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Is sampling transitional zone in patients who had prior negative prostate biopsy necessary?

Bayram Dogan · Ege Can Serefoglu · Ali Fuat Atmaca · Abdullah Erdem Canda · Ziya Akbulut · M. Derya Balbay

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Abstract
Objective To assess the necessity of transitional zone sampling of the prostate during repeat prostate biopsy procedures.
Methods Patients treated for lower urinary tract symptoms with transurethral resection of the prostate (TURP) from April 2004 to July 2009 whom had at least 1 negative prostate biopsy prior to this treatment were chosen as the study group. A histopathological analysis of surgical specimens was employed to determine cancer detection rates.
Results A total of 72 patients with the mean age of 66.1, mean prostate-specific antigen (PSA) of 10.4 ng/mL and mean prostate volume of 63.2 cc were included. Of the patients, 50 had 1 biopsy set, 17 had 2 sets, 4 had 3 sets and 1 patient had 4 sets of consecutive biopsies. All biopsy results were negative for prostate cancer. After the analysis of surgical specimens obtained during TURP, cancer was detected in 3 patients (4.2%). Transitional zone sampling during prostate biopsies did not significantly improve the cancer detection rate. Transitional zone sampling was performed in 29 biopsies taken from 20 patients, one of whom (5%) had prostate cancer. The remaining 71 biopsies were taken from 52 patients without transitional zone sampling, and cancer was detected in 2 (3.8%) of them.
Conclusions Since no significant difference was observed between patient groups (those with and those without transitional zone biopsies) in the detection of prostate cancer in the transitional zone, strategies for increasing the number of cores taken from transitional zone during repeat biopsies should be reconsidered.

Keywords Detection rate · Prostate biopsy · Prostate cancer · Screening · Transitional zone · Transurethral resection

B. Dogan · A. F. Atmaca · A. E. Canda · Z. Akbulut · M. Derya Balbay
Department of 1st Urology, Ataturk Training & Research Hospital, Ankara, Turkey

E. C. Serefoglu
Kiziltepe State Hospital, Mardin, Turkey

E. C. Serefoglu (✉)
Cinnah Caddesi No:47, 06680 Cankaya, Ankara, Turkey
e-mail: egecanserefoglu@hotmail.com

Introduction

Prostate cancer (PCa) is the most common cancer in men and serum prostate-specific antigen (PSA) assay is frequently used for screening of men 50 years of age and older for Pca [1, 2]. With the use of PSA as a screening tool, the estimated lifetime risk of being diagnosed with PCa has risen from 9 to 17% [3, 4]. Since its introduction in 1989 by Hodge et al. [5], systematic transrectal ultrasound (TRUS)-guided prostate biopsy (PBx) has started a new era in the

diagnosis of PCa. However, the accuracy of this method in detecting PCa has been argued and many studies have been conducted in order to improve its detection rate during subsequent years. In spite of these efforts, the answer to the question, how many biopsies are necessary to confirm or rule out the diagnosis of PCa, is still unclear [1]. In addition, there is no universally accepted repeat biopsy schema for patients with prior negative prostate biopsies and high PSA levels and/or suspicious digital rectal examination findings. Although some authors and recent guidelines recommend sampling the transitional zone in such cases [6, 7], to our knowledge, its effectiveness has not yet been validated.

Thus, the aim of this study was to evaluate the importance of transitional zone sampling in repeat biopsies to detect PCa, by showing the incidence of PCa detection in patients with at least one prior negative PBx, who underwent transurethral resection of prostate (TURP) due to lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH).

Materials and Methods

From April 2004 to July 2009, 387 patients with LUTS underwent TURP in our institution. Of those patients, 72 had one or more negative PBx before TURP and the medical records of those patients were evaluated retrospectivetely. Patient age, free and total PSA levels, number of biopsy sets, prostate volumes (measured via transabdominal or transrectal ultrasound), amount and histopathological results of the entire surgical specimens of TURP were recorded. The patients were divided into two groups: Group 1 consisted of 20 patients in whom transitional zone was sampled during previous biopsy sets and group 2 consisted of 52 patients without transitional zone sampling. Statistical analyses were performed with SPSS^{TM} (version 16), and the continuous data were compared using Mann–Whitney U test; whereas categorical variables were compared using chi-square test. Significance level was accepted as $p < 0.05$.

Results

Seventy-two patients with the mean age of 66.1 ± 7.3 years (range 49–85 years) underwent TURP after at least 1 negative TRUS-guided PBx. Mean total PSA and free PSA values were 10.4 ± 12.1 ng/ml (range 1.78–87.48) and 2.4 ± 3 (0.4–19.3), respectively. Mean prostate volume was 63.2 ± 20.1 cc (range 20–116), whereas mean resected prostate volume during surgery was 19.2 ± 7.9 grams (range 7–42). The characteristics of patients whose transitional zone was sampled (Group 1) and not (Group 2) can be seen in Table 1. There was no statistically significant difference between the characteristics of the patients in these two groups.

Overall, 100 sets of PBx were performed on 72 patients where 50, 17, 4 and 1 patients underwent 1, 2,

Table 1 Patients' characteristics and pathological results

	Transitional zone sampled (Group 1) (n = 20)	Transitional zone not sampled (Group 2) (n = 52)	*p* value[a]
Number of biopsies	29	71	
Age (mean)	65.2	66.5	0.5
Total PSA (mean) (ng/dl)	15.8	8.4	0.1
Free PSA (mean) (ng/dl)	2.8	2.3	0.7
Prostate volume (mean) (cc)	68.9	60.9	0.2
Resected prostate volume (mean) (cc)	20.2	18.8	0.5
TURP pathology	n(%)	n(%)	*p* value[b]
Benign	11(55)	31(59.6)	0.9
Inflammation	8(40)	19(36.5)	
HGPIN	–	–	
Adenocarcinoma	1(5)	2 (3.8)	

[a] Mann–Whitney U test

[b] Fisher's exact test

3 and 4 sets of PBx prior to TURP, respectively. The number of sampled cores during PBx varied from 8 to 61, and pathology results of those biopsies were as follows: benign 77 (77%), inflammation 22 (22%) and high-grade prostatic intraepithelial neoplasia (HGPIN) 1 (1%).

PCa was detected in the TURP specimen of 3 (4.2%) patients. Interestingly, 1 (5%) of those patients was from Group 1, who had undergone PBx 4 times (10–27 cores) prior to TURP and his transitional zone was sampled in 3 of these biopsy sets, where no PCa was detected. On the other hand, in Group 2, PCa was detected in the TURP specimen of 2 patients (3.8%) (Table 1). Pathology results of other TURP procedures performed in Group 1 and 2 are demonstrated in Table 1. There was no significant difference between Group 1 and 2 in terms of pathological examination results of TURP specimens ($p = 0.930$).

Discussion

Although there is no universally accepted biopsy fashion, today, the classical sextant biopsy technique is considered inadequate and recent guidelines have recommended a minimum of 8 cores be taken [6]. Moreover, many studies were carried out and many authors suggest different biopsy schemas to increase the detection rate of PCa. Levine et al. [8] demonstrated that performing 2 sets of consecutive biopsies increases the success of detection and diagnosis of PCa. In another study, Babaian et al. [9] reported that sextant PBx misses 20–25% of PCa and its accuracy is insufficient. He also argued that 11 quadrant PBx is more efficient in detecting PCa [9].

In subsequent years, the tendency of increasing the number of cores sampled continued to rise and many authors suggested that 8, 10, 12, 18 and 20 quadrant or even saturation PBxs are more efficient [10–12]. In order to decrease false-negative results of biopsy procedures, sampling more lateral regions was suggested, and in a prospective controlled randomized study, sampling lateral peripheral cores in addition to the standard 6 core biopsy protocol found to increase the diagnose rate from 14 to 35% [13]. In a recent meta-analysis, Chun et al. [14] highlighted the fact that the PBx regimen should be individualized according to patient characteristics and the number of systematic cores at initial PBx was recommended to be between 10 and 18 in patients with smaller (<50 cm^3) prostates.

If the first PBx is negative and PCa is still highly suspected, repeat biopsy is essential. Several studies demonstrated 10–34% cancer detection with repeat biopsies, following initial negative biopsy [15–20]. However, to whom, when and how these re-biopsies should be performed remains unclear. Although transitional zone sampling during repeat biopsies is recommended by several authors [6, 21], detecting cancer in this region is still only 1.4–6.9% [22–27].

In this study, we investigated the rational of transitional zone sampling in repeat PBx, by searching the incidence of PCa detection in patients with at least one prior negative PBx who underwent TURP for treatment of LUTS. We found that PCa was detected in the transitional zone of <5% of patients who previously had negative PBx results. Moreover, our data revealed that transitional zone sampling during previous PBx does not make any difference in detecting PCa that is later diagnosed upon TURP, where the entire transitional zone is resected and analyzed. Similarly, PCa detection rates with diagnostic/therapeutic TURP in patients with previous negative PBx have been evaluated by several authors and found to range between 7.9 and 33% [1, 27–30]. Although these rates are all higher than cancer detection rates of sampling transitional zone with PBx, guidelines do not recommend the use of diagnostic TURP instead of repeat biopsies [6]. Considering these facts, we believe that TURP must be considered as an alternative diagnostic procedure for patients who have persistently high PSA levels and suspected PCa, especially for those with concurrent LUTS.

Our study is not without limitations. First of all, there were only 3 PCa patients in the study population who were diagnosed on TURP. Therefore, further studies with larger study population are necessary to confirm our findings. In addition, only 20 men with negative transition zone biopsies could be included, which is mainly due to our biopsy protocol. Since transitional zone sampling was not performed during initial biopsy and it was reserved for 2nd, 3rd and 4th sets, the number of patients in this group remained limited.

Conclusions

Since there was no significant difference between patient groups (with or without transitional zone

biopsies) in the detection of PCa in the transitional zone, strategies for increasing the number of cores taken from the transitional zone of the prostate during repeat biopsies and potential diagnostic value of TURP should be reconsidered.

Conflict of interest The authors declare that they have no conflict of interest.

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