

Serum Levels of Prostate Specific Antigen Are Elevated after Colonoscopy

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The risks of prostate cancer and colorectal carcinoma increase with age. So, colonoscopy and measurement of serum prostate specific antigen (PSA) may be performed during a short term in a given patient. We aimed to evaluate whether colonoscopy affects serum PSA levels and to evaluate the relationship between prostate volume and elevation in serum PSA levels after colonoscopy. This study included 44 consecutive male patients, who underwent colonoscopy. The mean age of the patients was 56.05 ± 9.27 years. The mean time required for colonoscopy was 30 min. Serum PSA levels were measured 48-72 hours before colonoscopy, immediately after performing laxative enema, and at 24-48th hour, the 7th day, and the 14th day after colonoscopy in each patient. The serum PSA level was elevated after enema and at 24-48th hour and 7th day after colonoscopy from the baseline ($p < 0.05$), and declined to the baseline by 14th day. When the cut off value of 20 cm³ for normal prostate volume was taken into account, the serum PSA levels were significantly higher at the 24-48th hour and the 7th day in patients with larger prostate volume (> 20 cm³) than those with normal prostate volume ($p = 0.013$ and $p = 0.009$). These results suggest that PSA is easily released by manipulations from the larger prostate. In conclusion, serum PSA levels were elevated during 7 days after colonoscopy. Before performing invasive procedures, patients with high serum PSA levels should be asked whether colonoscopy was performed prior to the measurement.

Keywords: PSA level; colonoscopy; cancer screening; prostate cancer; colon cancer

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Prostate specific antigen (PSA) is a 33-kDa glycoprotein that contains 7% carbohydrate and acts as a serine protease. It is secreted from ductal and aciner epithelium of the prostate (Oesterling 1991). The main function of PSA is the liquefaction of the seminal fluid. Normally, less than 1% of the secreted PSA is released to the circulation (Lilja et al. 1991; Mikolajczyk et al. 2002). Serum PSA level is used as a tumor marker in the screening and monitoring of prostate cancer (Björk et al. 1996; Partin et al. 2002). It is recommended that serum PSA level to be measured annually after the age of 50 years in low risk men and after the age of 40 years in high-risk men along with rectal examination in the screening of prostate cancer (American Urological Association 1992; Mettlin et al. 1993).

Elevation in serum PSA level is due to the leakage of PSA to the circulation which results from any injury to the prostate gland or defects in the basal membrane barrier. Serum PSA level increases as a result of benign prostate

hyperplasia (BPH), prostatitis and manipulations to the prostate (i.e. prostate massage, prostate biopsy, urethral catheterization, transrectal ultrasonography) as well as prostate cancer. Although rectal examination causes elevation in serum PSA level, it is not clinically significant and rarely leads to false positivity. Elevation in serum PSA level after traumas, such as prostate biopsy, normalizes within 4 weeks (Crawford et al. 1992; Oesterling et al. 1993; Tarhan et al. 2005). In fact, PSA is eliminated from plasma by the liver. Serum half-life of PSA is 2 to 3 days after prostatectomy. Free PSA is eliminated by the kidneys within 2 to 3 days, too (Stamey et al. 1987; Oesterling et al. 1988).

Currently, colonoscopy is frequently performed in the diagnosis and treatment of colonic diseases. The risk of prostate cancer increases with age and serum PSA level is frequently measured in this aging population. As colonic diseases, such as colon cancer, increase with age, colonoscopy is also performed frequently. So, colonoscopy and

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measurement of serum PSA level may be performed during a short term in a given patient. Although there is a report (Oesterling et al. 1993) evaluating the effects of diagnostic urinary procedures on serum PSA levels, there are no established data whether colonoscopy has any effect on serum PSA levels. The results of studies in this field are controversial (Schwartz et al. 1999; Barbatzas et al. 2004).

We aimed to evaluate whether colonoscopy has any effect on serum PSA levels. We also aimed to evaluate the relationship between prostate volume and elevation in serum PSA levels and normalization time of serum PSA levels after colonoscopy if colonoscopy causes elevation in serum PSA levels.

Methods

Forty-four consecutive male patients, in whom colonoscopy was performed in our endoscopy unit, were enrolled in this study. Patients who had a history of prostate cancer, prostatectomy, bilateral orchiectomy, prostate biopsy, urologic procedure 30 days prior to the colonoscopy, transrectal ultrasonography, rectal examination 7 days prior to the colonoscopy, or current antiandrogen or 5 alpha reductase inhibitor therapy were excluded. Patients, in whom colonoscopy procedure took a long time period (i.e. polypectomy) and in whom any manipulation was performed to the rectum, were also excluded.

Serum PSA levels were measured 48-72 hours prior to the colonoscopy, immediately after performing laxative (phosphate) enema, at the 24-48th hour after the colonoscopy, on the 7th day and on the 14th day after the colonoscopy in each patient. Serum PSA levels were measured with chemiluminescence method using Beckman DXI 800[®] analyser (Beckman Coulter Hybritech PSA, Ireland). The normal ranges of PSA level was 0-4 ng/ml. Bowel cleansing was done using polyethylene glycol + sodium sulphate + sodium bicarbonate + sodium chloride + potassium chloride (Golytely[®]) solution in 4 L water one day prior to the colonoscopy. Midazolam (2-3 mg) and pethidine (20-30 mg) were intravenously administered to all patients during colonoscopy. Colonoscopy was performed by a single endoscopist using 40 F flexible colonoscope. Distal rectum was examined via retroflexion maneuver in all patients. Time period was obtained for each

colonoscopy procedure. All patients underwent transrectal ultrasonography to evaluate prostate volume by a single radiologist at the 14th day after the colonoscopy.

Written informed consent was taken from all patients. The study was approved by Haydarpaşa Numune Education and Research Hospital ethic committee

Statistical analysis

Statistical analysis was performed with NCSS (Number Cruncher Statistical System) 2007 program for Windows. Levene's test was used to determine whether PSA variable showed normal distribution and then statistical analysis was performed with logarithmic transformation. Besides standard descriptive statistical calculations (e.g. geometric mean and median (IQR)), repeated measures of ANOVA were used to determine the differences in measurement in each group at each time point. When $p < 0.05$, student Newman Keuls multiple comparisons tests were used for pairwise comparisons. The results were evaluated within a 95% confidence interval. Statistical significance level was established at $p < 0.05$.

Results

Totally, 44 male patients were included in this study. The mean age of the patients was 56.05 ± 9.27 years. The mean time used for colonoscopy was 30 min (20-45 min).

The PSA levels before colonoscopy, after enema, and at the 24-48th hour, the 7th day and the 14th day after colonoscopy were 0.87 ± 1.75 , 1.03 ± 1.81 , 0.98 ± 1.68 , 0.93 ± 1.84 and 0.90 ± 1.84 ng/ml, respectively (Fig. 1). Basal serum PSA levels were significantly lower than the levels at postenema, the 24 - 48th hour and the 7th day ($p = 0.006$, $p = 0.036$, and $p = 0.039$, respectively). Importantly, the serum PSA levels were returned to the basal levels after 14 days (Table 1).

When the cut off value of 20 cm^3 for normal prostate volume was taken into account (Edwards 2008), the PSA levels before colonoscopy, after enema, and at the 24-48th hour, the 7th day and the 14th day after colonoscopy were 0.71 ± 1.75 , 0.88 ± 1.81 , 0.75 ± 1.68 , 0.71 ± 1.85 , and 0.73 ± 1.84 ng/ml in patients with normal prostate volume,

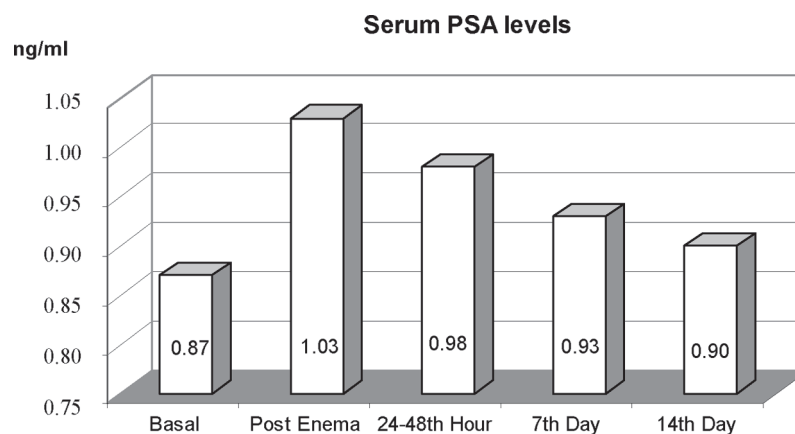


Fig. 1. Time-dependent changes in serum PSA levels.

Serum PSA levels (ng/ml) were elevated during 7 days after colonoscopy and then gradually decreased to the baseline level at the 14th day.

respectively (Table 2). They were 0.87 ± 1.67 , 1.04 ± 1.85 , 0.98 ± 1.52 , 1.05 ± 1.75 , and 1.01 ± 1.91 ng/ml in patients who had a prostate volume $> 20 \text{ cm}^3$, respectively. Thus, the serum PSA levels before colonoscopy, postenema, and at the 14th day after colonoscopy were similar between the two groups of patients (Table 2). In contrast, the serum PSA levels were significantly higher at the 24-48th hour and the 7th day in patients who had a prostate volume $> 20 \text{ cm}^3$ than those with normal prostate volume of $\leq 20 \text{ cm}^3$ ($p = 0.013$ and $p = 0.009$) (Table 2).

In summary, serum PSA levels were increased after enema and colonoscopy when compared to the baseline levels. However, the serum PSA level did not reach 4 ng/dL, a cut off value for prostate cancer, except for 2 patients (4.55%). The serum PSA levels of these 2 patients were close to 4 ng/dL prior to the colonoscopy. These patient's prostat volumes were 27 and 30 cm^3 .

Discussion

Prostate cancer and colorectal cancer are among the most common cancers in American men (Jemal et al. 2009).

Table 1. Comparison of serum PSA levels before and after colonoscopy.

	<i>p</i>
Basal vs Postenema	0.006
Basal vs 24-48 th hour	0.036
Basal vs 7 th day	0.039
Basal vs 14 th day	0.096
Postenema vs 24-48 th hour	0.130
Postenema vs 7 th day	0.054
Postenema vs 14 th day	0.357
24-48 th hour vs 7 th day	0.484
24-48 th hour vs 14 th day	0.600
7 th day vs 14 th day	0.305

The differences in serum PSA levels were statistically significant between baseline and postenema, baseline vs 24-48th hour, and baseline vs 7th day. The difference in serum PSA levels between baseline and 14th day was not statistically significant. The comparison was made with Newman Keuls multiple comparison tests.

Approximately 146,970 new cases of colorectal cancer (CRC) are diagnosed each year in the United States, of which 106,100 are colon and the remainder are rectal cancers (Jemal et al. 2009). Approximately 49,920 Americans die of CRC each year. In Turkey, prostate cancer is the 2nd most common cancer in men, whereas CRC is the 6th (<http://kanser.gov.tr/folders/file/kanser.pdf>). CRC is infrequent before age 40; however, the incidence increases progressively thereafter to 3.7/1000 per year by age 80. The lifetime incidence for patients at average risk is 5%, with 90% of cases occurring after age 50 (<http://seer.cancer.gov/statfacts/html/colorect.html>). Removal of premalignant adenomas can prevent the development of colorectal cancer and removal of localized cancer can prevent CRC-related deaths. Screening tests allow physicians to detect premalign adenomatous polyps, and early stage CRCs and to remove them.

In both prostate cancer and colon cancer, there are several tools to diagnose in earlier stages. Colonoscopy is the procedure of choice in the diagnosis of CRC especially in high risk population. On the other hand, digital rectal examination and serum PSA level measurement are the initial diagnostic methods in the evaluation of patients those are suspected to have prostate cancer.

Because CRC and prostate cancer are the diseases of aging population, screening and diagnostic studies for each disease can be performed in close time period in any given patient. It is suggested that colonoscopy may affect the serum PSA level. So, when measured soon after colonoscopy, serum PSA level may be falsely positive. This may lead clinicians to perform unnecessary invasive and expensive procedures.

In the present study, it seems possible that serum PSA levels can be affected by both laxative enema and colonoscopy. Serum PSA levels remained high until the 7th day after colonoscopy and decreased to basal level at the 14th day. Serum PSA levels were observed to increase more significantly in patients with high prostate volume. Because leakage of PSA to the circulation occurs as a result of rupture of the basal membrane of the secretory epithelium, high prostate volume might lead to higher elevations in serum PSA level in these patients. It was reported that serum PSA levels could fluctuate day by day in a ratio of

Table 2. Serum PSA levels and prostate volume.

	$\leq 20 \text{ cm}^3$	$> 20 \text{ cm}^3$	<i>p</i>
	PSA levels (ng/ml)	PSA levels (ng/ml)	
Basal	0.71 ± 1.75	0.87 ± 1.67	0.114
Postenema	0.88 ± 1.81	1.04 ± 1.85	0.073
24-48 th hour	0.75 ± 1.68	0.98 ± 1.52	0.013
7 th day	0.71 ± 1.85	1.05 ± 1.75	0.009
14 th day	0.73 ± 1.84	1.01 ± 1.91	0.053

Comparison of serum PSA levels before and after colonoscopy between patients with prostate volume $\leq 20 \text{ cm}^3$ ($n = 16$) and those with $> 20 \text{ cm}^3$ ($n = 28$).

30% (Crawford et al. 1996). However, the increase in serum PSA levels on the 7th day and the decline to the basal levels on the 14th day support that this elevation might be the result of colonoscopy itself rather than daily fluctuations.

The results of previous studies evaluating the effect of colonoscopy on serum PSA level were controversial. Schwartz and colleagues measured the serum PSA levels in 24 patients at the 24th hour, on the 7th and 30th days after colonoscopy and suggested that colonoscopy did not affect serum PSA levels (Schwartz et al. 1999). In another study, Barbatzas et al. (2004) measured serum PSA levels at the 24th hour, on the 7th and 30th days after colonoscopy and reported that colonoscopy increased serum PSA levels. But, these studies did not evaluate the relationship between prostate volume and serum PSA levels. The more significant elevations in serum PSA levels after colonoscopy in patients with high prostate volume suggest that serum PSA levels are affected more easily by manipulations in these patients.

In conclusion, both colonoscopy and serum PSA measurement are frequently performed screening methods. It must be kept in mind that serum PSA level may be high following 7 days after colonoscopy in comparison with baseline level. When evaluating patients with high serum PSA level, they should be asked whether colonoscopy was performed prior to the measurement. If yes, serum PSA levels should be repeated 14 days after colonoscopy before deciding prostate biopsy. This may preclude unnecessary invasive procedures.

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