Correlation of prostatic morphological parameters and clinical progression in aging Chinese men with benign prostatic hyperplasia: results from a cross-sectional study

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Abstract

Objectives Our study aimed to investigate the correlation of prostatic morphological parameters and benign prostatic hyperplasia (BPH) clinical progression in aging Chinese men. **Methods** In this retrospective study, a total of 1038 patients were reviewed. Prostatic morphology was measured by transrectal ultrasound (TRUS). Detailed medical history of all candidates were recorded and analysed after being classified by specific prostatic measurements. Univariate and multivariate logistic regression analyses were used to estimate the correlation between variables. **Results** The cumulative incidence of BPH clinical progression was 63.68% (661/1038) in study population. Prostate volume (PV), transitional zone volume (TZV), transitional zone index (TZI) and intravesical prostatic protrusion (IPP) were all positively associated with BPH progression (all $p < 0.001$). Patients with a PV > 60 mL, TZV > 15 mL, TZI > 0.5 or IPP > 5 mm had a significantly higher possibility of overall BPH clinical progression (adjusted odds ratio (OR): 2.485, 1.678, 1.886 and 1.924, respectively; 95% confidence interval (CI): 1.559-3.960, 1.131-2.489, 1.379-2.579 and 1.357-2.728, correspondingly). **Conclusion** Prostatic morphological parameters are significantly associated with BPH clinical progression. Patients with larger prostatic morphological parameters are more easily to progress. As a result, reasonable management should be timely considered for those patients before clinical progression occurs.

Abbreviations And Acronyms

ANOVA, analysis of variance

AUA, American Urological Association

AUR, acute urinary retention

BMI, body mass indexBPE, benign prostatic enlargement

BPH, benign prostatic hyperplasia

CI, confidence interval

DRE, digital rectal examination

IPP, intravesical prostatic protrusion

CVD, cardiovascular disease

DM, diabetes mellitus;

LUTS, lower urinary tract symptoms

MTOPS, Medical Therapy of Prostatic Symptoms

OR, odds ratio

PSA, prostate-specific antigen

PV, prostate volume

PVR, post-void residual urine volume

Qmax, maximum urinary flow rate

QoL, quality of life

SD, standard deviation

SE, standard error

tPSA, total prostate specific antigen

TRUS, transrectal ultrasound

TZI, transitional zone index

TZV, transitional zone volume

UTI, urinary tract infection

5-ARI, 5-alpha-reductase inhibitor

Introduction

Benign prostatic hyperplasia (BPH) is indisputable a common benign disease among aging males, which has a worldwide prevalence of over 50 % in men aged 60 years or older and as high as 88 % in men up to 80 years of age[1,2]. As people age, BPH has become an important global public health concern. Although BPH is not a life-threatening disease, it is associated with serious morbidities, including depression, an increased risk of falls and impaired quality of life (QoL)[3–5]. BPH is also a slowly progressive disease. If it's left untreated, lower urinary tract symptoms (LUTS) will get severer and serious complications such as hematuria, recurrent urinary tract infection (UTI), bladder stones, bladder diverticulum, acute urinary retention (AUR), and even renal insufficiency and failure can occur, which may be attributed to the disease progression[6] and requiring BPH-related surgical intervention[7].

Recent data suggest that adverse events of BPH have either increased or persisted in hospitalized patients over the past decade[8]. Surgical interventions, including minimally invasive treatment are usually performed to improve symptoms and decrease disease progression in BPH patients who have developed BPH related complications[9]. However, surgery associated morbidities, including blood loss, sexual dysfunction, instrument associated injury and even the resultant economic burden, etc. come out to be a real consideration.

A few trials have investigated to elucidate patients' characteristics that portend worse prognoses, and discovered that incidence of BPH clinical progression increased with aging, increased body mass index (BMI), post-void residual urine volume (PVR), prostate-specific antigen (PSA) levels and total prostate volume (PV), decreased maximum urinary flow rate (Qmax), and aggravated severity of LUTS[10–12]. However, none of these trials studied the correlation of prostatic morphological parameters and BPH clinical progression, and the relationship was still unclear.

Moreover, China is a rapidly aging society. According to the sixth national population census in 2010, 13.26 % of the Chinese population was older than 60 years [13]. And this percentage is estimated to reach to 16.7 % in 2020[14]. Population aging has been a challenge for healthcare systems in China, because BPH is one of the most common diseases in advance-aged males and has high annual healthcare costs [15,16]. Thus, knowledge of the clinical and demographic factors that may increase the incidence of disease progression and to provide seasonable and reasonable management before progression occurs are of great importance, especially for Chinese BPH patients.

From these viewpoints, we have investigated the correlation of prostatic morphological parameters and clinical progression in patients with BPH at their first outpatient or emergency visiting in our hospital, with the goal of helping clinicians to better understand the relevant factors of BPH clinical progression, and to make the most optimized clinical strategies for BPH management.

Patients And Methods

Study Design and Patient Selection

This was a retrospectively observational cross-sectional study conducted on patients diagnosed with BPH at their first outpatient or emergency visiting in our hospital. All of those objects corresponded to the following conditions. (1) Outpatient or emergency visiting due to LUTS or BPH associated complications; (2) Digital rectal examination (DRE) and transrectal ultrasound (TRUS) proved the existence of benign prostatic enlargement (BPE); (3) A systematic prostate biopsy was applied to patients with total PSA (tPSA) of over 4.0 ng/mL, and no malignant components were found. The exclusion criteria were: (1) immunodeficiency; (2) with any malignant diseases; (3) with medical history of BPH, irrespective of undergoing intervention or not; (4) with medical history of manual or instrumental urological intervention, pelvic or neurological surgery; (5) with comorbidities like neurogenic bladder, urethrostenosis, bladder neck fibrotic contracture, Parkinson's disease, cauda equine syndrome or any other neurological diseases that could affect patients' voiding function; (6) with history of urinary system abnormality, hematuria, urolithiasis, renal insufficiency, hydronephrosis, bladder diverticulum, etc. that were not secondary to BPH.

During Apr 2013 to Nov 2017, a total of 1038 patients were reviewed. Detailed information of age, BMI, tPSA, clinically routinely measured prostatic morphological parameters by TRUS (PV, transitional zone volume (TZV), transitional zone index (TZI) and intravesical prostatic protrusion (IPP)), LUTS (mainly referring to nocturia), comorbidities (cardiovascular disease (CVD), diabetes mellitus (DM)) and the medical history of BPH related complications (hydronephrosis, AUR, bladder stone, bladder diverticulum) were recorded.

All procedures performed in this study were in accordance with the ethical standards of the Ethics Committee of our hospital and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Formal informed consent is exempted.

Assessments

Nocturnal voiding frequency was as a representative of LUTS severity in this study, because nocturia is a highly prevalent and easy-to-measure symptom, and also one of the most bothersome components in men with LUTS/BPH [17,18]. Nocturia was defined by the International Continence Society as urinating one or more times a night[19].

BPH related complications assessed in this study included hydronephrosis, AUR, bladder stone and bladder diverticulum, surrogating the clinical progression of BPH[6]. Hydronephrosis had to be secondary to BPH and was assessed as any pelvicalyceal or ureteral dilation observed on radiographic reports of renal ultrasonography. AUR referred to a severe complication of BPH characterized by a sudden and painful inability to void voluntarily[22]. Bladder stone and bladder diverticulum should also be secondary to BPH and confirmed by radiographic reports of ultrasonography of the urinary system.

Details of the assessment of prostatic morphology have been previously published[20]. The ultrasound machine made by Siemens sequoia 512 (EV8C4-S, frequency 3~8 MHz) was used to estimate PV (mL), TZV (mL) and IPP (mm). Measurements of the PV and TZV were calculated using the prostate

ellipsoid formula ($\text{height} \times \text{width} \times \text{length} \times \pi/6$). TZI was calculated by dividing TZV by PV[24]. Considering the practical clinical significance, TZI was presented as TZI (%) when used as a continuous variable to incorporate into logistic regression model [21]. PV were divided into 30 mL, 30–60 mL and 60 mL subgroups, TZV 15 mL, 15–30 mL and 30 mL subgroups, TZI 0.5, 0.5–0.7 and 0.7 subgroups, and IPP 5 mm, 5–10 mm and 10 mm subgroups, respectively, according to the commonly chose clinical grouping strategies[22,23,10], in order to fit the clinical practice and extrapolate the results to clinical application.

The fasting serum level of tPSA was analyzed by using Hybritech calibrated Access tPSA assays[20]. BMI was calculated by dividing the body weight (kg) by square of height (m^2).

Statistical Analysis

All statistics were performed using PASW Statistics 18.0 (IBM Corp., NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD). The intergroup differences were tested using the analysis of variance (ANOVA). Categorical variables were expressed as frequency (percentage). The intergroup differences were tested using Chi-square test. Multiple imputation (SPSS-based EM method) was used to generate new data and process the data missing. Univariate and multivariate logistic regression analyses were used to investigate the relevant factors of BPH clinical progression. Variables that changed the effect value by more than 10 % were incorporated into the adjusted models[28]. Statistical significance was defined as a $p < 0.05$.

Results

Demographics and Clinical Characteristics

A total of 1038 patients were reviewed. Of this cohort, 86 patients had missing data in BMI. Multiple imputation was used to generate new data and process the data missing, and no statistical differences were found between the original and the interpolated data (Supplement table 1). Recorded clinical and demographic characteristics of all men and those subgroups divided upon specific prostatic measurements were shown in Table 1 and Table 2. Prostatic morphological parameters were positively associated with age, tPSA and nocturia (Table 2). These factors should be considered as potential confounders when estimating the correlation of prostatic measurements and BPH clinical progression.

Overall incidence of BPH clinical progression

A total of 661 (63.68 %) BPH patients were suffering or had the history of one or more BPH associated complications at their first outpatient or emergency visiting (Table 1). The majority of the patients with disease progression only presented 1 complication. The cumulative incidences of 1, 2, 3, 4 complications were 47.50 % (493/1038), 14.06 % (146/1038), 1.93 % (20/1038) and 0.19 % (2/1038), respectively. BPH related complications were mostly attributable to AUR and bladder stone, with rates of 45.09 % (468/1038) and 25.92 % (269/1038), correspondingly. Bladder diverticulum and hydronephrosis were much less happened, with rates of 1.73 % (18/1038) and 9.54 % (99/1038), respectively (Table 1).

Results of ANOVA showed the cumulative incidence of BPH related complications was positively associated with prostatic morphology (all $p < 0.001$). Patients with a greater prostate size had a higher probability of BPH clinical progression, especially the occurrence of AUR and hydronephrosis (Table 2).

Correlation of prostatic morphological parameters and BPH clinical progression

Univariate logistic regression analysis was performed on all clinical variables to evaluate the relevant factors of disease progression (Table 3). PV (odds ratio (OR): 1.017, 95 % confidence interval (CI): 1.012 to 1.021), TZV (OR: 1.022, 95 % CI: 1.016 to 1.027), TZI (OR: 1.042, 95 % CI: 1.033 to 1.051), IPP (OR: 1.075, 95 % CI: 1.055 to 1.096), age (OR: 1.056, 95 % CI: 1.040 to 1.072), tPSA (OR: 1.069, 95 % CI: 1.044 to 1.095) and nocturnal voiding frequency (OR: 1.432, 95 % CI: 1.292 to 1.587) were found to be positively associated with disease progression, while BMI showed a negative association (OR: 0.940, 95 % CI: 0.902 to 0.980).

Multivariate analysis was used to calculate the adjusted ORs and p values for adjusting the influences of confounding factors. The confounders included age, tPSA and nocturnal voiding frequency when the criterion that variables changing the effect value by more than 10 % was applied. Results showed additional adjustment for the confounding variables did not significantly reduce the ORs for the association between the prostatic morphological parameters and BPH clinical progression.

PV

Multivariate logistic regression analysis confirmed that a PV of greater than 60 mL (adjusted OR: 2.485, 95 % CI: 1.559–3.960) was associated with a significantly higher possibility of BPH progression relative to that of subjects with PV less than 30 mL ($p < 0.001$). But there was no statistical difference in BPH progression between patients with a PV of less than 30 mL and those with PV of 30 to 60 mL ($p = 0.108$) (Table 4).

TZV

Patients who had a TZV of 15 to 30 mL (adjusted OR: 1.678, 95 % CI: 1.131–2.489), and 30 mL (adjusted OR: 2.481, 95 % CI: 1.684–3.654) were both demonstrated having a significantly greater likelihood of overall BPH clinical progression relative to that of patients with TZV less than 15 mL ($p = 0.010$, 0.001 , respectively) (Table 4).

TZI

Those BPH patients with a TZI of 0.5 to 0.7 (adjusted OR: 1.886, 95 % CI: 1.379–2.579), and 0.7 (adjusted OR: 2.286, 95 % CI: 1.477–3.538) had a significantly higher possibility of BPH progression compared to patients with TZI of 0.5 or less (both $p 0.001$) (Table 4).

IPP

Similarly to other prostatic morphological parameters, subjects with an IPP of 5–10 mm (adjusted OR: 1.924, 95 % CI: 1.357–2.728), and 10 mm (adjusted OR: 2.521, 95 % CI: 1.775–3.582) had a significantly greater probability of BPH progression compared to patients with IPP less than 5 mm (both $p 0.001$) (Table 4).

Discussion

BPH is highly prevalent and can progress over time, but not all patients with BPH have the similar risk for progression [29,30]. Figuring out factors of this risk has been an ongoing process over the past decades. A few trials have investigated to elucidate patients' characteristics that portend worse prognoses [10–12]. But these trials mainly focused on the demographic and clinical factors, like age, BMI, PSA, PV, PVR, Qmax, LUTS severity, etc., and very rarely mentioned about the influences of prostatic morphology. Consequently, in order to elucidate the correlation of prostatic morphological parameters and BPH clinical progression, this research was conducted.

The main findings of our study are that: PV, TZV, TZI and IPP are all positively associated with BPH progression. Patients with larger prostatic measurements are more easily to clinically progress. Reasonable and seasonable management should be considered for patients with PV 60 mL, TZV 15 mL, TZI 0.5 or IPP 5 mm, before clinical progression occurs.

Clinical progression of BPH is mainly referred as LUTS getting severer and serious complications such as hematuria, recurrent UTI, bladder stones, bladder diverticulum, AUR, and even renal insufficiency and failure occurring [6]. The trial of Medical Therapy of Prostatic Symptoms (MTOPS) used the definition of disease progression as the first occurrence of an increase over baseline of at least 4 points in the American Urological Association (AUA) Symptom Score, AUR, urinary incontinence, renal insufficiency or recurrent UTI [6]. However, since not all of the clinical centers are capable of routinely assessing renal function, or the AUA Symptom Score in a primary care setting for BPH patients, and sometimes it's even hard to distinguish the pathogenesis of recurrent UTI and urinary incontinence, we attempted to make our work more broadly applicable by creating a simplified BPH clinical progression model with easily and routinely measured clinical and radiographic factors (hydronephrosis, bladder stone, AUR, bladder diverticulum). We defined BPH clinical progression as the occurrence of any of the BPH related complications mentioned above. Sarma et al. reported that disease progression occurred in 14 % of the BPH patients left untreated over a follow-up period of 5 years[24]. Guo et al. investigated 2271 BPH patients and found 1078 (47.5 %) had BPH-related complications [25]. However, when we used the simplified BPH clinical progression model, the cumulative incidence of disease progression was much higher (63.68 %). But intriguingly, this result was in accordance with the Chinese habit of delayed doctor visiting until the symptoms become severe. In this study, the mean (SD) age of these first hospital visiting BPH patients was 70.61 (9.11) years, which was much elder than in other countries[26,10], confirming this special phenomenon from the other aspect. But actually, this simplified model need to be validated by further larger-scale and better-designed studies conducted in multicenter before extrapolating the present findings to patients with BPH presenting in real life.

Nocturia is a highly prevalent and easy-to-measure bladder storage symptom, and also one of the most bothersome components in men with LUTS/BPH [17,18]. Frequently voiding twice or more per night can have a substantial impact on an individual's QoL, with sleep disruption leading to chronic fatigue, increased risk of falls and fractures, as well as mortality [27,28]. Therefore, nocturia is widely used to evaluate the severity of LUTS [29]. In China, it's unpractical to systemically evaluate LUTS severity of patients in their first outpatient or emergency visiting using PVR, Qmax, IPSS or other index score in most situations because of the unbalance of patient-clinician ration and the inspection related economic burden, especially at primary hospitals. And as an attempt to make our work more broadly applicable by creating a simplified model with easily measured factors, we used nocturnal voiding frequency as the only indicator to represent the severity of LUTS in this study. It was found that 94.70 % (983 / 1038) of the patients presented nocturia in our study, and nocturnal voiding frequency showed a significant OR (OR: 1.432, 95% CI: 1.292–1.587, $p 0.001$) with BPH progression using univariate logistic regression analysis, which meant utilizing nocturia to represent LUTS is partially reasonable, but still needed to be further validated.

5-alpha-reductase inhibitor (5-ARI) is used as the first-line pharmacological therapy for men with moderate-to-severe LUTS, mainly for modifying the natural history of BPH by delaying the disease progression [37,38]. Results of MTOPS showed finasteride could manifest a 34 % risk reduction in overall BPH clinical progression compared to placebo. Treatment of 5-ARI for over 2 years have also been demonstrated to significantly reduce prostatic measurements[30]. Thus, taken together all of these findings with our results that patients with larger prostatic morphological parameters are more easily to progress may be useful to clinicians and patients in deciding on appropriate treatment options.

A potential limitation of this study is that it was a retrospective cross-sectional study conducted in a single institution and the usage of the unverified simplified BPH clinical progression model. This needs to be borne in mind in extrapolating the present findings to patients with BPH presenting in real life, in clinic settings. Consequently, further perspective larger-scale and better-designed studies conducted in multicenter will be expectant.

In a nutshell, prostatic morphological parameters are significantly associated with BPH clinical progression. Patients with larger prostatic morphological parameters are more easily to progress. Utilizing these parameters permits estimation of individual patient risk for clinical progression. Novel clinical decision strategies based on our results will allow urologists to weigh patient-specific benefits against possible risks of adverse effects for a given patient, which will be helpful in developing more cost-effective treatment strategies for BPH management. But our results need to be further validated before extrapolating in clinical application.

Declarations

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All procedures performed in this study were in accordance with the ethical standards of the Ethics Committee of Xinhua Hospital and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIAL

The data that support the findings of this study are available from the corresponding author, Yu Wu, upon reasonable request.

COMPETING INTERESTS

The authors declare that they have no competing interests

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AUTHORS' CONTRIBUTIONS

Subo Qian: study design, data collection and management, data analysis, manuscript writing

Haibo Shen: study design, data collection and management, data analysis, manuscript editing

Shun Zhang: data collection, data analysis

Jun Qi: manuscript editing, supervision

Yu Wu: study design, data collection and management, data analysis, manuscript editing, supervision

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Tables

Table 1 Patients’ characteristics (mean (SD) or n (%))

	Demographic Data		Demographic Data
Number of patients (n)	1038	Hydronephrosis, n (%)	99 (9.54)
Mean (SD) Age (years)	70.61 (9.11) †	AUR, n (%)	468 (45.09)
Mean (SD) BMI (kg/m ²)	24.21 (3.07) †	Bladder stone, n (%)	269 (25.92)
Mean (SD) tPSA (ng/mL)	6.84 (8.34) †	Bladder diverticulum, n (%)	18 (1.73)
Mean (SD) PV (mL)	68.13 (37.57) †	Overall complications, n (%)	661 (63.68)
Mean (SD) TZV (mL)	41.29 (31.19) †	Complication=0, n (%)	377 (36.32)
Mean (SD) TZI	0.55 (0.16) †	Complication=1, n (%)	493 (47.50)
Mean (SD) IPP (mm)	9.27 (7.47) †	Complication=2, n (%)	146 (14.06)
CVD, n (%)	458 (44.12)	Complication=3, n (%)	20 (1.93)
DM, n (%)	154 (14.84)	Complication=4, n (%)	2 (0.19)
Nocturia, n (%)	983 (94.70)		

Abbreviations: AUR, acute urinary retention; BMI, body mass index; CVD, cardiovascular disease; DM, diabetes mellitus; IPP, intravesical prostatic protrusion; PV, prostate volume; SD, standard deviation; tPSA, total prostate-specific antigen; TZI, transitional zone index; TZV, transitional zone volume

Complication=0 meant patients without BPH related complications, and Complication=1, 2, 3, 4 meant patients with corresponding quantity of complications.

† Column statistics.

Table 2 Patients’ characteristics according to prostatic morphological parameter distribution

Characteristics		PV				TZV				TZI				IPP			
Number of patients (n)	<30 mL (n=122)	30-60 mL (n=385)	>60 mL (n=531)	p value	<15 mL (n=214)	15-30 mL (n=242)	>30 mL (n=582)	p value	<0.5 (n=387)	0.5-0.7 (n=456)	>0.7 (n=195)	p value	<5 mm (n=287)	5-10 mm (n=320)	>10 mm (n=431)	p value	
Mean (SD) Age (years)	66.46 (10.92)	68.75 (8.66)	72.92 (8.30)	<0.001 ^{****}	65.65 (10.12)	69.08 (8.35)	73.07 (8.10)	<0.001 ^{****}	66.76 (9.37)	72.51 (8.25)	73.83 (7.78)	<0.001 ^{****}	67.21 (10.04)	71.56 (8.51)	72.17 (8.27)	<0.001 ^{****}	
Mean (SD) BMI (kg/m ²)	23.80 (2.93)	24.35 (3.08)	24.20 (3.08)	0.232 [†]	24.23 (2.93)	24.45 (3.09)	24.10 (3.10)	0.324 [†]	24.42 (2.97)	23.97 (3.06)	24.34 (3.24)	0.080 [†]	24.56 (2.95)	24.05 (3.03)	24.09 (3.16)	0.073 [†]	
Mean (SD) tPSA (ng/mL)	1.62 (1.92)	4.24 (5.42)	9.93 (9.66)	<0.001 ^{****}	1.98 (3.50)	4.89 (7.33)	9.44 (8.97)	<0.001 ^{****}	3.76 (6.57)	7.61 (7.12)	11.18 (11.31)	<0.001 ^{****}	3.77 (7.36)	6.40 (6.15)	9.22 (9.57)	<0.001 ^{****}	
Mean (SD) PV (mL)	-	-	-	-	28.96 (7.69)	48.14 (9.84)	90.84 (34.77)	<0.001 ^{****}	41.69 (19.57)	74.40 (28.48)	105.94 (44.22)	<0.001 ^{****}	38.60 (20.19)	62.89 (24.79)	91.68 (38.97)	<0.001 ^{****}	
Mean (SD) TZV (mL)	7.96 (2.62)	22.14 (8.59)	62.83 (29.35)	<0.001 ^{****}	-	-	-	-	16.23 (10.04)	45.66 (19.55)	80.81 (35.16)	<0.001 ^{****}	17.22 (15.69)	36.71 (21.33)	60.72 (32.62)	<0.001 ^{****}	
Mean (SD) TZI	0.34 (0.08)	0.48 (0.13)	0.65 (0.11)	<0.001 ^{****}	0.33 (0.07)	0.48 (0.09)	0.66 (0.09)	<0.001 ^{****}	-	-	-	-	0.40 (0.14)	0.55 (0.14)	0.64 (0.11)	<0.001 ^{****}	
Mean (SD) IPP (mm)	0.68 (1.92)	6.18 (5.61)	13.49 (6.62)	<0.001 ^{****}	1.16 (2.52)	6.93 (5.56)	13.23 (6.50)	<0.001 ^{****}	4.07 (5.19)	11.55 (6.86)	14.30 (6.53)	<0.001 ^{****}	-	-	-	-	
CVD, n (%)	47 (38.52)	158 (41.04)	253 (47.64)	0.058 [‡]	82 (38.32)	100 (41.32)	276 (47.42)	0.044 ^{**}	154 (39.79)	202 (44.30)	102 (52.31)	0.016 [*]	114 (39.72)	151 (47.19)	193 (44.78)	0.170 [‡]	
DM, n (%)	23 (18.85)	44 (11.43)	87 (16.38)	0.047 ^{**}	35 (16.36)	28 (11.57)	91 (15.64)	0.256 [‡]	60 (15.50)	71 (15.57)	23 (11.79)	0.415 [‡]	51 (17.77)	47 (14.69)	56 (12.99)	0.210 [‡]	
Nocturia, n (%)	102 (83.61)	359 (93.25)	522 (98.31)	<0.001 ^{****}	180 (84.11)	230 (95.04)	573 (98.45)	<0.001 ^{****}	346 (89.40)	444 (97.37)	193 (98.97)	<0.001 ^{****}	252 (87.80)	302 (94.38)	429 (99.54)	<0.001 ^{****}	
Hydronephrosis, n (%)	4 (3.28)	23 (5.97)	72 (13.56)	<0.001 ^{****}	8 (3.74)	14 (5.78)	77 (13.23)	<0.001 ^{****}	20 (5.17)	54 (11.84)	25 (12.82)	0.001 ^{***}	13 (4.53)	24 (7.50)	62 (14.38)	<0.001 ^{****}	
AUR, n (%)	28 (22.95)	129 (33.51)	311 (58.57)	<0.001 ^{****}	43 (20.09)	91 (37.60)	334 (57.39)	<0.001 ^{****}	111 (28.68)	235 (51.54)	122 (62.56)	<0.001 ^{****}	74 (25.78)	136 (42.50)	258 (59.86)	<0.001 ^{****}	
Bladder stone, n (%)	25 (20.49)	106 (27.53)	138 (25.99)	0.302 [‡]	47 (21.96)	71 (29.34)	151 (25.94)	0.200 [‡]	87 (22.48)	134 (29.38)	48 (24.62)	0.067 [‡]	61 (21.25)	98 (30.62)	110 (25.52)	0.031 ^{**}	
Bladder diverticulum, n (%)	3 (2.46)	8 (2.08)	7 (1.32)	0.554 [‡]	4 (1.87)	4 (1.65)	10 (1.72)	0.984 [‡]	6 (1.55)	7 (1.54)	5 (2.56)	0.615 [‡]	2 (0.70)	7 (2.19)	9 (2.09)	0.284 [‡]	
Overall complications, n (%)	50 (42.62)	211 (54.80)	400 (75.33)	<0.001 ^{****}	85 (39.72)	143 (59.09)	433 (74.40)	<0.001 ^{****}	183 (47.29)	325 (71.27)	153 (78.46)	<0.001 ^{****}	124 (43.20)	212 (66.25)	325 (75.41)	<0.001 ^{****}	

Abbreviations: AUR, acute urinary retention; BMI, body mass index; CVD, cardiovascular disease; DM, diabetes mellitus; IPP, intravesical prostatic protrusion; PV, prostate volume; SD, standard deviation; tPSA, total prostate-specific antigen; TZI, transitional zone index; TZV, transitional zone volume

[†] ANOVA; [‡] Chi-square test; * meant p<0.05, ** meant p<0.01, *** meant p<0.001, were assumed as statistically significant.

Table 3 Univariate analysis of relevant factors of BPH clinical progression

BPH clinical progression				
Variables	Estimate	SE	p value	OR (95% CI) †
PV (mL)	0.016	0.002	<0.001***	1.017 (1.012-1.021)
TZV (mL)	0.022	0.003	<0.001***	1.022 (1.016-1.027)
TZI (%)	0.041	0.004	<0.001***	1.042 (1.033-1.051)
IPP (mm)	0.072	0.010	<0.001***	1.075 (1.055-1.096)
tPSA (ng/mL)	0.067	0.012	<0.001***	1.069 (1.044-1.095)
Age (years)	0.054	0.008	<0.001***	1.056 (1.040-1.072)
BMI (kg/m ²)	-0.062	0.021	0.004**	0.940 (0.902-0.980)
Nocturnal voiding frequency (times)	0.359	0.052	<0.001***	1.432 (1.292-1.587)
CVD	0.210	0.131	0.109	1.233 (0.955-1.593)
DM	-0.002	0.182	0.990	0.998 (0.699-1.424)

Abbreviations: BPH, benign prostatic hyperplasia; CI, confidence interval; CVD, cardiovascular disease; DM, diabetes mellitus; IPP, intravesical prostatic protrusion; OR, odds ratio; PV, prostate volume; SE, standard error; TZI, transitional zone index; TZV, transitional zone volume

† Binary univariate logistic regression analysis; ** meant p<0.01, *** meant p<0.001, were assumed as statistically significant.

Table 4 Multivariate analysis of the correlation of prostatic morphological parameters and BPH clinical progression

BPH clinical progression				
Variables	Unadjusted OR (95% CI) †	p	Adjusted OR (95% CI) ‡	p value
PV (continuous variable, mL)	1.017 (1.012-1.021)	<0.001***	1.009 (1.004-1.014)	0.001**
PV (tertiles)	-	-	-	-
<30 mL	1	-	1	-
30-60 mL	1.746 (1.156-2.639)	0.008**	1.430 (0.925-2.210)	0.108
>60 mL	4.397 (2.914-6.634)	<0.001***	2.485 (1.559-3.960)	<0.001***
TZV (continuous variable, mL)	1.022 (1.016-1.027)	<0.001***	1.013 (1.006-1.019)	<0.001***
TZV (tertiles)	-	-	-	-
<15 mL	1	-	1	-
15-30 mL	2.192 (1.507-3.190)	<0.001***	1.678 (1.131-2.489)	0.010*
>30 mL	4.410 (3.167-6.141)	<0.001***	2.481 (1.684-3.654)	<0.001***
TZI (continuous variable, %)	1.042 (1.033-1.051)	<0.001***	1.028 (1.018-1.038)	<0.001***
TZI (tertiles)	-	-	-	-
<0.5	1	-	1	-
0.5-0.7	2.766 (2.081-3.676)	<0.001***	1.886 (1.379-2.579)	<0.001***
>0.7	4.061 (2.734-6.031)	<0.001***	2.286 (1.477-3.538)	<0.001***
IPP (continuous variable, mm)	1.075 (1.055-1.096)	<0.001***	1.045 (1.024-1.067)	<0.001***
IPP (tertiles)	-	-	-	-
<5 mm	1	-	1	-
5-10 mm	2.580 (1.857-3.586)	<0.001***	1.924 (1.357-2.728)	<0.001***
>10 mm	4.030 (2.926-5.552)	<0.001***	2.521 (1.775-3.582)	<0.001***

Abbreviations: CI, confidence interval; IPP, intravesical prostatic protrusion; OR, odds ratio; PV, prostate volume; TZI, transitional zone index; TZV, transitional zone volume

Adjusted OR: influences of confounders included age, tPSA and nocturnal voiding frequency were adjusted.

† Binary univariate logistic regression analysis; ‡ Binary multivariate logistic regression analysis; * meant $p < 0.05$, ** meant $p < 0.01$, *** meant $p < 0.001$, were assumed as statistically significant.

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