



Role of Transition Zone Index in the Prediction of Clinical Benign Prostatic Hyperplasia

Klinik Benign Prostat Hiperplaziyi Öngörmeye Transizyon Zon İndeksinin Yeri

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What's known on the subject? and What does the study add?

Role of transition zone index in the prediction of clinical benign prostatic hyperplasia.

ABSTRACT

Objective

The objective of this study was to determine the role of the transition zone (TZ) index (TZI) in the prediction of clinical benign prostatic hyperplasia (BPH) in patients who underwent transurethral prostatectomy (TUR-P) and to analyze the correlation between the amount of resected tissue and TZ volume (TZV).

Materials and Methods

Twenty-six male clinical BPH patients with obstructive complaints and 17 male benign prostate enlargement (BPE) patients without any complaints were included in the study. Both the groups were over the age of 50. Clinical BPH patients underwent complete TUR-P. Statistical analysis was done with SPSS. Sensitivity, specificity, positive and negative predictive values of TZI-as a method of assessing clinical BPH-were measured.

Results

There was a statistically significant difference in prostate volume, uroflowmetry patterns, prostate-specific antigen (PSA), International prostate symptom score (IPSS), TZV and TZI between the two groups. There was a correlation between TZV and the amount of resected tissue ($r=0.97$; $p<0.0001$). TZI also correlated with IPSS, quality of life (QL) and maximum flow rate (MFR) ($r=0.58$, $p<0.0001$; $r=0.56$, $p<0.0001$; $r=-0.70$, $p<0.0001$, respectively).

Conclusion

TZI >0.40 has a high level of sensitivity and specificity in the prediction of clinical BPH among patients who undergo TUR-P due to obstructive symptoms and reported as BPH. There is a strong correlation between the amount of resected tissue and TZV. TZI is a valuable tool in diagnosis, and TZV gives valuable information about the patient to the surgeon.

Keywords

Clinical benign prostatic hyperplasia, transurethral prostatectomy, tissue amount, transition zone volume, transition zone index

ÖZ

Amaç

Transüretral prostatektomi (TUR-P) yapılan hastalarda transizyon zon indeksinin (TZİ) klinik benign prostat hiperplazisini (BPH) öngörmedeki rolünü ve rezeke edilen doku miktarı ile transizyon zon volümü (TZV) arasındaki korelasyonu araştırmaktır.

Gereç ve Yöntem

Obstrüktif yakınması olan 26 klinik BPH'lı ve yakınması olmayan benign prostatik büyümesi (BPE) olan 17 erkek hasta çalışmaya alındı. Her iki grup 50 yaş üzerindedir. Klinik BPH'lı hastalara komplet TUR-P yapıldı. SPSS ile istatistiksel çalışma yapıldı. Klinik BPH tanısı öngörmeye TZİ için duyarlılık, özgüllük, pozitif öngörü değeri ve negatif öngörü değeri ölçüldü.

Bulgular

Prostat volümü, üroflowmetri paternleri, prostat spesifik antijen (PSA), Uluslararası prostat semptom skoru (IPSS), TZV, TZİ iki grup arasında istatistiksel olarak farklıydı. TZV ile rezeke edilen doku miktarı arasında korelasyon vardı ($r=0.97$, $p<0.0001$). TZİ ile IPSS, yaşam kalitesi (QL) ve maksimal akım hızı (MFR) arasında korelasyon tespit edildi (sırasıyla; $r=0.58$, $p<0.0001$; $r=0.56$, $p<0.0001$; $r=-0.70$, $p<0.0001$).

Sonuç

Obstrüktif yakınması nedeniyle TUR-P yapılan ve patolojisi BPH olarak rapor edilen hasta grubunda klinik BPH'yı öngörmeye TZİ'nin 0,40 üstündeki değerlerinin duyarlılığı ve özgüllüğü oldukça yüksektir. Rezeke edilen doku ile TZV arasında yüksek korelasyon vardır. TZİ tanı koymada ve TZV ise hasta hakkında cerraha değerli bilgiler sunmaktadır.

Anahtar Kelimeler

Klinik benign prostat hiperplazisi, transüretral prostatektomi, doku miktarı, transizyonel zon volümü, transizyonel zon indeksi

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Introduction

Benign prostatic obstruction (BPO) or benign prostatic hyperplasia (BPH), which is more commonly used, is one of the factors that lead to lower urinary tract symptoms (LUTS) in elderly men (1). BPH primarily develops in the transition zone (TZ) (2). TZ volume (TZV) differs between patients with and without BPH (3). An increase in TZV is paralleled by age (4,5). The tissue resected either by transurethral prostatectomy (TUR-P) or open surgery is the TZ.

The correlation between BPH and TZV and TZ index (TZI) has been examined in the literature (6,7,8).

In this study, the role of the TZI in the prediction of clinical BPH in patients who undergo TUR-P is determined and the correlation between the amount of resected tissue and TZV is analyzed.

Materials and Methods

Twenty-six male patients who applied to the urology outpatient clinic with obstructive symptoms and diagnosed with clinical BPH and 17 male patients who applied to the urology outpatient clinic and diagnosed with BPE without obstructive symptoms were enrolled in the study.

Prostate specific antigen (PSA), uroflowmetry, urea and creatinine tests were done and transrectal ultrasonography (TRUS) and abdominal ultrasonography (USG) were performed. Patients with the following manifestations were excluded: malignancy, neurogenic bladder, systemic neurological disease, post void residual urine (PVR) over 350 ml, urethral stenosis, pelvic radiation, previous prostatic surgery, bladder stone, and previous medical therapy due to infravesical obstruction symptoms.

The enrollment criteria were as follows: obstructive symptoms, International Prostate Symptom Score (IPSS) 13 and above, quality of life (QL) score 3 and above, maximum flow rate (MFR) 10 ml/sec and below, prostate weight 15 gram and above, voiding volume in uroflowmetry 150 ml and above, and age 50 and above. This group of patients was deemed as clinical BPH group.

Patients over the age of 50, without obstructive symptoms, with IPSS and QL scores of 12 and below and 2 and below, respectively, were deemed as the control group. Informed consent was taken from all patients.

Patients with a voiding volume of 150 ml and above were subjected to uroflowmetry analysis twice. Uroflowmetry was made using a Dantec Menuec 3.1 water cystometry device. MFRs were recorded.

Abdominal USG was performed to examine the upper urinary system and to determine PVR.

Zonal distribution of prostatic hyperplasia was evaluated using TRUS. Prostate volume and TZV were measured. Measurements were made using Siemens Sonoline SL-1 device and Siemens Endo-P5/7.5 MHZ multiplanar transrectal transducer. Prostate was scanned in transaxial and longitudinal planes and measured.

Prostate volume and TZV were automatically calculated by the ellipsoid formula ($\pi/6 \times \text{width} \times \text{length} \times \text{depth}$). The ratio of TZV to the total prostate volume was calculated. This is the TZI. TZV was multiplied by coefficient 1 to calculate the weight. (9).

The same physician evaluated all the patients (MG, M.D.). TUR-P procedure was performed in all clinical BPH patients by the same surgeon (ZK, M.D.).

SPPS was used for statistical analysis. Distribution of data was evaluated. Patient data were presented as an arithmetic mean + 1 standard deviation. Correlation analysis was made. The Mann-Whitney U test was used for the data that follow nonparametric distribution, and Student's t-test was used for the data that follow parametric distribution.

Sensitivity, specificity, positive and negative predictive values (PPV) (NPV) of TZI-as a method of assessing clinical BPH-were measured and coherence analysis was made. Kappa statistics was used for coherence.

Results

Clinical BPH patients with obstructive symptoms were classified as group A and BPE patients without any symptoms were classified as group B. The mean age difference between the two groups was not statistically significant. However, MFR, prostate volume, PSA, TZV and TZI were different in two groups and the difference was statistically significant.

The breakdown of the tested parameters in both groups is in given Table 1.

Patients with a PSA level between 4 and 10 ng/ml were evaluated by PSA-density and age-adjusted PSA. TRUS-guided biopsy was performed. Patients with malignancy were excluded.

Correlation among the parameters tested is given in Table 2.

Correlation between the amount of resected tissue and TZ calculated before the surgery are given in Table 3. The highest correlation is reported in TZV.

Cut-off values and accuracy rates for TZI are given in Table 4.

The mean TZV in patients who underwent TUR-P was 28.62 cc (minimum 6, maximum 86), and the mean resected tissue amount was 26.27 gr (minimum 8, maximum 75). There was a strong correlation between these two parameters. ($r=0.97$, $p<0.0001$; Pearson correlation). The weight of the tissue was calculated in grams by multiplying TZV by coefficient 1.

Discussion

TZ is the primary zone for BPH (2). TZV and TZI are parameters directly correlated with BPH. These parameters give information on the clinical status of BPH.

The size, weight and shape of the prostate always keep the attention of urologists. The size of the prostate is generally measured to decide for the method of surgery. Prostate size is important to plan the surgery, to envisage the length of the procedure, to know the amount of tissue to be resected, and to schedule the surgery (10). Today, thanks to TRUS, the prostate can be examined in details (9). Although the central and peripheral glands cannot be differentiated clearly in young patients in sonography, it is easily recognizable when BPH is developed (11,12). TZ is mildly hypo-echoic in sonography. Its border with peripheral zone can be easily recognized (13,14).

Table 1. Mean parameters and statistical significance as per the groups

		Clinical BPH	BPE	p
Age		66.0±7.9 (50-81)	60.5±7.43 (50-75)	Ns ^a
IPSS		20.2±7.0 (13-35)	4.9±4.1 (0-13)	<0.00001 ^b
QL		3.7±0.9 (3-6)	1.1±0.8 (0-3)	<0.00001 ^b
MFR (ml/sn)		8.6±1.6 (3-10)	21.8±6.6 (14-38)	<0.00001 ^b
PSA (ng/ml)		3.43±3.23 (0.1-10)	1.38±0.83 (0.3-4)	<0.01 ^b
Prostate volume	Abdominal USG (cc)	58.8±28.4 (10-126) ^c	36.1±18.5 (11-77) ^d	<0.005 ^b
	TRUS (cc)	49.5±28.0 (15-161) ^c	29.1±10.3 (15-48) ^d	<0.001 ^b
TZV (cc)		28.62±24.1 (6-86)	9.9±4.9 (3-32)	<0.00001 ^b
TZI		0.6±0.1	0.3±0.1	<0.00001 ^b
Tissue amount (cc)		26.27 (8-75)		

^aNo statistical significance, ^bMann-Whitney U, ^cNo statistical difference between the volumes, BPH: Benign prostatic hyperplasia, BPE: Benign prostate enlargement, IPSS: International Prostate Symptom Score, QL: Quality of life, MFR: Maximum flow rate, PSA: Prostate-specific antigen, USG: Ultrasonography, TZV: Transition zone volume, TZI: Transition zone index, TRUS: Transrectal ultrasonography

Table 2. Correlation between the tested parameters and transition zone index and transition zone volume (Pearson method)

	IPSS	QL	MFR	Abdominal USG	TRUS	TZV-TZI
TZV						
r	0.22	0.30	-0.46	0.78	0.96	0.72
p	0.11	0.03	0.001	0.0001	0.0001	0.0001
TZI						
r	0.58	0.56	-0.70	0.54	0.56	0.72
p	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001

IPSS: International Prostate Symptom score, QL: Quality of life, MFR: Maximum flow rate, USG: Ultrasonography, TRUS: Transrectal ultrasonography, TZV: Transition zone volume, TZI: Transition zone index

Table 3. Correlation between the tissue amount and other parameters (Pearson method)

	Abdominal USG	TRUS	TZV	TZI
Tissue amount				
r	0.73	0.95	0.97	0.55
p	0.001	0.0001	0.0001	0.002

USG: Ultrasonography, TRUS: Transrectal ultrasonography, TZV: Transition zone volume, TZI: Transition zone index

Intraprostatic structure is clearly explored by TRUS. Along with this development, now the focus is on TZ, which is the primary zone for BPH. Greene demonstrated that TZV was larger in patients with BPH (3). Collins classified (4) TZV based on age groups and demonstrated that prostate volume, TZV and TZI show a parallel increase with aging. TZI is 0.36 when the patient is 20 years old. However, it is 0.60 when the patient is over the age of 50. A similar increase was also revealed by Liu (5).

TZV and TZI have been used in many studies. For instance, in one study, TZV was used to evaluate the outcomes of the medical therapy (15,8). Follow-up of patients given finasteride or dutasteride therapy was based on the changes to be observed in the levels of TZV and MFR. The possibility of responding to therapy was 38% in patients with a TZI below 0.51, whereas it was 100% in patients with a TZI above 0.51. It is concluded in this study that follow-up based on TZV in patients receiving finasteride treatment is accurate (15).

Table 4. Accuracy rates for transition zone index based on various cut-offs

TZI	Sensitivity	Specificity	PPV	NPV	Coherence (Kappa analysis)
	%	%	%	%	%
0.25	0	31	0	70	24 (48)
0.30	0	25	0	64	22 (6)
0.35	0	19	0	47	16 (2)
0.40	97	91	97	64	86 (70)
0.45	91	87	94	82	90 (80)
0.50	100	68	76	100	84 (68)
0.55	100	56	61	100	74 (2)
0.60	100	54	58	100	72 (45)

TZI: Transition zone index, PPV: Positive predictive values NPV: Negative predictive values

It is demonstrated that TZI accurately predicts acute urinary retention in BPH patients, and that it might be helpful to decide for medical therapy or surgery (16,17), and that it has a PPV for the progression and severity of the disease (18), and that it predicts the necessity of TUR-P procedure (19). It is confirmed that TZI and TZV predict the efficiency of TUR-P procedure pre-operatively (7), and that more than 60% of the TZV should be resected to benefit from TUR-P (20).

A recent study confirmed that MFR improvement is much better with combined medical therapy in BPH patients with a TZI of over 0.50. Multivariate analysis demonstrates that TZI is the strongest independent factor predicting the increase in MFR (21).

In our study, the mean TZV was 28.62 mL and the weight of the resected tissue was 26.27 g. There is a strong correlation between these two parameters ($r=0.97$, $p<0.0001$). The difference in between was only 2.35 (10%). Tissue loss during resection was the cause of this difference (22).

Another study using TZV as a method of assessment indicated a correlation between TUR-P and the amount of resected tissue (23). A study comparing TUR-P and open prostatectomy demonstrated a correlation between TZV and tissue amount. In this study, 120 patients underwent TUR-P. The mean TZV and the mean removed tissue weight were found to be 25.43 mL and 22.9 g, respectively. The difference between TZV and resected tissue weight was only 2.53 (11%) (24). Another study confirms that TUR-P is strongly correlated with TZV and TZI, although the same study indicates that prostate volume is ineffective in the prediction of efficiency of TUR-P procedure (7). All the studies listed above underline the correlation between TZV and weight of the resected tissue. Our study confirms a strong correlation in between as well (Table 3).

Kaplan et al. (6) did one of the first studies exploring the role of TZV and TZI in the diagnosis of BPH. This study was focused on American Urological Association symptom score index, prostate and TZV measurements by TRUS and urodynamic analysis. The authors concluded that there was a strong correlation with TZI, if the cut-off value for TZI was 0.50. Our study revealed a similar result for TZI. There is one more recent study on the same subject. In this study, it is reported that $TZI \geq 0.50$ has a strong correlation with MFR improvement (21).

The reliability and relevance of TZI, which is calculated by dividing TZV by total prostate volume, draws great interest among the scientific circles. The rationale behind is as follows: TZ is enlarged macroscopically and creates a static mass, which causes obstruction leading to symptomatic BPH.

In our study, the correlation coefficient between MFR and TZI was higher than TZV ($r=-0.70$; $r=-0.46$, respectively). The correlation of TZI with IPSS, QL, MFR was much stronger than the correlation between TZV and the parameters in question. This is an indication that TZI has a stronger predictive role when compared to TZV (Table 2).

There was no significant correlation between IPSS and TZV, whereas IPSS correlated with TZI ($r=0.58$, $p<0.0001$). There was a similar correlation between QL and TZV and TZI. In other words, the increased volume, per se, does not cause symptoms. Increased TZV in total volume (TZI) leads to the formation of symptoms.

Our study revealed there was statistically significant difference in TZI between clinical BPH group and control group. According to our results, the cut-off value for TZI is 0.40 or 0.45, 0.40 has the highest sensitivity and specificity, whereas, 0.45 has the highest coherence, and Kappa analysis is almost perfect. If 0.50, 0.55 and 0.60 are taken as the cut-off values for TZI, the NPV and sensitivity increase up to 100%, however, specificity decreases. Specificity reaches its peak value, when TZI is 0.40 and 0.45. When the cut-off value is 0.40, 3% of

patients are left undiagnosed and 10% of patients are misdiagnosed (Table 4). Another study revealed that patients responded to medical therapy 100% when the cut-off value for TZI was over 0.51 (15). Yet another study reported a strong correlation when the cut-off value for TZI was 0.50 (6). The same cut-off for TZI, 0.50, was also confirmed in the most recent study (21). Our cut-off values 0.40 and 0.45 are in line with the above-cited studies.

A cut-off value of 0.40 for TZI has high sensitivity and specificity. TZI with a cut-off value of 0.40 and above is a reliable factor predicting clinical BPH.

There is a strong correlation between resected tissue and TZV. This parameter gives valuable information to the surgeon. It helps not only to predict the length of TUR procedure to schedule surgeries, but also to plan the surgery in patients with high volumes.

Correct diagnosis with a single examination is the ultimate goal of every physician. It is the optimum goal in terms of cost and patient compliance. Efforts will continue to reach this goal. In a recent study, it has been demonstrated that there was a correlation between BPH and resistive indices of prostate and urethral blood flows. The authors concluded that resistive index of prostate blood flow might be used for diagnostic purpose (25). In the same study the rate of diagnosis was reported to be 97% with this single examination.

Radiological examination of TZ, being the primary zone for BPH, which leads to lower urinary tracts symptoms, gives valuable information. Findings following a detailed examination of TZ will help to have a better clinical prediction. We believe that studies with larger series of patients including control group comprised of controls under the age of 50 will highlight the real predictive value of TZI and/or TZV.

Study Limitations

Our study has some limitations to be pointed out; namely, the small patient population and the age of the patients in the control group.

Conclusion

TZI predicts clinical BPH with high sensitivity and specificity in patients with obstructive symptoms who underwent TUR-P and reported as BPH. The strong correlation between TZV and resected tissue gives the surgeon valuable information about the patient before the surgery.

Ethics

The study were approved by the Yüksek İhtisas Training and Research Hospital of Local Ethics Committee (2011-KAEK-25 2016/15-14), Informed Consent: Consent form was filled out by all participants.

Peer-review: Internal peer-reviewed.

Authorship Contributions

Concept: Muhammet Güzelsoy, Ziya Kirkali, Design: Muhammet Güzelsoy, Ziya Kirkali, Data Collection or Processing: Muhammet Güzelsoy, Analysis or Interpretation: Muhammet Güzelsoy, Ziya Kirkali, Literature Research: Muhammet Güzelsoy, Writing: Muhammet Güzelsoy, Ziya Kirkali.

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