

# ORIGINAL ARTICLES

## Urological Oncology

### Changes in Serum Prostate-Specific Antigen Level after Prostatectomy in Patients with Benign Prostatic Hyperplasia

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#### ABSTRACT

**Introduction:** The goal of this study was to investigate the effect of transurethral resection of the prostate and open prostatectomy on the serum prostate-specific antigen (PSA) level in men with benign prostatic hyperplasia.

**Materials and Methods:** Serum prostate-specific antigen levels were determined before and 6 months after operation in 86 patients with benign prostatic hyperplasia who had undergone transurethral resection of the prostate or open prostatectomy. We measured the prostate volume by means of transrectal ultrasonography and weighed the surgical specimen. Changes in serum PSA levels and their correlation with prostate volume and the resected prostate weight were evaluated.

**Results:** Of 86 patients, 45 underwent transurethral resection of the prostate and 41 underwent open prostatectomy. Mean PSA levels were reduced by 67.4 % (range, 0.40 ng/mL to 7.60 ng/mL) in the patients who had undergone transurethral resection of the prostate and 80.7% (range, 1.00 ng/mL to 14.50 ng/mL) in the patients with open prostatectomy. Removal of 1g of prostate tissue reduced serum PSA levels by an average of 0.15 ng/mL in those who underwent transurethral resection of the prostate and 0.10 ng/mL in those treated with open prostatectomy ( $P = .018$ ). Forty patients (88.9%) in the group who underwent transurethral resection of the prostate and 39 (95.1%) in the open prostatectomy group exhibited a postoperative PSA level of less than 2.00 ng/mL ( $P = .20$ ).

**Conclusion:** A modified reference range seems necessary for the screening of prostate cancer via PSA level in men who have undergone prostatectomy for benign prostatic hyperplasia.

**KEY WORDS:** prostate-specific antigen, benign prostatic hyperplasia, prostatectomy

#### Introduction

Prostate-specific antigen (PSA), a useful marker for malignant prostate disease, is produced by prostate epithelial cells. The increased PSA level in patients with benign prostatic hyperplasia (BPH) is caused by the enlargement of the transitional zone.<sup>(1)</sup> After the resection of an

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adenoma of the prostate, PSA levels are expected to decrease to the reference range.<sup>(2)</sup> Stamey and colleagues<sup>(3)</sup> have demonstrated that after adenectomy for BPH, serum PSA levels are reduced drastically in direct proportion to the volume of tissue removed. A modified reference range of PSA levels after BPH adenectomy has been suggested.<sup>(4)</sup> In this study, we investigated the effect of transurethral resection of the prostate (TURP) and open prostatectomy (OP) on serum PSA level in men with BPH.

### Materials and Methods

Between March 2001 and February 2003, 104 patients with BPH were referred to our medical center for surgical treatment. The inclusion criteria for this clinical trial were as follows: age older than 50 years, the existence of urinary retention and persistent gross hematuria, and failure of prior medical therapy. Patients with a malignancy, liver disease, or a history of prostate surgery or treatment with either antiandrogenic drugs or finasteride were excluded from this study. Eighty-six patients were enrolled, and 18 were excluded (5 because of postoperative death, 5 because of adenocarcinoma, and 8 who refused to participate).

All patients were evaluated by digital rectal examination (DRE), determination of the serum PSA level, and transrectal ultrasonography (TRUS) before surgical operation. Long (L) and short (S) diameters and depth (D) were measured, and prostate volume was obtained by means of a prostate ellipse volume calculation ( $L \times S \times D \times 0.5236$ ), as described previously.<sup>(5)</sup> The serum PSA level was measured with the Microwell Elisa Kit (Diagnostic Systems Laboratories Inc, Calabasas, California, USA) with a normal cutoff point of 4 ng/mL. In subjects with a PSA level greater than 4 ng/mL or a suspicious result from DRE, TRUS-guided biopsy was performed, and 3 tissue specimens were obtained from each lobe. The PSA density was calculated by dividing the serum PSA level by the prostatic volume.

Based on the results of DRE, TRUS, and cystoscopy, we decided to perform TURP in 45 patients and OP in 41 (the TURP and OP groups, respectively). Two weeks after operation, patients were examined, and their urine culture results and the report of pathologic examination were recorded. The serum PSA level was measured 6 months after surgery.

Statistical analyses were performed with SPSS software (Statistical Package for the Social Sciences, version 9.0, SSPS Inc, Chicago, Ill, USA), and the Student *t* test, the paired *t* test, the chi-square test, the Mann-Whitney test, and the Pearson correlation were used as appropriate (significance,  $P < .05$ ).

### Results

Forty-five (52.3%) and 41 (47.7%) patients underwent TURP and OP, respectively. The mean serum PSA level before surgery was  $5.35 \pm 3.68$  ng/mL (range, 0.80 ng/mL to 17.50 ng/mL). Of 86 patients, 43 (50%) had a preoperative serum PSA value below the normal reference range ( $< 4$  ng/mL). The mean preoperative prostate volume was  $57.96 \pm 33.82$  mL (range, 15.00 mL to 190.00 mL).

The preoperative PSA level correlated with the prostate volume determined by TRUS (Figure 1;  $r = 0.699$ ,  $P < .001$ ). This correlation was also seen in the OP and TURP groups ( $r = 0.606$ ,  $P < .001$  and  $r = 0.595$ ,  $P < .001$ ). Overall, the preoperative PSA density was  $0.09 \pm 0.05$  (range, 0.03 to 0.33).

The mean serum PSA level after the surgery was  $1.08 \pm 0.68$  ng/mL (range, 0.20 ng/mL to 3.10 ng/mL). None of the patients in our study had a postoperative serum PSA level greater than 4 ng/mL (Table 1). Forty patients (88.9%) in the TURP group and 39 (95.1%) in the OP group had a postoperative PSA less than 2 ng/mL ( $P = .20$ ).

Serum PSA levels decreased postoperatively in all patients, and the mean PSA levels were reduced by 67.4 % (range, 0.40 ng/mL to 7.60 ng/mL) and 80.7% (range, 1.00 ng/mL to 14.50 ng/mL) in the patients in the TURP and OP groups, respectively. The mean decrease in serum PSA level was  $4.28 \pm 3.5$  ng/mL ( $P < .001$ ; confidence interval: 3.51 to 5.04). This variable

**TABLE 1.** Distribution of serum PSA levels before and after the procedures

PSA (ng/mL)	Preoperative Number of Patients (%)	Postoperative Number of Patients (%)
$\leq 2$	11 (12.8)	81 (91.9)
$\leq 4$	44 (51.2)	86 (100)
$\leq 10$	76 (88.4)	-
$> 10$	10 (11.6)	-

PSA: prostate serum-specific antigen

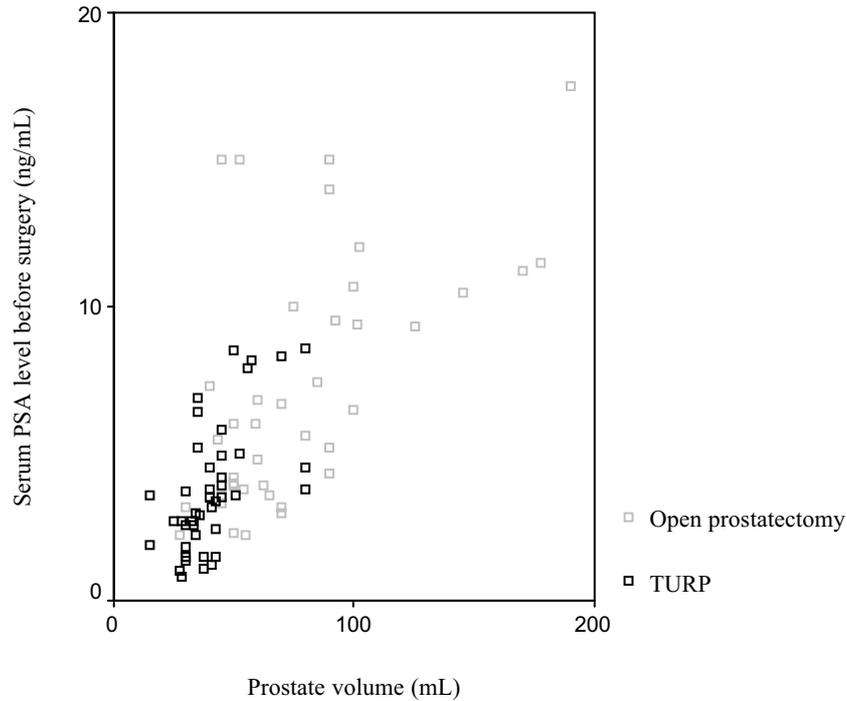


FIG. 1. Estimated ultrasonographic correlation of the preoperative serum PSA level with prostate volume.

was  $2.63 \pm 1.97$  ng/mL ( $P < .001$ ; confidence interval: 2.03 to 3.22) in the patients in the TURP group and  $6.08 \pm 4.02$  ng/mL ( $P < .001$ ; confidence interval: 4.81 to 7.35) in those in the OP group (Figure 2;  $P < .001$ ; confidence interval, 4.79 to 2.11). The preoperative serum PSA level correlated with the mean decrease in the serum PSA level (Figure 3;  $r = 0.95$ ,  $P < .001$ ; OP group:  $r = 0.97$ ,  $P < .001$ ; TURP group:  $r = 0.88$ ,  $P < .001$ ).

The mean weights of the resected adenomas in the TURP and OP groups were  $18.67 \pm 10.33$  g (range, 6.00 g to 50.00 g) and  $65.00 \pm 38.32$  g (range, 13.00 g to 200.00 g,  $P < .001$ ; confidence interval, 58.13 to 34.53). There was a significant correlation between the preoperative prostatic volume determined by TRUS and the weight of the resected adenomas (Figure 4;  $r = 0.87$ ,  $P < .001$ ). This correlation in the TURP and OP

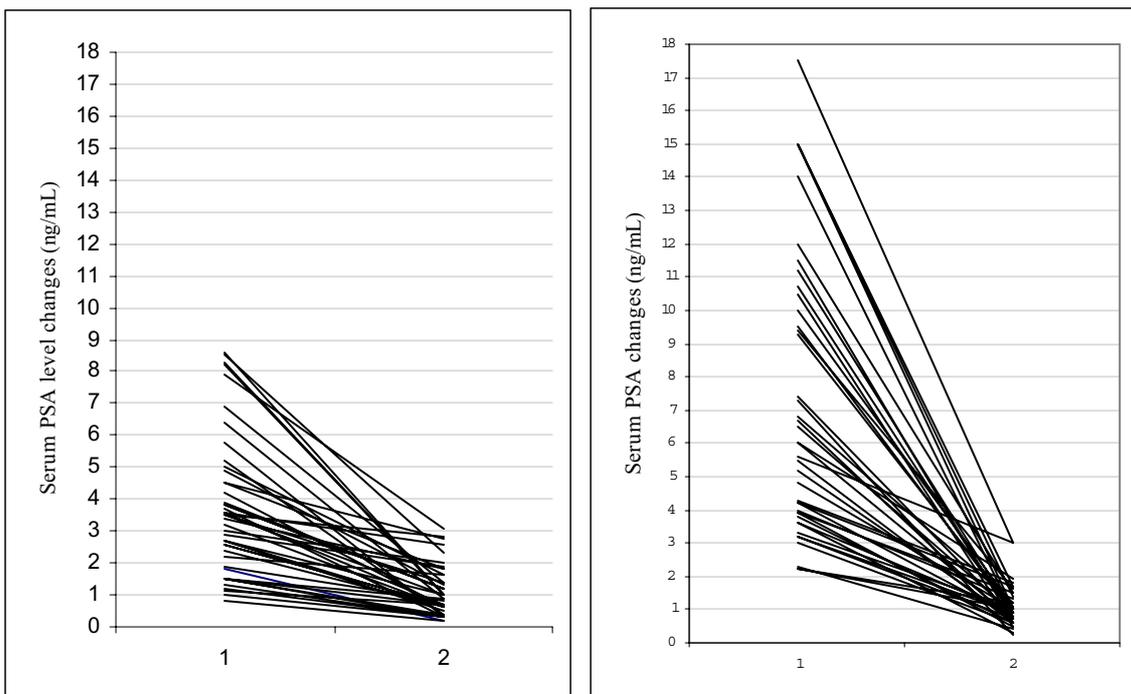
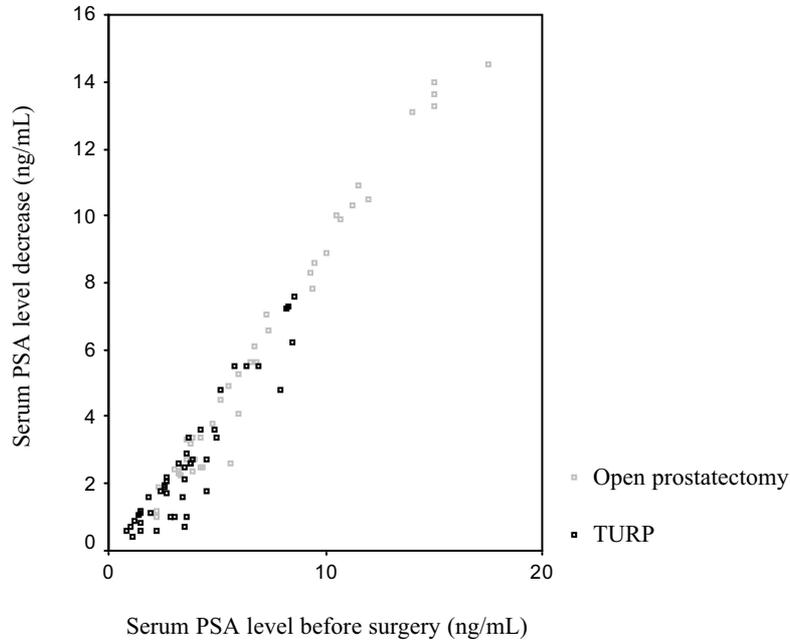


FIG. 2. Changes in the postoperative serum PSA level in patients who underwent TURP or OP.

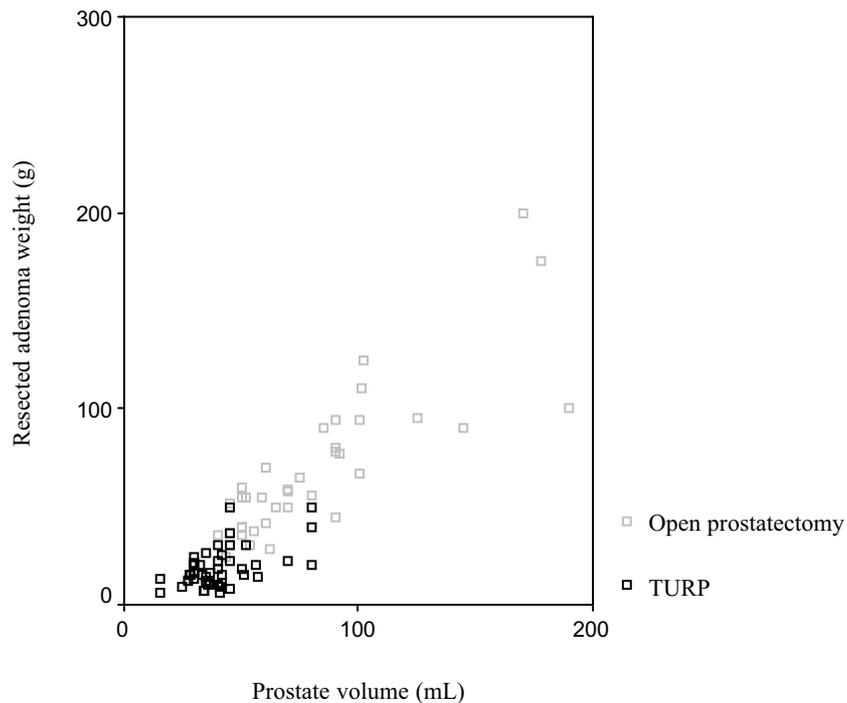


**FIG. 3.** The correlation between the preoperative serum PSA level and the postoperative decrease in the PSA level in all patients.

groups was also significant (TURP group:  $r = 0.53$ ,  $P < .001$ ; OP group:  $r = 0.85$ ,  $P < .001$ ).

The correlation coefficient between the mean postoperative decrease in the serum PSA level and the weight of the adenoma in the TURP and OP groups was 0.475 ( $P = .001$ ) and 0.58.7 ( $P < .001$ ), respectively (Figure 5). The mean ratio

of the postoperative decrease in the serum PSA level to the adenoma weight in 86 patients was  $0.13 \pm 0.09$  ng/mL/g (range, 0.03 ng/mL/g to 0.51 ng/mL/g). This ratio in the patients in the TURP and OP groups was  $0.15 \pm 0.12$  ng/mL/g and  $0.10 \pm 0.06$  ng/mL/g, respectively ( $P = .018$ ).



**FIG. 4.** The relationship between prostate volume estimated ultrasonographically and the resected adenoma weight.

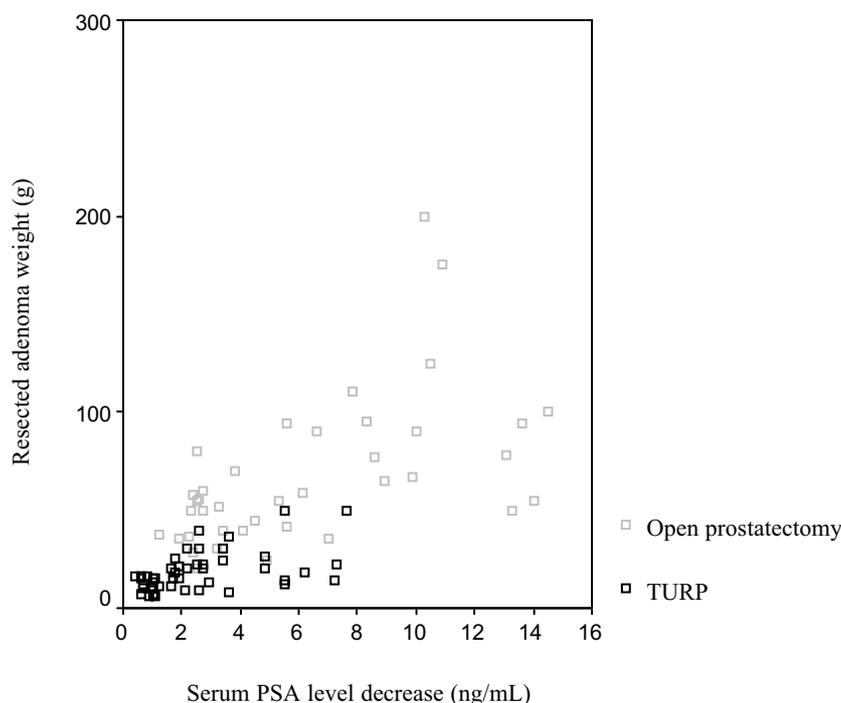


FIG. 5. The correlation between the decrease in PSA levels and the resected adenoma weight.

### Discussion

In this study, half of the patients with BPH exhibited a preoperative serum PSA value above the normal reference range ( $> 4$  ng/mL). In addition, the mean preoperative prostate volume was approximately 58 mL.

Furuya and colleagues<sup>(2)</sup> have reported a smaller mean prostate volume ( $38.8 \pm 23.9$  mL), and 48.7% of their patients had exhibited preoperative PSA levels above 4 ng/mL. Aus and colleagues<sup>(6)</sup> have demonstrated a preoperative serum PSA value above normal reference range in 50% of their patients and a mean prostate volume of 47.9 mL. Considering prostate volume, our patients had relatively lower serum PSA levels.

Using a transrectal biopsy specimen from the prostate in patients with a moderately elevated level of serum PSA, Catalona and colleagues<sup>(7)</sup> identified cancer in only one-third of the patients studied. Kehinde and colleagues<sup>(8)</sup> have demonstrated that BPH and BPH with prostatitis appear to be more frequent causes of serum PSA levels greater than 10 ng/mL in Arab men than in male Caucasians in the United States and Europe. This suggests that in our geographic region (the Middle East), BPH may be a more common cause of elevated serum PSA ( $> 4$  ng/mL) than is cancer. Moreover, the calculated PSA density revealed in our study is

similar to that demonstrated by Lloyd and colleagues (0.068),<sup>(1)</sup> but it is much lower than that in the study by Furuya and colleagues (0.17).<sup>(2)</sup>

Aus and colleagues<sup>(6)</sup> have reported a decrease in serum PSA levels by 70% (range, 6 ng/mL to 1.9 ng/mL) after TURP. They have also noted that prostate volume was reduced by 58% (range, 63.3 mL to 26.5 mL). In our study, the patients who underwent OP or TURP had a reduction in the mean serum PSA level by 80.7% and 67.4%, respectively. In addition, we noted a reduction in prostate volume by 84% in the OP group and 54.2% in the TURP group. Our findings show that in patients who underwent OP, the greater the volume of transitional zone removed, the greater the reduction in the mean serum PSA level.

The PSA reduction per gram of resected adenoma weight was 0.10 in patients who underwent OP, 0.15 in those treated with TURP, and 0.12 overall. In 2 studies, similar results were found in patients who underwent TURP,<sup>(1,4)</sup> but Furuya and colleagues<sup>(2)</sup> reported a higher ratio (0.18 ng/mL/g) in Japanese patients. Because large prostate glands contain more epithelial tissue than do smaller prostates, the incomplete maturation of epithelial cells and their secretory dysfunction may be a reason for which the PSA level decreases less after OP than after TURP. The main reason for that difference is not clear,

and additional research is necessary to clarify that issue.

In this study, postoperative serum PSA levels were less than 2 ng/mL in 91.9% of patients and between 2 and 4 ng/mL in 8.13%, regardless of operative technique. No patients exhibited a postoperative serum PSA level greater than 4 ng/mL. There was no significant difference between the results of the 2 techniques in achieving postoperative serum PSA levels of less than 2 ng/mL. Aus and coworkers<sup>(6)</sup> have reported a postoperative PSA value of less than 4 ng/mL after TURP in 90% of patients. Our patients exhibited much greater reductions in postoperative serum PSA levels, which might have been resulted from the use of OP in our study. Long-term follow-up for patients who underwent TURP in a study by Marks and colleagues<sup>(4)</sup> showed that the subjects with prostatic cancer had a mean PSA level of 1.4 ng/mL. Considering the low accuracy of rectal examination after prostatectomy, a modified reference range of PSA seems necessary for the screening of prostate cancer in men who undergo prostatectomy for BPH.

### Conclusion

After either TURP or OP for BPH, the serum PSA level decreases significantly. Because rectal examination is not accurate in the early detection of prostate cancer and because the likelihood of this malignancy remains even after TURP or OP, the serum PSA level cannot be determined

accurately when BPH is treated by these operations. Thus, further studies to find a modified cutoff point for the serum PSA level in such patients are warranted.

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