Does Rigid Cystoscopy Affect the Total Serum Prostate-Specific Antigen Levels?

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Abstract In the present study, we aim to prospectively evaluate the effect of performing rigid cystoscopy (CPE) in urological patients on the total serum prostate-specific antigen (PSA) levels. The study design was a prospective observational study. After giving informed consent, urological patients visiting the outpatient clinic of our institution from November 2010 to March 2012 who satisfied our protocol entry/exclusion criteria were recruited into the present study. Blood sample was withdrawn 1 h prior to CPE for serum PSA estimation, and CPE was performed

with a 17-Fr rigid cystoscope. Blood was again withdrawn at 1 and 24 h after CPE for serum PSA estimation. The study used paired samples test (two tailed) for statistical analysis. A total of 50 patients with mean age of 60 years underwent CPE. The baseline, 1-h, and 24-h post CPE mean serum PSA levels were 1.98 ± 2.25 (0.02–12.33), 2.90 ± 2.81 (0.3–14.26), and 3.04 ± 2.95 (0.2–15.03) ng/dl, respectively. The paired samples test (two tailed) revealed that the rise in the baseline PSA versus 1-h PSA and baseline PSA versus 24-h PSA was highly significant at $P < 0.001$ and $P < 0.002$, respectively; however, the 1-h PSA versus 24-h PSA rise was not so significant ($P < 0.043$). The present study demonstrated that rigid cystoscopy may be associated with a variable rise in the serum PSA that may persist for a period of up to or beyond 24 h. Thus, we believe that the history of recent cystoscopy must be taken into consideration while interpreting the serum PSA value in the routine urological setting, as this will reduce unnecessary prostate biopsies in patients with an elevated serum PSA. Therefore, it may be advisable to wait for 24–48 h before withdrawing blood for serum PSA estimation in patients with history of CPE in the previous 24–48 h.

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Key messages: This study was a prospective observational study designed to evaluate the effect of routine office rigid cystoscopy on the serum PSA levels which was conducted on 50 consecutive urological patients. This study demonstrates that cystoscopy may elevate serum PSA levels for up to at least 24 h. Thus, one must wait for 1–2 days for prior to estimating serum PSA levels in patients, particularly in those with a recent history of cystoscopy. There are variable data presented in the published English literature (PubMed™) on the effect of cystoscopy on serum PSA levels.

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Introduction

Serum prostate-specific antigen (PSA) is produced by benign/malignant prostatic epithelial cells and serves to cause liquefaction of the seminal fluid [1], and disruption of cellular architecture within the prostate gland can increase PSA levels [2]. Although present in large amount in prostate tissue and semen, PSA has also been detected in other body fluids and tissues. Serum PSA levels may be elevated in

Table 1 Statistical analysis (by paired samples two-tailed test) of the serum total PSA levels 0, 1, and 24 h after cystoscopy

	Mean	No.	Std. deviation	Standard error of the mean
Variance 1	1.9820	50	2.25989	0.31960
Variance 2	2.9004	50	2.81988	0.39879
Variance 3	3.0488	50	2.95127	0.41737

Variance 1 serum t PSA at 0 h (baseline), *Variance 2* serum t PSA at 1 h after CPE, *Variance 3* serum t PSA at 24 h after CPE

prostate diseases, prostatic manipulations, and urological diagnostic and therapeutic procedures. Since PSA estimation is frequently used in conjunction with digital rectal exam (DRE) for early diagnosis and management of prostate cancer, it is used as a tumor marker for early detection, screening, staging, and posttreatment monitoring of patients with suspected prostate cancer. Thus, it is necessary to study the effect of various factors (CPE) on serum PSA levels that may impact its interpretation. The precise impact of CPE on serum PSA is also not well defined in the literature. In this study, we attempt to prospectively evaluate the effect, if any, of rigid cystoscopy on the serum PSA levels in urological patients. We believe this may help in better interpretation of false positives in patients with elevated serum PSA levels. To the best of our knowledge, we could not locate any similar Indian study in the published English literature (PubMedTM). This forms the rationale for undertaking the present study.

Methods

After obtaining institutional ethics clearance and administering an informed consent, a prospective observational study was undertaken in the outpatient clinic of our institution from November 2010 to March 2012. Patients satisfying our entry criteria (all adults 40–80 years of age with urological complaints warranting a cystoscopy) were enrolled into the current study. Patients with active or untreated urinary tract infection,

recent history of sexual activity/ejaculation in the preceding 1 week, history of drug therapy (antiandrogens and/or alpha-blockers), history of transurethral resection of the prostate (TURP) and prostatic biopsy in the preceding 6 weeks, history of DRE in the preceding 1 week, and patients with diagnosed prostate cancer were excluded from the present study. Venous blood (2 ml) was withdrawn 1 h prior to cystoscopy and was sent for serum PSA assay. About 10 ml of 2 % xylocaine jelly was pushed through the meatus. Diagnostic rigid cystoscopy was performed using a 17-Fr compact-type rigid cystoscope in OT in the usual manner. After performing rigid cystoscopy, 2 ml of venous blood was again withdrawn 1 and 24 h after the cystoscopy. All blood samples withdrawn were sent for serum total PSA estimation.

The specimens were centrifuged to separate the serum from the cells and stored at 2–8 °C till assay. All serum samples were assayed within 48–72 h of their being withdrawn. All samples were quantitatively analyzed by a microplate immunoassay technique using an enzyme-linked immunosorbent assay (ELISA) kit (Weldon Biotech) [3, 4]. Each ELISA titer plate contained 96 wells for PSA testing. The standard laboratory reference range for serum PSA of 0–4.0 ng/ml was used in this study. Statistical significance of differences between means of total serum PSA levels was determined by Student's *t* test, and paired *t* test was used to compare serum PSA levels before and at 1/24 h after cystoscopy. $P < 0.05$ was considered to be statistically significant. In patients with serum PSA levels > 4 ng/ml, prostatic biopsy was performed to rule out prostate cancer. All the patients were found to be negative for prostate cancer and had evidence of benign prostatic hyperplasia (BPH).

Results

Our study was conducted on a total of 50 patients (40–80 years with mean age of 60 years) with urological complaints for which cystoscopy was warranted in 19, 14, 9, 8, and 1 patient for evaluation of BPH, hematuria, urethral

Table 2 Statistical comparison of total serum PSA levels at 0 and 1 h after cystoscopy

	Paired differences					<i>t</i>	<i>df</i>	Significance (two tailed)
	Mean	Standard deviation	Standard error of the mean	95 % Confidence interval of the difference				
				Lower	Upper			
Variance 1–variance 2	−0.91840	1.49726	0.21174	−1.34392	−0.49288	−4.337	49	0.000

df degrees of freedom, *Variance 1* serum tPSA at 0 h (baseline), *Variance 2* serum tPSA at 1 h after CPE

Table 3 Statistical comparison of total serum PSA levels at 0 and 24 h post CPE

	Paired differences					<i>t</i>	<i>df</i>	Significance (two tailed)
	Mean	Standard deviation	Standard error of the mean	95 % Confidence interval of the difference				
				Lower	Upper			
Variance 1–variance 3	−1.06680	1.55224	0.21952	−1.50794	−0.62566	−4.860	49	0.000

CPE cystoscopy, *df* degrees of freedom, *Variance 1* serum tPSA at 0 h (baseline), *Variance 3* serum tPSA at 24 h after CPE

stricture, recurrent urinary tract infection, and nocturnal enuresis, respectively.

The paired samples statistics, correlation, and *t* test are depicted in Tables 1 to 3. The serum total PSA (tPSA) was measured before (0 h) and 1 and 24 h after performing rigid cystoscopy. Serum tPSA at 0 h was 0.02–12.33 ng/ml (mean, 1.9820 ± 2.25989), whereas the serum tPSA was 0.3–14.26 ng/ml (mean, 2.9004 ± 2.8198) 1 h after cystoscopy and 0.2–15.03 ng/ml (mean, 3.0488 ± 2.95127) 24 h after CPE, as depicted in Table 1.

The mean serum tPSA values at 0 and 1 h following cystoscopy were compared using two-tailed paired *t* test to find out the significance of differences between the values, and a mean rise of -0.91840 was noted in serum PSA value, as depicted in Table 2.

The change in serum PSA value at 1 h after rigid cystoscopy was found to be highly significant as the *P* value was 0.000 ($P < 0.05$). Serum PSA value at 0 h was compared with PSA at 24 h following cystoscopy, and the mean change of -1.06680 was noted in serum PSA values which was found to be highly significant as the *P* value was 0.000 ($P < 0.05$), as shown in Table 3. A summary depiction of the effect of CPE on serum PSA levels is given in Fig. 1.

Discussion

Although PSA is mainly present in the prostate tissue and semen, it has also been detected in malignant breast tumors [5–7], normal breast tissue [8], breast milk [9], and adrenal and renal carcinomas [10]. Serum PSA levels may be increased in BPH [11, 12], prostatitis [12], prostate cancer [13], and following prostate biopsy/massage [14], DRE [15, 16], colonoscopy [17], and cystoscopy [18]. Serum PSA has been traditionally used as a diagnostic tool in conjunction with DRE for the early diagnosis and management of prostate cancer. Studies on the effect of ejaculation on serum PSA have shown either insignificant change [19] or a significant decrease in serum PSA [20, 21] in younger patients, whereas they showed an increase in serum PSA in older patients [22, 23]. Finasteride (5 mg) and other 5- α -reductase inhibitors have been shown to lower PSA levels by an average of 50 % after 6 months of treatment [24].

Therefore, interpretation of PSA levels should always consider the presence of prostate diseases, previous diagnostic and therapeutic procedures, and prostate-directed treatments because these may alter serum PSA levels. Data from prior studies evaluating PSA change in relation to

Fig. 1 A graphic depiction of the serum PSA levels at baseline (a), at 1 h postcystoscopy (b), at 24 h postcystoscopy (c), and the comparative overall effect of cystoscopy at various intervals on serum PSA levels (d)

Table 4 A review of salient features of the various published studies evaluating the effect of cystoscopy/prostate manipulation on the serum PSA levels

No.	Reference	Study	Conclusion
1.	Rodriguez-Rubio et al. [18]	Effect of DRE and flexible CPE on free and total PSA and % free PSA in 67 men	Fourfold ↑ in serum PSA values
2.	Lynn et al. [25]	Effect of prostatic manipulation/DRE/Flex CPE/prostate biopsy in 92 men on serum PSA level	No significant rise in complexed PSA levels while tPSA ↑ significantly
3.	Dew T et al. [26]	Effect of flexible and rigid CPE, TRUS and TURP on serum PSA in 60 men	Statistically significant variable rise in serum PSA 1 day post rigid cystoscopy
4.	Deliveliotis et al. [27]	Influence of CPE, TRUS, DRE, and prostate biopsy on serum PSA levels in 170 men	No significant effect on serum PSA levels
5.	Long et al. [28]	Effect of prostatic manipulations on tPSA and cPSA levels in 113 men	Statistically significant difference in tPSA. cPSA is less prone to variations compared to tPSA.
6.	Bastani et al. [29]	Effect of CPE on tPSA level in 190 men	tPSA ↑ after CPE and is higher in men with urinary retention
7.	Oesterling et al. [30]	Effect of CPE, prostate biopsy, and TURP on tPSA levels in 101 men	No significant change in tPSA level after CPE. tPSA after flexible/rigid CPE is accurate and reliable.
8.	Collins et al. [31]	Effect of DRE/Flex CPE/TRUS on free/tPSA and free/total PSA ratio in 82 men	Significant ↑free/total PSA ratio after each maneuver. No significant ↑ tPSA after CPE
9.	De Castro and Baker [32]	Effect of flexible CPE on tPSA in 40 men	Statistically significant difference in t/free/% free PSA. None clinically significant.
10.	Rezakhaniha et al. [33]	Effect of rigid CPE on tPSA in 102 men	No/insignificant effect on PSA
11.	Lin et al. [34]	Effect of DRE, prostate biopsy, TURP urethral catheterization, suprapubic prostatectomy, and rigid CPE on tPSA/fPSA/t:tPSA in 160 men	DRE, catheterization, and CPE had no crucial effect on tPSA.
12.	Present study	Effect of rigid CPE on tPSA levels in 50 men	Significant rise in serum PSA levels up to 48–72 h after rigid cystoscopy

DRE digital rectal examination; CPE cystoscopy, tPSA total serum PSA, cPSA complexed PSA, fPSA free PSA

cystoscopy have shown variable results, as serum PSA level may either increase or remain the same following cystoscopy. We believe, while it is well accepted, that no urologist may consider an elevated PSA after CPE to be pathological; nevertheless, there is scarcity in published studies evaluating the precise effect of rigid cystoscopy on serum PSA levels, as a recent review of literature suggests that the serum PSA level may increase or remain unaltered following rigid cystoscopy (Table 4) [18, 25–34]. While the effect of rigid cystoscopy on serum PSA has not been clearly defined in the published literature (Table 4), in our study, we observed a significant rise in the serum PSA levels both at 1 and 24 h following cystoscopy. Urological conditions necessitating cystoscopy may alter the levels of serum PSA, and we believe that this ought to be taken into consideration while evaluating serum PSA levels for diagnosis of any prostate disease (BPH, prostate cancer) in order to avoid false positives.

The current study demonstrated a rise in serum PSA levels at 1 and 24 h following rigid cystoscopy. This increase in serum PSA was seen to be statistically highly significant with a *P* value of 0.000 (*P*<0.05). Therefore, we believe that one should postpone the estimation of serum PSA levels by at least 24 h particularly in patients with a history of recent cystoscopy in the previous 24–48 h. The

present study was limited by its small size and by lack of symptomwise stratification of patients with various urological disorders, as we believe that these too may have impacted the serum PSA levels.

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