

# Prostate Specific Antigen Levels Following Transurethral Resection of the Prostate

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## ABSTRACT

*Objective:* Determine how serum prostate-specific antigen (t-PSA) levels and free PSA (f/t PSA) ratio change following transurethral resection of the prostate (TURP).

*Materials and Methods:* Thirty men with a mean age of  $67.0 \pm 4.2$  years (range 46 to 84 years) underwent TURP for BPH between May 2005 and October 2005. Preoperative assessment included symptom evaluation with the International Prostate Symptom Score (I-PSS) and the prostate volume estimation by transrectal ultrasound. Total PSA and f/t PSA ratio were assessed before the procedure, as well as 30, 60 and 180 days after the TURP.

*Results:* Clinical improvement after TURP, reflected by I-PSS score, was demonstrated as early as 30 days and remained stable until the end of the follow-up. Mean t-PSA declined 71% after TURP and 60 days after surgery the reduction reached its peak, stabilizing afterwards. It varied from  $6.19 \pm 7.06$  ng/mL before surgery to  $1.75 \pm 1.66$  ng/mL on day 60 ( $p < 0.001$ ). The mean baseline f/t PSA ratio was  $18.2\% \pm 3.4\%$  and was not significantly changed at any given time point in the postoperative period ( $p = 0.91$ ). There were also no statistically significant differences in t-PSA or f/t PSA between patients with and without prostatitis at any time point ( $p = 0.23$ ). Resected prostate fragments weighed  $29.9 \pm 19.6$  g, corresponding to 39.1% of the estimated preoperative prostate volume. Each gram of tissue resected decreased PSA by  $0.15 \pm 0.11$  ng/mL, while 1% prostate volume resected led to a reduction of  $2.4\% \pm 0.4\%$  in serum PSA from baseline.

*Conclusions:* PSA decreases drastically in patients who undergo TURP. These low levels stabilize within 60 days after surgery. The f/t PSA ratio did not change, and the finding of chronic prostatitis did not affect the levels of these variables.

*Key words:* prostate-specific antigen; benign prostatic hyperplasia; transurethral resection of prostate

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## INTRODUCTION

Benign prostatic hyperplasia (BPH) is the most prevalent prostatic pathology, and transurethral resection of the prostate (TURP) is one of the surgeries most commonly performed by urologists, and considered the gold standard for the surgical treatment of BPH.

Prostate-specific antigen (PSA) is a tumor marker whose role in the diagnosis and follow-up of patients with prostatic diseases has continuously evolved. PSA behavior after transurethral resection of the prostate is crucial during patient follow-up. It is known that serum PSA levels increase temporarily in the first few days following a TURP procedure, decreasing gradually afterwards and reaching stable

values within 3-6 months (1). However, serum PSA level stabilization apparently depends on several aspects, namely, patient's age, PSA levels before surgery, prostate volume and prostate volume resected. Thus, there is not a cutoff value established for normal PSA in patients who undergo TURP (2,3).

Although different factors may affect PSA reduction after the procedure, an approximate 72% decrease from baseline is expected, even with a proportionally lower reduction in prostate volume (2). This occurs because resection affects basically the transition zone of the prostate, which produces more PSA per gram of tissue (4).

Total serum PSA is found in its free form and bound to plasma proteins. Clinically, both total PSA (t-PSA) and free PSA ratio (f/t PSA) are important for the diagnosis and follow-up of prostatic diseases. In the past few years, great importance has been attributed to free PSA, which is usually reduced in patients with adenocarcinoma. Previous studies suggested that f/t PSA ratio tends to remain stable after TURP in patients with benign prostatic hyperplasia (2,5).

Prostatic inflammation has probably a not clearly understood impact on PSA levels in the postoperative period. Although many studies suggest that the presence of prostatic inflammation can contribute to increasing total PSA levels, the mechanism by which such histological changes induce the prostatic acinus marker to move to the systemic circulation is still controversial (6).

In this study, we analyzed how total PSA and f/t PSA ratio change with time in patients with BPH who undergo TURP, as well as the impact of prostatitis on these parameters, in an attempt to contribute to clarifying some of these important aspects concerning patient follow-up.

## MATERIALS AND METHODS

During one year, 40 patients with lower urinary tract symptoms associated with benign prostatic hyperplasia were selected to undergo TURP and evaluated prospectively. Preoperative assessment included clinical history, physical examination of the

prostate, the International Prostate Symptom Score (I-PSS), urine culture, measurement of prostatic volume by transrectal ultrasound of the prostate (TRUS), and determination of t-PSA and f/t PSA serum levels.

Patients with suspected abnormality on digital rectal examination or PSA  $\geq 4.0$  ng/mL underwent prostate biopsy. Patients with adenocarcinoma were excluded from the study, as well as those with atypical small acinar proliferation (ASAP) or intra-epithelial neoplasia, patients on finasteride in the last 6 months, patients with urinary retention, patients with neurological diseases that could have an impact on the urinary tract, and those with history of pelvic radiotherapy or lower urinary tract surgeries. Patients with urinary infection were treated, and their PSA levels were measured 30 days after a negative urine culture.

The study protocol was approved by the hospital's Research Ethics Committee. All patients were duly informed about the study and signed the informed consent form. Ten patients were excluded from the study because they did not return for postoperative assessment.

The TURP was performed according to the standard technique, and the fragments were immediately weighed and further analyzed by the same pathologist.

Outcome measures were IPSS, t-PSA and f/t PSA ratio after 1,3 and 6 months. These parameters in different time points were correlated with preoperative prostatic volume, total volume of tissue resected, percentage of volume resected and the histopathological finding of chronic prostatitis.

The analysis of variance test (ANOVA) and the Turkey's test were used to compare serum PSA level variations at different time points. The Pearson's correlation coefficient was used to evaluate the association between patients' age and the reduction of PSA levels after TURP. The Student's t-test was used to compare PSA level progression in patients with and without chronic prostatitis. The significance level adopted was 5%. Statistical data were analyzed using commercially available software.

## RESULTS

Patients' ages ranged from 46 to 84 years (mean  $67.0 \pm 4$  years). Preoperative IPSS ranged from 18 to 29, mean  $22.5 \pm 2.9$ .

Preoperative t-PSA ranged from 0.79 ng/mL to 33.46 ng/mL, mean  $6.19 \pm 7.06$  ng/mL. Preoperative f/t PSA ratio ranged from 8.3% to 39.0%, mean  $18.2 \pm 4.0\%$ .

Baseline prostatic volume, as measured by TRUS, ranged from 29.0 cc to 130.0 cc, mean  $71.8 \pm 24.0$  cc. Prostate fragments resected weighed from 11 g to 102 g, mean  $29.9 \pm 19.6$  g. In terms of percentage, the volume resected ranged from 21.6% to 78.4%, mean 39.1% (Table-1).

On the histopathological examination, 12 patients (40%) were diagnosed with both benign prostatic hyperplasia and chronic prostatitis, and 18 patients (60%) were diagnosed with benign prostatic hyperplasia only. There were no statistically significant

differences between patients with and without prostatitis regarding age, IPSS, t-PSA, f/t PSA ratio and prostate weight resected (Table-2).

Before surgery, mean I-PSS was  $22.5 \pm 2.9$ . It changed to  $12.6 \pm 2.0$  on day 30,  $11.6 \pm 1.6$  on day 60, and  $11.3 \pm 1.8$  on day 180 following surgery. At all time points assessed after surgery, I-PSS values were lower than in the preoperative period ( $p < 0.001$ ). There were no significant differences in mean IPSS after 1, 3 and 6 months (Figure-1).

Before surgery, mean t-PSA was  $6.19 \text{ ng/mL} \pm 7.06 \text{ ng/mL}$ , decreasing to  $2.27 \pm 2.20 \text{ ng/mL}$  on day 30 (63% reduction from baseline),  $1.75 \pm 1.66 \text{ ng/mL}$  (71% reduction) on day 60, and  $1.79 \pm 1.26 \text{ ng/mL}$  (71% reduction) on day 180 following surgery. A significant difference was observed when preoperative t-PSA was compared with postoperative values on days 30, 60 and 180 ( $p < 0.001$  for all comparisons). A significant difference was also found when t-PSA on day 30 was compared with t-PSA on days 60 and 180 in the postoperative period ( $p = 0.035$ ). There was no statistically significant difference between mean t-PSA on days 60 and 180 (Figure-2). Age was not associated with the decline of PSA levels after TURP at all time points assessed ( $p = 0.151$ ).

Before surgery, mean f/t PSA ratio was  $18.2\% \pm 3.4\%$ , while in the postoperative period, it changed to  $17.8 \pm 8.6\%$  on day 30,  $18.7 \pm 9.9\%$  on day 60, and  $21.0 \pm 7.5\%$  on day 180 (Figure-3). There was no significant difference between preoperative and postoperative f/t PSA ratios at any time point in the postoperative period ( $p = 0.910$ ).

**Table 1** – Baseline values ( $n = 30$  patients).

Variable	Mean $\pm$ SD
Age (years)	$67.0 \pm 4.0$
IPSS	$22.5 \pm 2.9$
T-PSA (ng/mL)	$6.19 \pm 7.06$
F/t PSA (%)	$18.18 \pm 4.03$
Prostate volume (cc)	$71.8 \pm 24.0$
Weight resected (g)	$29.87 \pm 19.58$

**Table 2** – Baseline data, according to the presence of prostatitis.

	With Prostatitis ( $n = 12$ )	Without Prostatitis ( $n = 18$ )	p Value
Age (years)	$64.7 \pm 7.5$	$68.5 \pm 9.0$	0.223
IPSS	$23.2 \pm 3.2$	$22.0 \pm 2.8$	0.336
T-PSA (ng/mL)	$8.1 \pm 10.2$	$4.9 \pm 3.7$	0.342
F/t PSA (%)	$20.4 \pm 9.0$	$22.5 \pm 3.7$	0.451
Weight Resected (g)	$24.9 \pm 12.7$	$33.2 \pm 22.8$	0.216

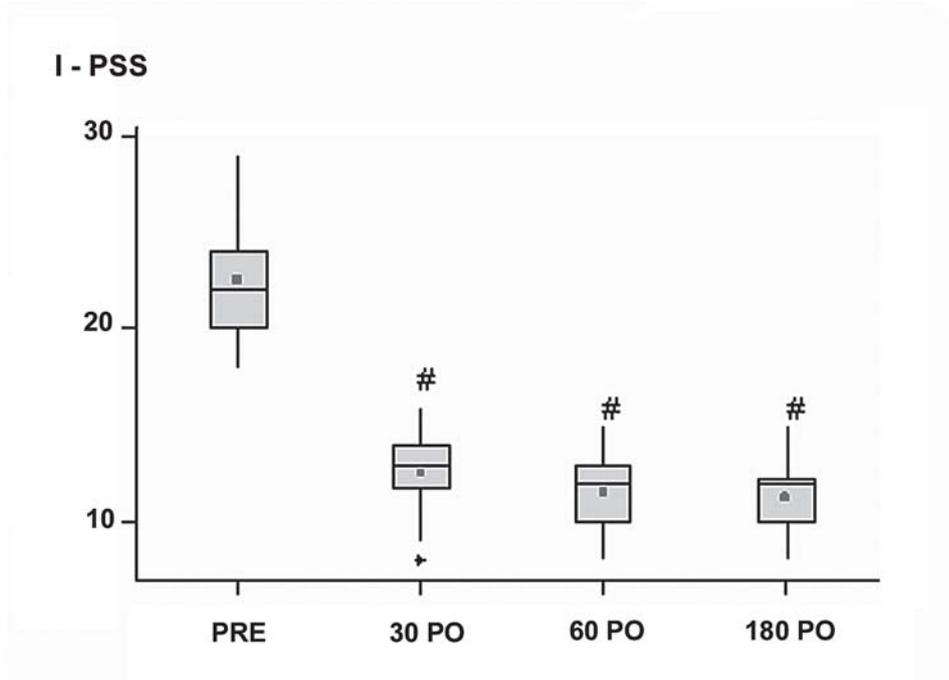


Figure 1 – IPSS at baseline and postoperative days 30, 60 and 180. (# =  $p < 0.001$  compared to preoperative)

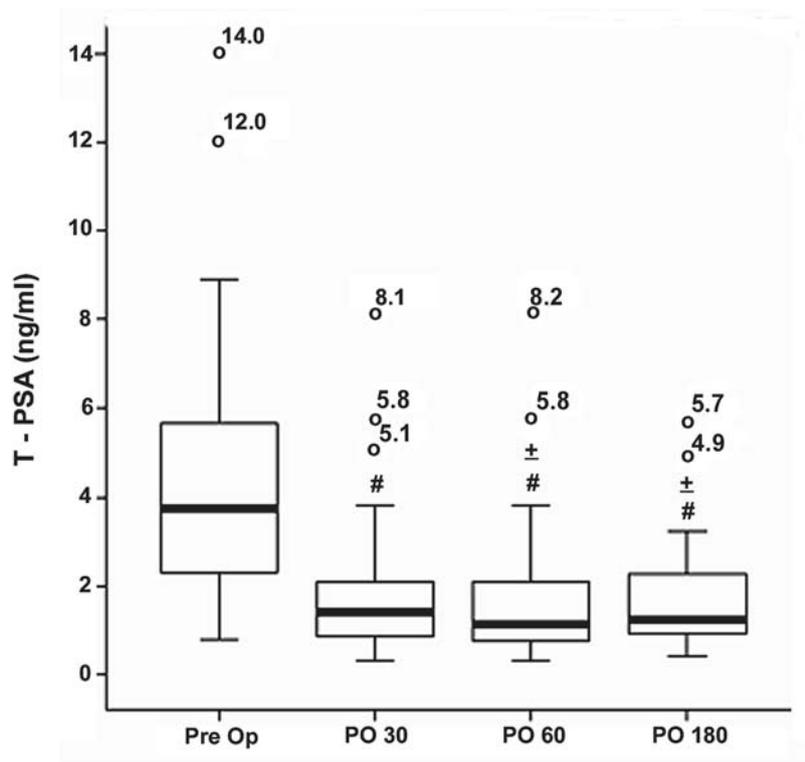


Figure 2 – T-PSA at baseline and postoperative days 30, 60 and 180. (#  $p < 0.001$  compared to preoperative;  $\pm p = 0.035$  compared to PO day 30)

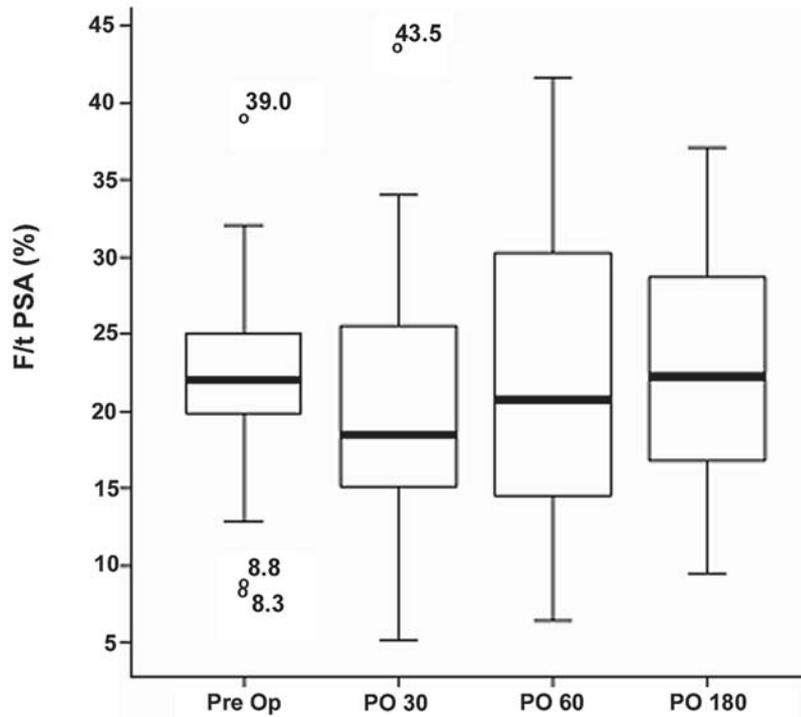


Figure 3 – F/t PSA at baseline and postoperative days 30, 60 and 180.

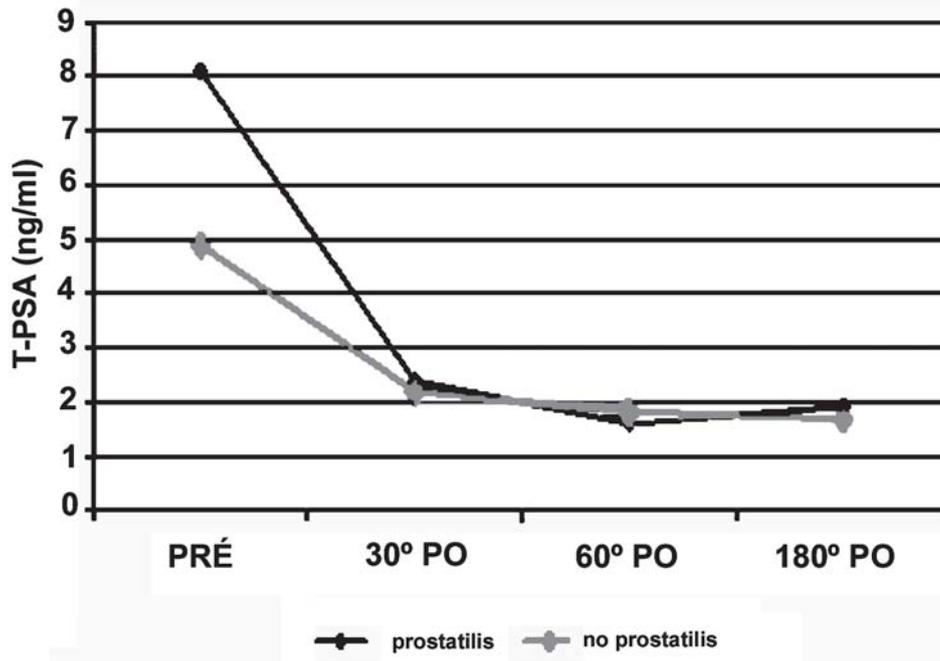


Figure 4 – T- PSA at baseline and postoperative days 30, 60 and 180 in patients with and without prostatitis.

Among the patients with prostatitis, preoperative t-PSA was  $8.1 \pm 10.2$  ng/mL, changing to  $2.4 \pm 2.3$  ng/mL,  $1.6 \pm 1.0$  ng/mL and  $1.9 \pm 0.9$  ng/mL, respectively, on days 30, 60 and 180 following surgery. Among the patients without prostatitis, t-PSA was reduced from  $4.9 \pm 3.7$  ng/mL to  $2.2 \pm 2.2$  ng/mL,  $1.8 \pm 2.0$  ng/mL and  $1.7 \pm 1.5$  ng/mL, respectively, on days 30, 60 and 180 (Figure-4). There was no statistically significant difference on t-PSA reduction between patients with and without prostatitis ( $p = 0.110$ ).

Similarly, f/t PSA ratios in patients with prostatitis did not differ significantly, at any moment, from f/t PSA ratios in patients without prostatitis.

In absolute values, the average reduction in t-PSA (measured at PO 60) was  $4.44 \pm 6.9$  ng/mL, corresponding to a  $71 \pm 22.8\%$  reduction compared to baseline. Mean weight of prostatic tissue resected in the TURP was  $29.9 \pm 19.6$  g, corresponding to  $39.2 \pm 13.8\%$  of the estimate ultrasound preoperative prostate volume. Based on these data, each gram of prostatic tissue resected caused a mean reduction in total serum PSA of  $0.14 \pm 0.11$  ng/mL, while 1% prostate volume resected led to a reduction of  $2.4 \pm 0.4\%$  in serum PSA from baseline.

## COMMENTS

Benign prostatic hyperplasia is one of the most frequent pathologies affecting men, and its prevalence rises progressively after the age of 40. Transurethral resection of the prostate is one of the surgeries most performed in men aged above 50 years. Its effectiveness in relieving symptoms in BPH patients has been extensively documented, and it is considered the gold standard for the treatment of BPH (7).

PSA is a valuable tool in the follow-up of these patients, but it is unknown what is the exact behavior of this marker following TURP; it probably depends on several factors. Vesey et al. (3) published one of the first studies evaluating the impact of TURP on PSA levels. They found a correlation between prostate size and preoperative PSA, noting that there is a temporary rise in PSA levels in the first few days following surgery. Oesterling et al. (8) published similar

results, suggesting that one should wait four to six weeks after TURP to make new PSA measurements. Aus et al. (1) measured PSA levels before surgery and three months after TURP in 190 patients with BPH. Mean PSA decreased 70%. After the TURP, 90% of the patients had PSA  $< 4$  ng/mL and 98% had PSA  $< 10$  ng/mL. The authors concluded that PSA levels should be kept below 4 ng/mL following TURP for BPH.

In a retrospective analysis of patients who developed prostate adenocarcinoma after TURP for BPH, Wolff et al. (9) noted that these patients stabilized their PSA levels above 2.0 ng/mL. Thus, they proposed that patients with either PSA  $> 2.0$  ng/mL or an early rise in PSA following TURP should be checked for prostate cancer.

The population studied in this series was similar to the ones in most of the previous studies in terms of age, symptom severity, free and total PSA, prostate weight and prostate weight resected. Clinical improvement observed following TURP, as measured by I-PSS, was quite significant. One month after surgery, the mean reduction of I-PSS was 44%, stabilizing around 50% within 60 days. Such variation in I-PSS following TURP is consistent with the results reported by other authors (10,11).

In this study, mean PSA before surgery was 6.19 ng/mL. Thirty days after TURP, it decreased to 2.27 ng/mL (63%). After 60 days, it was reduced to 1.75 ng/mL (71% reduction), stabilizing at this level until day 180. This indicates that t-PSA measurement before 60 days may not reflect postoperative PSA nadir, so it is necessary to wait at least 2 months after surgery. Apparently, the low PSA levels found 60 days after surgery are sustained for years, resulting in a population with serum markers similar to those seen in men who did not develop BPH (12).

In this study, f/t PSA ratio did not change following surgery. This observation is consistent with literature findings, which did not show significant variation after TURP (2). In benign prostatic hyperplasia, t-PSA is mainly produced in the transition zone (4). Free PSA is produced in the same proportion in both transition and peripheral zones in these patients. As the transition zone is resected during TURP, there is a significant reduction in t-PSA, but not in free PSA.

As free PSA is not altered after TURP, this parameter can be used to monitor patients after surgery, similarly to what is done in the normal population (2).

Prostate inflammation is a common histological finding in patients with symptomatic BPH without symptoms of chronic prostatitis or history of acute prostatitis. Clinical significance of chronic prostatitis in patients with BPH and its impact on PSA levels are not fully understood (13). Kiehl et al. (6) studied the effect of chronic prostatitis on PSA levels and demonstrated that, when the inflammatory process reaches glandular epithelial cells, serum PSA levels rise above cutoff values. They also noted that increased PSA levels were directly proportional to the severity of the inflammatory process. This increase in total prostate-specific antigen levels is well established in literature in patients with acute prostatitis, but there are controversies regarding chronic prostatitis, whose influence on PSA levels is not fully understood (14,15). In this study, 12 (40%) patients had histologically defined chronic prostatitis. There was no difference between patients with and without prostatitis concerning age, symptom severity (as measured by I-PSS), mean t-PSA and f/t PSA. The comparison of t-PSA and f/t PSA levels in patients with and without prostatitis on days 30, 60 and 180 following surgery did not show significant differences between the groups. However, due to the limited size of the studied population, only compelling differences would have been shown and we cannot affirm that the presence of chronic prostatitis does not affect serum t-PSA and f/t PSA levels before and after TURP. Additionally, we did not evaluate the epithelial cell inflammation and the severity of the inflammatory process, which, according to Kiehl et al., (4) are the main aspects of chronic prostatitis that can affect PSA.

Stamey et al. (16), estimated that each gram of prostatic tissue resected reduces PSA levels by 0.3 ng/mL. Lloyd et al. (17) analyzed preoperative prostate volume, adenoma volume and the amount of tissue resected, finding a reduction of 0.09 ng/mL in serum PSA. We found a reduction of 0.14 ng/mL  $\pm$  0.2 ng/mL per gram of prostatic tissue resected in our patients. Marks et al. (5) found a mean reduction of 0.11 ng/mL in PSA per gram of prostatic tissue

resected. The differences among different series appear to be secondary to differences in patient populations as well as technical changes in PSA measurement methods, which used to be enzymatic, but have changed to radioimmunoassay in the last 15 years.

In terms of percentage, TURP has led to a 71% decrease in PSA in our series, corresponding to a mean reduction of 2.4% per each 1% of prostate volume resected. We did not find in medical literature the estimates of PSA reduction based on the percentage of prostatic tissue resected, and we believe it could be a quite useful parameter because it allows for the prediction of mean PSA reduction based on two parameters that may independently affect postoperative PSA, namely, the preoperative prostate volume and the prostate volume resected.

## CONCLUSIONS

Our results confirm that PSA levels are clearly reduced after TURP, stabilizing after 2 months. Free PSA does not change after surgery, and the presence of chronic prostatitis does not affect postoperative progression of t-PSA and f/t PSA levels. There is not an absolute serum PSA value below which patients undergoing TURP can be surely free of developing cancer, because postoperative PSA depends on several factors like preoperative PSA, prostate volume and prostate volume resected. However, PSA reduction may be estimated based on preoperative prostate volume and prostate volume resected.

## CONFLICT OF INTEREST

None declared.

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