pressure of detrusor at Qmax; BOOI, bladder outlet obstruction index; BCI, bladder contractility index.
[a]: One-way analysis of variance, [b]: Kraskal-Wallis test, [c]: Pearson Chi-square test.

(Table 3).

DISCUSSION

The pathophysiology of BPH is complex. Prostatic adenoma enlargement increases urethral resistance and leads to BOO, further resulting in compensatory changes in bladder function. However, the elevated detrusor pressure required to maintain urinary flow in the presence of increased outflow resistance occurs at the expense of normal bladder storage function, which is the source of DO. With the continuation of obstruction, decompensation of the detrusor and DUA will eventually take place. The degree of BOO is correlated with the severity of obstruction-relevant symptoms, and the recovery of BOO is used to evaluate the efficacy of treatment of BPH. Furthermore, the baseline degree of BOO was recently found to influence the outcome of treatment. Research has shown that patients with BOO have better outcomes from TURP than do those without BOO [11-14]. One research study showed that patients with BOO will still have a favorable surgical outcome even if they have DO or DUA [14]. Therefore, some hospitals use urodynamics as a routine preoperative examination to confirm whether the candidates have explicit BOO and good detrusor contractility. However, urodynamic study is not totally innocuous, with significant evidence of discomfort and urinary infections associated with performing the examination, as well as imposing additional cost to the patient or to the institution. For this reason, some research has been initiated to find less-invasive or noninvasive examinations for evaluating the degree of BOO. IPP measured as the shortest distance connecting the protruded end of the prostate into the bladder based on the bladder neck in the sagittal plane reflects the maximum longitudinal length of the prostate and may help in assessing the obstructive level of the prostate. Nose et al. [15] first studied the correlation between IPP and the BOOI in 30 male outpatients in 2005 and found that IPP grading correlated well with the BOOI. Keqin et al. [16] analyzed 206 BPH patients classified by different IPP grade and found that the IPP value positively correlated with TPV, PSA, PVR, Qmax, PdetQmax, and BOOI as well as the incidence of AUR, bladder trabeculation, detrusor overactivity, and low bladder compliance. Ku et al. [17] analyzed 260 men with LUTS and found that the BOOI was higher in patients with apparent IPP than in those without. The TZI calculated as TZV divided by TPV may also correlate with the obstructive level because higher volumes of the transition zone will result in harder pressure on the urethra. Kaplan et al. [18] evaluated 61 men with symptomatic BPH and found a significant correlation between TZI and symptoms, Qmax, and PdetQmax. Wang et al. [19] analyzed 116 BPH patients and found that TZI and TZV were both positively correlated with BOOI and IPSS. Milonas et al. [20] reported that lower TZI was an independent predictor of ineffective surgical outcome. In the present study, we found significant correlations in surgical patients between both TZI and IPP with parameters reflecting the level of BOO, such as Qmax, PdetQmax, and BOOI. These results are consistent with the results of former research and suggest that TZI and IPP may be appropriate parameters in diagnosing and classifying BOO. For a long period, TURP has been the gold standard surgical procedure based on the concept of removing the whole enlarged adenoma involved in static and dynamic urethral obstruction. However, the development of medication such as alpha-adrenergic blockers and 5-alpha-reductase inhibitors has decreased the progression of BPH and the operation rate in patients in recent years. However, some patients cannot achieve favorable recovery from drug therapy and need a surgeon to relieve the symptoms. The patients needing surgical therapy in our research were found to have higher values of both IPP and TZI than the patients needing only drug therapy. This result suggests that IPP and TZI could measure the disease progression in BPH patients receiving medication and might have predictive value for medication efficacy. Higher IPP grade was found to correlate with higher voiding symptom score, which demonstrated that IPP could reflect the severity of BPH from not only an objective aspect but also a subjective aspect. AUR is one of the most serious complications of BPH and an indication for surgical intervention. This research has found positive correlations

TABLE 3. Model summary of multiple linear regression with the parameters from TRUS and urodynamics

	Qmax		PdetQmax		BOOI	
	Standardized coefficients	p-value	Standardized coefficients	p-value	Standardized coefficients	p-value
TPV	-0.729	0.490	0.136	0.052	0.394	0.159
TZV	-0.747	0.502	0.017	0.077	0.560	0.122
TZI	-0.630	0.004	0.809	0.013	0.702	0.028
IPP	-0.821	0.038	0.524	0.059	0.028	0.043
PRV	-0.058	0.223	0.021	0.039	0.142	0.640
R Square	0.955		0.943		0.826	

TRUS, transrectal ultrasonography; Qmax, maximum urinary flow; PdetQmax, pressure of detrusor at Qmax; BOOI, bladder outlet obstruction index; TPV, total prostate volume; TZV, transitional zone volume; TZI, transitional zone index; IPP, intravesical prostatic protrusion; PRV, postvoiding residual volume.

between not only IPP but also TZI and the incidence of AUR, which further suggests that these 2 factors might be used to predict the progression of BPH and the possibility of undergoing surgical therapy.

CONCLUSIONS

In general, this research investigated TZI and IPP from TRUS in BPH patients and found positive correlations between these indexes and symptoms, BOO level, and the incidence of AUR. TZI and IPP were also found to differ significantly between BPH patients receiving medication and those undergoing surgical therapy. The results demonstrated that the two parameters had favorable value for assessing severity and progression in patients with BPH. However, this research was retrospective only, with inevitable bias from subject selection and follow-up time. Therefore, more prospective research should be launched to investigate the predictive value of the two parameters for the progression and treatment efficacy of BPH.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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