

# Comparison of Transrectal Ultrasound-guided Biopsy of the Prostate and Transurethral Resection of the Prostate for Detection of Prostate Cancer in Patients With Moderate Lower Urinary Tract Symptoms

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**Background:** To compare transrectal ultrasound (TRUS)-guided biopsy of the prostate and transurethral resection of the prostate (TURP) for detection of prostate cancer (PCa) in patients with moderate lower urinary tract symptoms (LUTS) by retrospective chart review.

**Methods:** Between January 2004 and December 2008, a total of 520 patients, aged 50.3–81.5 years, with moderate LUTS (International Prostate Symptom Score, 8–19), and elevation of prostate-specific antigen ( $\geq 4$  ng/mL), or abnormal findings by digital rectal examination, were enrolled for evaluation. All the patients were recommended to receive TRUS-guided biopsy of the prostate (TRUS biopsy group) or TURP (TURP group) due to the possibility of PCa, according to their choice after full explanation by the doctors.

**Results:** There were 379 patients in the TRUS biopsy group and 141 in the TURP group. PCa was detected in 80 patients (21.1%) in the TRUS group and in 27 (19.1%) in the TURP group. Clinically localized PCa (T1–2N0M0) was found in 46 patients (57.5%) in the TRUS biopsy group and in 16 (59.3%) in the TURP group. Bone metastasis was noticed in 22 (27.5%) patients in the TRUS biopsy group and in 7 (25.9%) in the TURP group. The percentage of low-grade tumor was significantly higher in the TURP group than in the TRUS biopsy group (11.1% vs. 5%).

**Conclusion:** TURP was not superior to TRUS-guided biopsy of the prostate for detection of PCa in patients with moderate LUTS and prostate-specific antigen  $\geq 4$  ng/mL. [*J Chin Med Assoc* 2010;73(11):568–572]

**Key Words:** prostate cancer, prostate-specific antigen, transrectal ultrasound biopsy, transurethral resection of the prostate

## Introduction

Prostate cancer (PCa) is a leading cause of male cancer mortality in the USA.<sup>1</sup> Diagnosis of PCa can be made by transrectal ultrasound (TRUS)-guided biopsy of the prostate or transurethral resection of the prostate (TURP). Prostate-specific antigen (PSA) has been proved to be a very useful tumor marker for the prostate, but it is not specific for PCa.<sup>2</sup> An abnormal digital rectal examination (DRE) and/or elevated serum

PSA can indicate PCa. The technique of TRUS-guided biopsy of the prostate has changed from the sextant biopsy in 1980 to saturation biopsy nowadays. It is suggested that the more biopsy cores that are taken, the more cancer one finds.<sup>3</sup> Most PCa is located in the peripheral zone, which is easily confirmed by TRUS-guided biopsy, but it is hard to diagnose PCa in the transitional zone.<sup>3,4</sup> Therefore, biopsies in the transitional zone of the prostate have been suggested for patients with elevated PSA and negative results from extended



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multisite biopsies.<sup>5-7</sup> Puppo et al have suggested that diagnostic TURP has a high diagnostic power for PCa,<sup>8</sup> but risk of morbidity with TURP should not be ignored.<sup>3</sup> However, other authors have reported a lower diagnostic yield (range, 20–30%) for TURP.<sup>3</sup> Kitamura et al concluded that many cancers diagnosed by TURP might be clinically insignificant.<sup>9</sup>

van Renterghem et al reported that their patients with mild lower urinary tract symptoms (LUTS), elevated PSA and negative multisite biopsies underwent TURP, and 9.8% of them had PCa.<sup>10</sup> Patients with moderate LUTS [International Prostate Symptom Score (IPSS), 8–19] and elevated PSA ( $\geq 4$  ng/mL) or abnormal findings by DRE are recommended to receive TRUS-guided biopsy of the prostate or TURP, but which procedure is better for diagnosis of PCa needs further evaluation. To compare TRUS-guided biopsy of the prostate and TURP for diagnosis of PCa in patients with moderate LUTS, we conducted a retrospective study.

## Methods

PSA, DRE, TRUS and IPSS were routinely checked for evaluation of all the patients (age  $\geq 50$  years) with LUTS, and TRUS was performed by using real-time scanning with a rotating 7.5-MHz transducer (Bruel & Kjaer, Copenhagen, Denmark) at our hospital. Between January 2004 and December 2008, 601 patients with moderate LUTS (IPSS, 8–19) and PSA  $\geq 4$  ng/mL, or abnormal findings by DRE (such as palpable nodule or hard consistency), were included for evaluation. All the patients were initially treated with  $\alpha$ -blocker, and no patients received 5 $\alpha$  reductase inhibitor. Eighty-one patients with a history of acute urinary retention, acute prostatitis, urethritis, or refusal to undergo further examinations were excluded. The remaining 520 patients, aged 50.3–81.5 years, satisfied the inclusion criteria and were enrolled for evaluation. These 520 subjects were recommended to receive TRUS-guided biopsy of the prostate (TRUS biopsy group) or TURP (TURP group) because of the possibility of PCa, according to the patients' choice after full explanation by the doctors. Patients in the TURP group did not have previous biopsy, and they chose TURP because there was no specific improvement or side effects after  $\alpha$ -blocker treatment. PSA was checked every 3–6 months for patients without PCa in the TURP group, and patients were recommended to receive biopsy if an increase in PSA was noticed. Prostate volume was measured by TRUS, with the formula being  $0.52 \times \text{length} \times \text{width} \times \text{height}$ .

Biopsy of the prostate was done with a spring-loaded automatic biopsy gun under TRUS guidance and local anesthesia (application of xylocaine jelly over the rectum). We used 12-core biopsy including 6 laterals, 2 from the transitional zone and 4 from the lateral peripheral zone, in addition to the conventional sextant biopsies, as described by Durkan et al to detect PCa.<sup>5</sup> Repeated biopsy was recommended if high-grade prostatic intraepithelial neoplasia or increased PSA (higher than previous level) was noted 6 months after the first negative biopsy. A continuous-flow resectoscope was used to perform TURP until the surgical capsule was found (nearing perforation), without suprapubic cystostomy drainage. All surgical specimens were weighed and sent for pathological examinations. Bone scanning (whole-body bone scintigraphy) and computed tomography or magnetic resonance imaging were performed in all the patients for clinical staging when PCa was confirmed. Tumor grading was classified as low (2–4), intermediate (5–7) or high (8–10) according to the Gleason score. Clinically insignificant PCa (T1N0M0) was defined as low-grade tumor, PSA  $< 10$  ng/mL,  $< 5\%$  of PCa in the resected tissue by TURP, and no evidence of metastasis. The study was approved by the institutional review board of Taipei City Hospital.

The  $\chi^2$  test and Mann–Whitney  $U$  test were used for statistical analysis, with  $p < 0.05$  considered to be statistically significant.

## Results

Of the 520 patients, 379 (72.9%) were in the TRUS biopsy group and 141 (27.1%) in the TURP group. PCa was detected in 80 (21.1%) patients in the TRUS biopsy group and in 27 (19.1%) in the TURP group. The baseline characteristics of all 520 patients and 107 with PCa are illustrated in Table 1. No significant differences in age, PSA, IPSS and prostate volume were noted between the 2 groups (Table 1). Patients in the TURP group had lower maximal urine flow rate than those in the TRUS biopsy group ( $12.5 \pm 3.7$  vs.  $12.9 \pm 4.1$  mL/sec; Table 1), but the difference was not significant ( $p = 0.63$ ). The mean number of TRUS-guided biopsies that were undertaken in 80 patients with PCa was 1.4 (1 in 52 patients, 2 in 22, 3 in 5, and 4 in 1). Of 299 subjects without PCa in the TRUS biopsy group, 30 had undergone prior biopsy at another hospital, and the number of biopsies was 1 in 199, 2 in 80, and 3 in 20 patients. The mean weight of TURP specimen was 28.9 g (range, 13–53 g). The PCa detection rates were 0%, 12.1%, 17.9%, 21.6% and 53.4% in the TRUS biopsy group and 6.8%,

**Table 1.** Baseline characteristics of all the patients and those with prostate cancer\*†

	Group 1 (n = 379)	Group 2 (n = 141)	<i>p</i>	PCa in Group 1 (n = 80)	PCa in Group 2 (n = 27)	<i>p</i>
Age (yr)	64.5 ± 11.5 [186]	66.2 ± 12.6 [72]	0.61	63.7 ± 12.9 [38]	66.4 ± 14.2 [12]	0.73
PSA (ng/mL)	21.1 ± 16.4 [241]	14.1 ± 13.7 [103]	0.08	22.2 ± 17.0 [37]	15.5 ± 15.1 [13]	0.07
< 4	2.9 ± 1.0 [6] (n = 12)	2.8 ± 0.9 [30] (n = 58)	0.86		2.9 ± 1.0 [2]	0.02
PCa detection rate				0% (n = 0)	6.8% (n = 4)	
4–10	7.1 ± 1.9 [90] (n = 165)	6.9 ± 1.8 [21] (n = 36)	0.75	7.8 ± 2.1 [12]	7.1 ± 2.0 [5]	0.45
PCa detection rate				12.1% (n = 20)	19.4% (n = 7)	0.72
10–20	15.3 ± 3.8 [28] (n = 56)	15.0 ± 3.2 [10] (n = 20)	0.73	16.1 ± 3.9 [6]	15.5 ± 3.3 [2]	0.67
PCa detection rate				17.9% (n = 10)	20.0% (n = 4)	0.95
20–30	25.4 ± 3.6 [46] (n = 88)	24.9 ± 3.8 [4] (n = 9)	0.69	26.2 ± 4.1 [11]	25.7 ± 4.3 [1]	0.62
PCa detection rate				21.6% (n = 19)	22.2% (n = 2)	0.65
> 30	62.5 ± 22.5 [32] (n = 58)	57.4 ± 23.8 [11] (n = 18)	0.25	66.3 ± 26.5 [18]	63.9 ± 25.6 [6]	0.26
PCa detection rate				53.4% (n = 31)	58.8% (n = 10)	0.51
IPSS	13.1 ± 3.9 [190]	14.0 ± 4.2 [70]	0.51	12.9 ± 3.9 [39]	13.8 ± 4.3 [13]	0.54
Maximal flow rate	12.9 ± 4.1 [191]	12.5 ± 3.7 [71]	0.63	12.7 ± 4.0 [41]	12.3 ± 3.8 [14]	0.61
Clinically localized PCa				57.5% (n = 46)	59.3% (n = 16)	
Bone metastasis				27.5% (n = 22)	25.9% (n = 7)	
Prostate volume (cm <sup>3</sup> )	40.4 ± 12.5 [188]	38.5 ± 11.8 [72]	0.56	38.9 ± 12.2 [42]	37.4 ± 11.5 [13]	0.63

\*Data are presented as mean ± standard deviation [mean rank]; †Mann-Whitney U and  $\chi^2$  tests were used for statistical analysis, with  $p < 0.05$  considered significant. Group 1 = TRUS biopsy group; Group 2 = TURP group; PCa = prostate cancer; PSA = prostate-specific antigen; IPSS = International Prostate Symptom Score.

19.4%, 20%, 22.2% and 58.8% in the TURP group when PSA was < 4 ng/mL, 4–10 ng/mL, 10–20 ng/mL, 20–30 ng/mL, and > 30 ng/mL, respectively (Table 1). Significantly higher PCa detection rate was noted in patients in the TURP group than the TRUS biopsy group when PSA was < 4 ng/mL (Table 1). IPSS significantly decreased from  $14.0 \pm 4.2$  to  $5.5 \pm 2.5$  after TURP. Major complication rate for TURP (including TURP syndrome and blood transfusion due to severe hematuria) was 3.5% (5/141), and for TRUS-guided biopsy (including urinary sepsis and blood transfusion due to severe hematuria) was 1.3% (5/379).

There was bone metastasis in 22 patients (27.5%) in the TRUS biopsy group and 7 (25.9%) in the TURP group; the difference was not significant. Of the 22 patients in the TRUS group with bone metastasis, PSA was > 30 ng/mL in 19, 20–30 ng/mL in 2, and 10–20 ng/mL in 1. Of the 7 patients in the TURP group with bone metastasis, PSA was > 30 ng/mL in 6, and 20–30 ng/mL in 1. Clinically localized PCa (T1–2N0M0 proved by computed tomography or

magnetic resonance imaging) was found in 46 (57.5%) patients in the TRUS biopsy group and 16 (59.3%) in the TURP group, with no significant difference between the 2 groups. The proportion of cancer in the resected prostate tissue was < 5% in 10 patients, 5–10% in 8 and > 10% in 9, and 37% (10/27) was clinically insignificant tumor by TURP. The percentage of low-, intermediate- and high-grade tumor was 5% (4/80), 51.3% (41/80), and 43.7% (35/80) in patients in the TRUS group, and 11.1% (3/27), 51.9% (14/27), and 37% (10/27) in patients in the TURP group, respectively. The percentage of low-grade tumor was significantly higher in patients in the TURP group than the TRUS group (11.1% vs. 5%). Of 299 patients without PCa in the TRUS biopsy group, 35 received TURP and 2 had PCa. Of 114 subjects without PCa in the TURP group, 20 underwent TRUS biopsy due to increasing PSA and 2 had PCa. In these 4 patients with PCa, PSA was 35 ng/mL, 45 ng/mL, 52 ng/mL, and 38 ng/mL, respectively.

## Discussion

Patients with elevated PSA or abnormal DRE findings are recommended to receive TRUS-guided biopsy of the prostate initially, and repeat biopsy is recommended unless PSA is normalized. In addition, Chappell and McLoughlin<sup>3</sup> reported that repeat biopsy is suggested for patients with high-grade prostatic intraepithelial neoplasia,<sup>11</sup> low ratio of free to total PSA, high PSA density, or family history of PCa. However, extended multisite biopsies are not harmless and might cause discomfort to the patient.<sup>12</sup> Most PCa in the transition zone is located anteriorly and is not detected if the biopsy needle is only directed at the center of the tumor.<sup>13,14</sup> PCa in the transition zone is more often of low grade and has less chance of capsular penetration and metastasis than peripheral zone cancers.<sup>15</sup> In the present study, in patients with PSA < 4 ng/mL, no cancer (0/12) was found by needle biopsy, but 4 cancers (4/58) were found by TURP. Additionally, all 4 cancers were clinically insignificant (<5% in resected tissue) and low grade (Gleason score, 2–4) tumors. Furthermore, the specimens from TURP were not obtained with a whole-mount procedure, so the detection rate of PCa might have been underestimated.

van Renterghem et al reported that patients with mild LUTS and elevated PSA might have bladder outlet obstruction and benefit from TURP.<sup>10</sup> Lin et al suggested that the chance of detecting PCa beyond a third biopsy is low, and TURP might be an alternative procedure, especially in patients with elevated PSA and obstructive symptoms.<sup>16</sup> However, how many biopsies are adequate remains debatable. Startsev et al stated that TURP could detect cancer in the transitional zone in patients with LUTS and negative prostate biopsy.<sup>17</sup> Reich et al suggested that TURP is very effective and durable in alleviating LUTS due to benign prostate hyperplasia.<sup>18</sup> Patients with severe LUTS might be prone to select TURP, and patients with mild LUTS could be more likely to choose prostate biopsy if cancer is suspected. In addition, TRUS biopsy might be suggested first for younger patients (<70 years) and PSA > 10 ng/mL. In the present study, we included patients with moderate LUTS (IPSS, 8–19) for evaluation. Patients with moderate LUTS had significant improvement after TURP, and about 20% had PCa, but all these patients had elevated PSA or abnormal DRE findings. Therefore, patients with moderate LUTS and elevated PSA might have a higher incidence of PCa than those without LUTS, but the etiology needs further evaluation. Furthermore, TURP was not superior to TRUS-guided biopsy for diagnosis of PCa in patients with moderate LUTS and PSA  $\geq$  4 ng/mL.

In the study by Puppo et al,<sup>8</sup> 7 patients (20%) had PCa diagnosed by TURP and biopsy of the peripheral zone of the prostate after repeated negative needle biopsy and elevated PSA. Also, the proportion of cancer in the resected prostate tissue was 2–4% in 5 cases, 6% in 1, and 8% in another. In the present study, we found that about 37% (10/27) of patients had clinically insignificant tumor (<5% of PCa in the resected tissue) by TURP without previous needle biopsy. In addition, of the 10 patients, 4 had PSA < 4 ng/mL and 6 had PSA between 4 and 10 ng/mL. Furthermore, the percentage of low-grade tumor was higher in the patients who underwent TURP than in those who received needle biopsy. Until now, there has been controversy about the role of diagnostic TURP.<sup>8,9,13,16,19–21</sup> Bratt reported that diagnostic TURP might be of value for patients with large prostate and continuously rising PSA,<sup>22</sup> and if no cancer is found and PSA is increasing after TURP, the remaining smaller prostate can be more easily sampled by TRUS-guided biopsy. van Renterghem et al concluded that TURP can be a useful diagnostic tool for PCa in patients with mild LUTS but elevated PSA,<sup>10</sup> and that special attention is needed over the lateral and anterior part of the prostate during diagnostic TURP. Shen et al<sup>23</sup> suggested that TURP combined with additional systemic prostate biopsy can increase the detection rate of PCa, and is a relatively safe treatment. In the present study, TURP could resect all the tumors completely, and might have increased the diagnostic yield of PCa and detected more clinically insignificant tumor, especially in patients with moderate LUTS and PSA < 4 ng/mL. Additionally, the lower prevalence of PCa and smaller prostate in Asian patients might explain why diagnostic TURP had a higher chance of detecting PCa than needle biopsy in patients with PSA < 4 ng/mL. Therefore, TURP might have a higher PCa detection rate than needle biopsy in patients with moderate LUTS and PSA < 4 ng/mL. Although the baseline characteristics between the 2 groups were similar, they could be different in nature. Lack of random allocation was a major limitation of the present study. However, TRUS biopsy and TURP were simultaneously and equally provided for all the patients after full explanation to avoid selection bias.

D'Ambrosio et al<sup>24</sup> reported that a prior history of TURP does not affect outcome in patients who subsequently develop PCa. Eastham et al<sup>25</sup> suggested that patients with clinically localized PCa managed without curative intent have about a 15% risk of local progression within 10 years. Akgul et al<sup>26</sup> suggested that TURP can cause cautery artifacts in resected prostate tissue, which might influence interpretation by pathologists. Therefore, more effort should be taken to

evaluate the scientific basis for TURP as a diagnostic tool for PCa, and whether it will affect the outcome of further treatment.

In conclusion, TURP was not superior to TRUS-guided biopsy of the prostate for detection of PCa in patients with moderate LUTS and PSA  $\geq$  4 ng/mL. However, TURP might have had a greater chance for detection of clinically insignificant and low-grade PCa than TRUS-guided biopsy of the prostate in patients with moderate LUTS, and abnormal DRE findings and PSA < 4 ng/mL, but the case number was small and lacked random allocation. Therefore, we need more subjects, longer follow-up, and a prospective study design for further clarification.

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