Effects of prostate manipulation on serum total and free prostate specific antigen, and free-to-total prostate specific antigen ratio

Yun-Hua Lin, MM, Yong-Guang Jiang, MD, Ming-Chuan Li, MM, Yong Luo, MD, Jun-Sheng Wang, BM.

ABSTRACT

الأهداف: دراسة آثار الطرق المختلفة لمعالجة البروستاتا على مولدات الأجسام المضادة الحرة داخل البروستاتا (fPSA) وكذلك على مجموع مولدات الأجسام المضادة داخل البروستاتا (tPSA) بالإضافة إلى تأثيرها على نسبة المولدات الحرة إلى مجموع المولدات داخل االبروستاتا (f/tPSA).

الطريقة: لقد شملت الدراسة 160 ذكراً وذلك خلال الفترة من يناير 2006م إلى ديسمبر 2009م في مستشفى أنزين التابع للجامعة الطبية، بكين، الصين. خضع 23 مريضاً من هؤلاء المرضى للفحص الشرجي (DRE)، و21 مريضاً لقسطرة الاحليل، و28 مريضاً لتنظير المثانة، فيما تم أخذ عينة من البروستاتا لتشريحها من 35 مريضاً، وخضع 35 مريضاً لعملية قطع البروستاتا عن طريق الاحليل (TURP)، و18 مريضاً خضعوا لاستئصال البروستاتا فوق العانة. سُحبت عينات الدم من المرضى قبل هذه العمليات وتمت مقارنتها بعينات الدم المأخوذة بعد هذه العمليات بأربع وعشرين ساعة وبعدها بأربع أسابيع.

النتائج: لم يكن للفحص الشرجي تأثيراً واضحاً على مولدات الأجسام المضادة داخل البروستاتا، فيما أدت القسطرة وتنظير المثانة إلى زيادة واضحة في مجموع مولدات الأجسام المضادة داخل البروستاتا بعد العملية بأربع وعشرين ساعة، غير أن هذه الزيادة الطفيفة قد لا تكون مهمة من الناحية السريرية، فيما لم يتغير كثيراً معدل مولدات الأجسام المضادة الحرة وكذلك نسبة المولدات الحرة إلى مجموع المولدات. أظهر تشريح البروستاتا تغيراً واضحاً في معدل مولدات الأجسام المضادة الحرة ومجموع الأجسام المضادة مع نقص في نسبة المولدات الحرة إلى مجموع المولدات بعد هذه العملية بأربع وعشرين ساعة. ولم يتغير معدل مولدات الأجسام المضادة الحرة ومجموع مولدات الأجسام المضادة ونسبة هذه المولدات لبعضها البعض بعد عمليات القسطرة، وتنظير المثانة والتشريح بأربع أسابيع. لقد أدى قطع البروستاتا عن طريق الاحليل واستئصال البروستاتا فوق العانة إلى زيادة واضحة في معدل هذه المولدات مع نقص في نسبة هذه المولدات لبعضها البعض وذلك بعد العملية بأربع وعشرين ساعة، ولكن أصبحت هذه المولدات أقل من معدلها الطبيعي بعد القطع والاستئصال بأربع أسابيع فيما ظلت نسبة هذه المولدات لبعضها البعض ثابتة.

خاتمة: لم يكن للفحص الشرجي، وقسطرة الاحليل، وتنظير المثانة أثراً كبيراً على معدل مولدات الأجسام المضادة داخل البروستاتا. فيما أثر التشريح، وقطع البروستاتا عن طريق الاحليل واستئصال البروستاتا تأثيراً واضحاً على هذه المولدات، واعتماد طرق العلاج هذه لمدة طويلة يجب أن يؤخذ بعين الاعتبار وذلك عند تقييم المستويات المختلفة التي يصل إليها معدل مولدات الأجسام المضادة داخل البروستاتا.

Objectives: To evaluate the effects of the different types of manipulation on prostate total specific antigen (tPSA), free prostate specific antigen (fPSA), and free-to-total prostate specific antigen (f/tPSA).

Methods: A total of 160 males were enrolled from January 2006 to December 2009 in the Urology Department, Beijing Anzhen Hospital affiliated to the Capital Medical University, Beijing, China. Of these patients, 23 had digital rectal examination (DRE), 21 had urethral catheterization, 28 had rigid cystoscopy, 35 had prostate biopsy, 35 underwent transurethral resection of the prostate (TURP), and 18 underwent suprapubic prostatectomy. Blood samples were taken before, at 24 hours, and 4 weeks after the manipulation for PSA tests.

Results: The DRE had no significant effect on PSA. Catheterization and cystoscopy exerted significant increases in tPSA at 24 hours. However, these small increases may not be clinically significant. The fPSA and f/tPSA were not significantly changed. There was a marked increase in tPSA and fPSA, associated with a decrease in f/tPSA at 24 hours after biopsy. No significant alterations were found in tPSA, fPSA, and f/tPSA at 4 weeks after catheterization, cystoscopy, and biopsy. The TURP and prostatectomy caused significant increases in tPSA and fPSA at 24 hours, associated with decreases in f/tPSA. The tPSA and fPSA values were below the baseline levels at 4 weeks after TURP and prostatectomy, however, f/tPSA remained constant.

Conclusion: The DRE, catheterization, and cystoscopy had no crucial effect on PSA. Prostatic biopsy, TURP and prostatectomy significantly affected the PSA levels, and their longitudinal courses should be considered while evaluating different forms of PSA levels.

Saudi Med J 2010; Vol. 31 (9): 999-1004

From the Urology Department, Beijing Anzhen Hospital affiliated to the Capital Medical University, Beijing, China.

Received 26th May 2010. Accepted 27th July 2010.

Address correspondence and reprint request to: Dr. Yong-Guang Jiang, Urology Department, Beijing Anzhen Hospital, No.2 Anzhen Road, Chao Yang District, Beijing 100029, China. Tel. +86 13520877107. Fax. +86 (10) 64456491. E-mail: scalpel@163.com

Serum prostate specific antigen (PSA) is the most widely used tumor marker for detecting, staging, and monitoring prostate cancer. However, it lacks specificity at the widely applied cut-off level of 4.0 ng/mL.[1] Elevated PSA levels can be found in the presence of prostatic malignancy, prostatitis, and benign prostatic hyperplasia.[1] Clinical studies have shown that the free PSA (fPSA) and free-to-total PSA ratio (f/tPSA) may be used in conjunction with total PSA (tPSA) to enhance the specificity of cancer detection.[2-4] It was reported that various diagnostic and therapeutic procedures may affect serum tPSA and fPSA concentration level,[1] but to what extent and for how long the serum PSA will be modified remains controversial. Therefore, we performed a prospective study using several forms of prostate manipulation, including digital rectal examination (DRE), urethral catheterization, rigid cystoscopy, prostatic biopsy, transurethral resection of prostate (TURP) and suprapubic subcapsular prostatectomy and aimed to evaluate their impact on tPSA and fPSA levels in conjunction with f/t PSA ratio values.

Methods. A total of 160 males were enrolled in the study (mean age 68 years, range 50-85) from January 2006 to December 2009 at the Urology Department, Beijing Anzhen Hospital affiliated to the Capital Medical University, Beijing, China. Patients who had been catheterized, had urethral instrumentation, had symptoms of prostatitis, or had documented urinary tract infection within 6 weeks were excluded. Patient who had been on a 5-α reductase inhibitor within 6 months were also excluded. Patients were followed up for 4 weeks. The appropriate ethics committee approved the study, and informed consent was obtained prior to all types of prostate manipulation. The prostate manipulations included in the study were DRE, urethral catheterization, rigid cystoscopy, prostate biopsy, TURP, and suprapubic subcapsular prostatectomy. All procedures were performed by a Faculty Urologist in our hospital. Twenty-three patients that underwent DRE as a routine examination for benign prostatic hyperplasia (BPH) were enrolled. The urologists were advised to perform the DRE in the usual manner without vigorous massage. Twenty-one patients underwent 16 Foley (F) urethral catheterization according to postoperative routine procedure after general anesthesia, and none of them had lower urinary tract operations. The catheters were all removed the following day. Rigid cystoscopy was performed in 28 patients with either hematuria or superficial bladder cancer, with a 19.5F rigid cystoscope (Richard Wolf Medical Instruments, Knittlingen, Germany) after lubricating the urethra with 10 mL of 2% lidocaine gel. Transrectal prostate biopsies were performed in 35 patients with suspected prostate malignancy, using an 18 gauge disposable core biopsy needle (Bard Max Core, Bard Peripheral Vascular Inc, Tempe, AZ, USA). Ten-core biopsies were taken in all cases. The TURPs were performed in 35 patients using a 24F resectoscope (Richard Wolf Medical Instruments, Knittlingen, Germany) as an inpatient procedure. A total of 18 patients with BPH underwent suprapubic subcapsular prostatectomy. Blood samples were obtained before the prostate manipulation, and at 24 hours, and 4 weeks after the prostate manipulation. Venipuncture samples were immediately centrifuged and analyzed. The PSA was determined using the Abbott I2000 tPSA and fPSA immunoassay systems (Abbott Park, IL, USA).

General linear model repeated measures analysis was used to assess the differences of PSA and ratio values before and after the manipulation. Mann-Whitney U test was used to assess the differences between benign and malignant disease in patients who had biopsy. The significance level was set at $p<0.05$. Statistical analyses were performed using the Statistical Package for Social Sciences version 13.0 (SPSS Inc, Chicago, IL, USA). Values are expressed as mean with 95% confidence intervals (CI).

Results. The mean and 95% confidence intervals for tPSA, fPSA, and f/t PSA ratio are summarized in **Tables 1-3**. No significant longitudinal changes were found in tPSA, fPSA and f/t PSA ratio either at 24 hours or 4 weeks after DRE manipulation (**Table 1**). Both urethral catheterization and rigid cystoscopy caused a slight, but statistically significant increase in tPSA at 24 hours after manipulation, but not at 4 weeks. No significant changes were found in fPSA and f/tPSA at 24 hours, or at 4 weeks (**Table 1**). Among the subjects who underwent biopsy, 16 males (46%) were diagnosed with prostate cancer. There was a marked increase in tPSA and fPSA, but a decrease in f/tPSA at 24 hours after needle biopsy in both subgroups (**Table 2**). Baseline tPSA was higher for men with cancer ($p=0.003$). Baseline fPSA was similar for men with and without cancer ($p=0.205$). Mean f/t in the cancer group was 0.12 compared to 0.18 in those with benign disease ($p=0.009$, **Table 2**). The degree of change in tPSA ($p=0.257$), and f/tPSA ($p=0.461$) did not differ significantly between the 2 groups. However, the increase in fPSA was greater in the benign disease group ($p=0.007$). After 4 weeks, all variables returned to near baseline levels in the benign disease group. All patients in the cancer group received treatments after biopsy, and their data after 4 weeks were not available. Serum tPSA and fPSA were markedly increased, associated with f/tPSA decrease 24 hours after TURP, or suprapubic prostatectomy (**Table 3**). The tPSA and fPSA levels returned to below baseline levels at 4 weeks, and f/t PSA was not significantly changed at 4 weeks.

Table 1 - Effect of manipulation on tPSA, fPSA, and f/tPSA.

Types of manipulation	Before manipulation	24 hours after manipulation	*P*-value	4 weeks after manipulation	*P*-value
	Mean (confidence interval)				
Effect of digital rectal examination (n=23)					
tPSA (ng/ml)	1.96 (1.31-2.61)	1.97 (1.31-2.63)	*p=1	1.96 (1.30-2.62)	*p=1
fPSA (ng/ml)	0.52 (0.32-0.72)	0.52 (0.32-0.71)	p=1	0.52 (0.32-0.72)	p=1
f/tPSA	0.24 (0.20-0.27)	0.23 (0.20-0.27)	p=1	0.24 (0.21-0.27)	p=1
Effect of urethral catheterization (n=21)					
tPSA (ng/ml)	1.95 (1.36-2.54)	2.25 (1.57-2.94)	p=0.022	1.98 (1.39-2.57)	p=0.707
fPSA (ng/ml)	0.49 (0.30-0.68)	0.55 (0.36-0.75)	p=0.096	0.50 (0.32-0.68)	p=1
f/tPSA	0.24 (0.21-0.28)	0.24 (0.21-0.28)	p=1	0.24 (0.21-0.28)	p=1
Effect of rigid cystoscopy (n=28)					
tPSA (ng/ml)	2.23 (1.62-2.84)	2.56 (1.87-3.25)	p=0.018	2.26 (1.63-2.88)	p=1
fPSA (ng/ml)	0.59 (0.41-0.78)	0.65 (0.43-0.86)	p=0.226	0.58 (0.40-0.77)	p=1
f/tPSA	0.27 (0.23-0.30)	0.25 (0.21-0.29)	p=0.191	0.26 (0.23-0.29)	p=0.832

tPSA - total specific antigen, fPSA - free prostate specific antigen, f/tPSA - free-to-total prostate specific antigen, *p-value represents the post-hoc significance in repeated measure analysis as compared to the baseline value, significance level was set at p<0.05

Table 2 - Effect of prostate biopsy on tPSA, fPSA, and f/tPSA (n=35).

Subgroups	Before manipulation	24 hours after manipulation	*P*-value	4 weeks after manipulation	*P*-value
	Mean (confidence interval)†				
BPH					
tPSA (ng/ml)	8.32 (5.59-11.04)	21.50 (14.83-28.17)	*p<0.001	8.27 (5.73-10.81)	*p=1
fPSA (ng/ml)	1.24 (0.92-1.56)	2.81 (1.86-3.76)	p=0.001	1.29 (0.91-1.66)	p=1
f/tPSA	0.18 (0.14-0.21)	0.14 (0.11-0.18)	p=0.035	0.18 (0.14-0.21)	p=1
PCa					
tPSA (ng/ml)	18.41 (10.96-25.86)	27.82 (18.18-37.46)	p<0.001	NA	
fPSA (ng/ml)	1.98 (1.23-2.73)	2.47 (1.64-3.30)	p=0.001	NA	
f/tPSA	0.12 (0.10-0.14)	0.09 (0.08-0.11)	p<0.001	NA	

tPSA - total specific antigen, fPSA - free prostate specific antigen, f/tPSA - free-to-total prostate specific antigen, BPH - benign prostatic hyperplasia, PCa - prostate cancer, †CI - confidence interval, NA - not available, *p-value represents the post-hoc significance in repeated measure analysis as compared to the baseline value, significance level was set at p<0.05

Table 3 - Effect of operations on tPSA, fPSA, and f/tPSA.

Types of manipulation	Before manipulation	24 hours after manipulation	*P*-value	4 weeks after manipulation	*P*-value
	Mean (confidence interval)				
Effect of transurethal resection of the prostate (n=35)					
tPSA (ng/ml)	3.41 (2.34-4.48)	9.20 (6.49-11.91)	*p<0.001	2.05 (1.35-2.75)	*p<0.001
fPSA (ng/ml)	1.22 (0.70-1.73)	2.32 (1.54-3.09)	p=0.007	0.73 (0.40-1.05)	p<0.001
f/tPSA	0.33 (0.28-0.37)	0.26 (0.22-0.29)	p=0.001	0.32 (0.28-0.36)	p=1
Effect of suprapubic prostatectomy (n=18)					
tPSA (ng/ml)	3.20 (1.95-4.45)	10.33 (6.18-14.47)	p<0.001	1.59 (0.95-2.24)	p=0.001
fPSA (ng/ml)	0.89 (0.42-1.36)	2.09 (0.91-3.27)	p=0.013	0.42 (0.21-0.63)	p=0.010
f/tPSA	0.24 (0.19-0.29)	0.19 (0.14-0.23)	p=0.005	0.24 (0.19-0.28)	p=0.695

tPSA - total specific antigen, fPSA - free prostate specific antigen, f/tPSA - free-to-total prostate specific antigen, *p-value represents the post-hoc significance in repeated measure analysis as compared to the baseline value, significance level was set at p<0.05

The median weight of prostate tissue resected was 21 g (range: 13-58 g) in TURP, 68 g (range: 45-138 g) in prostatectomy, and no malignancy was found.

No significant changes in serum tPSA, fPSA and f/tPSA ratio were found either at 24 hours or at 4 weeks after digital rectal examination in this study. Although urethral catheterization and rigid cystoscopy caused a statistically significant increase in tPSA at 24 hours after manipulation, the change of mean values were slight, and not clinically significant. The tPSA levels returned to baseline at 4 weeks after urethral catheterization and rigid cystoscopy, and fPSA and f/tPSA ratio did not

change at any time point. Prostatic biopsy, TURP, and suprapubic subcapsular prostatectomy can induce a dramatic increase in serum tPSA and fPSA concentration, associated with f/tPSA ratio decrease at 24 hours after manipulation. All the PSA variables returned to baseline values 4 weeks after biopsy. The results of TURP and suprapubic prostatectomy manipulation at 4 weeks showed that f/tPSA ratio returned to baseline, however, both tPSA and fPSA values were below baseline level. The relative variations in the prostatectomy group were: from 3.20-1.59 ng/mL (tPSA [p=0.001]); from 0.89-0.42 ng/mL (fPSA [p=0.010]); and from 0.24-0.24 (f/tPSA [p>0.05]).

Discussion. Serum PSA was first purified in 1979, and is now accepted as a valuable aid for early detection of prostate cancer.[2-4] However, there are concerns on the high rate of false-positive results, although previous studies have demonstrated that the f/tPSA ratio can increase PSA specificity for prostate cancer.[2-4] It is well-documented that mechanical manipulation of the prostate can alter tPSA in serum, and it may take several weeks or even months for tPSA to return to baseline level.[1] However, little is known on the effect of mechanical manipulation on fPSA. It is important to know to what extent the PSA levels are affected by different types of manipulation, and for how long these alterations continue.

Previous findings regarding the effect of DRE on serum tPSA were inconsistent. Some studies showed minimal effect of DRE on serum PSA,[1,5] whereas, others observed a significant elevation of tPSA and fPSA immediately after manipulation,[6,7] which returned to baseline within 24 hours.[6] In our study, the effect of DRE on serum tPSA, fPSA, and f/tPSA was not statistically significant after 24 hours, or after 4 weeks. Previous studies showed that patients who had non-urological operations had no change in serum PSA levels after in-dwelling catheter.[1] Kravchick et al[8] found that the average PSA level of the in-dwelling catheter group was significantly elevated. Erdogan et al[9] compared the PSA levels before and after catheterization in patients with acute urinary retention. Elevations in PSA values was statistically significant in patients that underwent urethral catheterization, but not in patients that received suprapubic percutaneous cystostomy.[9] In our study, the elevation in tPSA (0.3 ng/ml) was slight and not clinically significant, although it was statistically significant. The increase in serum tPSA (0.33 ng/ml) level at 24 hours after rigid cystoscopy was statistically significant, but probably not clinically significant. The fPSA and f/tPSA were not significantly altered over time. Our results are consistent with other previous studies. Long et al[7] examined patients undergoing rigid (n=17), and flexible (n=28) cystoscopy, and found a median increase of 0.13 (p=0.02) in rigid cystoscopy and 0.68 (p<0.01) ng/mL in flexible cystoscopy. DeCastro et al[10] studied the effect of flexible cystoscopy on PSA after one, and 24 hours in 40 patients. They noted that although the small differences in tPSA, fPSA, and f/t before and after cystoscopy achieved statistical significance, none were clinically significant. The subgroup analysis (such as ethnicity, initial PSA level, age, gland size, cystoscopy indication, and findings) revealed either insufficient numbers for additional analysis, or no statistically significant differences in the mean tPSA, fPSA, and f/t values.[10] The rigid cystoscope is thicker than the flexible cystoscope and exerts more pressure on the prostate, which might explain why the change in PSA values in our group were more prominent than in some other studies.

It has been a consistent finding that prostatic biopsy causes dramatic serum PSA elevation, however, the magnitude of the increase and the length of time necessary for the PSA to return to baseline level varied in previous studies. In some early studies[1,6,11] the median increase was reported as high as 10 times the baseline PSA level, and the median time for return to baseline PSA was reported as 15 days - 6 weeks. Biopsies taking 3 or fewer cores resulted in a smaller magnitude of increase in serum PSA, and a proportionally shorter duration of PSA elevation than those taking 4 or more cores. Prostate size and the presence of cancer had no influence on the duration of PSA elevation following biopsy.[1,6,11] However, most early studies did not evaluate fPSA. Shao et al[12] studied the effect of biopsy in 36 men and found that prostatic biopsy caused a significant increase in tPSA at 10, 30, 60, and 90 minutes. The increase was most pronounced for patients without prostate cancer (p<0.05).[12]

Previous studies[5,13,14] reported a dramatic increase in median tPSA and percentage of fPSA one hour after biopsy. The degree of change in tPSA, fPSA and f/t did not differ greatly between the benign and malignancy groups, although a greater increase in fPSA in the benign disease group, and a corresponding lesser change in f/t ratio in the malignancy group was observed. Serum tPSA remained greater than the baseline levels after 24 hours, and in most male patients after one week. Serum fPSA returned to near baseline levels much more rapidly than tPSA. The percentage of fPSA decreased to less than baseline levels at 24 hours, and at one week. Baseline tPSA, and the change in tPSA following biopsy were similar for males with and without cancer. Males with cancer had a lower baseline percentage of fPSA that returned to baseline more slowly than those

without cancer.[5,13,14] In our study, the median increase in tPSA after 24 hours following biopsy was similar in males with and without cancer (9.41 ng/ml versus 13.18 ng/ml, $p>0.05$), but significant in fPSA in males with and without cancer (0.49 ng/ml versus 1.57 ng/ml, $p<0.05$). It was suggested that males with BPH released more fPSA than those with prostate cancer. However, the increase we observed in tPSA and fPSA were lower than reported in some of the aforementioned studies. It may due to the different baseline PSA levels, the fast clearance of fPSA from serum, and prolonged time between biopsy and venipuncture (24 hours) in our study. The f/tPSA value decreased 0.03 versus 0.04 in males with and without cancer ($p>0.05$) at 24 hours, mainly because the numerator fPSA decreased faster than the denominator tPSA. None of the median changes in tPSA, fPSA, and f/tPSA was statistically significant 4 weeks after biopsy in our study group.

For the group undergoing operation in our study, there was an increase at 24 hours postoperatively in the serum tPSA and fPSA (5.79 ng/m and 1.10 ng/ml in the TURP group, 7.13 ng/m and 1.20 ng/ml in the suprapubic subcapsular prostatectomy group). The f/t PSA ratio decreased by 0.07 in the TURP group and 0.05 in the prostatectomy group. Long et al[7] found a median increase of PSA level of 14.37 ng/ml 20 minutes after TURP. Oberpenning et al[15] collected intraoperative blood samples for tPSA and fPSA measurement every 15 minutes during 14 radical retropubic prostatectomies (RRP), and 10 radical cystoprostatectomies (RCP), and found significant elevations in both parameters. The mean fPSA levels showed a 4.3- (RRP), and 7.9-fold (RCP) increase, followed by a rapid decline after prostate removal. The tPSA increased 1.2- (RRP), and 1.3-fold (RCP), and declined more slowly. Postmanipulatory f/tPSA also increased significantly, reaching mean elevations of +0.29 during RRP, and +0.28 over preoperative ratios during RCP.[15] One possible explanation for the difference between our data and those from other investigators is that the amount of resected tissue may have differed. The larger the gland size, perhaps the greater quantity of PSA moved into the bloodstream. Another possibility is that the time to obtain the blood samples varied from intraoperative-at 24 hours postoperatively in different studies. The reason of the f/tPSA decrease at 24 hours postoperatively was similar to that in the biopsy group. Fonseca et al[16] assessed tPSA and f/tPSA ratio before the procedure, and at 30, 60, and 180 days separately after the TURP in 30 males. It was observed that the mean tPSA declined 71% after TURP, and 60 days after surgery. It varied from 6.19 ± 7.06 ng/mL before surgery to 1.75 ± 1.66 ng/mL on day 60 ($p<0.001$). The mean baseline f/tPSA was 18.2 ± 3.4%, and was not significantly changed at any time point in the postoperative period ($p=0.91$). Each gram of tissue resected decreased tPSA by 0.15 ± 0.11 ng/mL.[16] In our study, tPSA level decreased from 3.41 ng/mL to 2.05 ng/mL after 4 weeks in patients who underwent TURP, and fPSA level decreased from 1.22 ng/mL to 0.73 ng/mL. However, the mean change in f/tPSA did not achieve statistical significance. The relative variations were similar in the prostatectomy group. With resection of the prostate, the quantity of tPSA and fPSA secreted by the gland markedly declined, resulting in decreased serum tPSA and fPSA levels. The drop of fPSA concentration might be approximately in proportion to that of tPSA, so that the f/tPSA ratio remained constant over time. The magnitude of change in observed values may differ between studies as the size of the prostate, the weight of resected tissue, and the follow-up intervals varied. However, the trends of the change were consistent with each other.

There are limitations to this study. The small number of enrolled patients made it difficult to conduct further subgroup analysis (such as, age, gland size). And there are still other analytical or biological factors, which could possibly affect PSA levels, which we could not evaluate one by one. In addition, due to ethnicity and chronological differences, one should therefore pay caution when our present findings were directly compared with other studies.

In conclusion, diagnostic and therapeutic procedures including prostatic biopsy, TURP, and suprapubic subcapsular prostatectomy might affect the serum PSA concentration levels. In future studies, the effects of prostate manipulation and their longitudinal course need to be taken into account while evaluating different forms of serum PSA levels.

References

1. Carter HB, Partin AW. Diagnosis and Staging of Prostate Cancer. In: Walsh PC, Retik AB, Wein AJ, Darracott-Vaughan E Jr, editors. Campbell's Urology. 8th ed. Philadelphia (PA): WB Saunders Co; 2002. p. 3055-3064.
2. Elabbady AA, Khedr MM. Free/total PSA ratio can help in the prediction of high gleason score prostate cancer in men with total serum prostate specific antigen (PSA) of 3-10 ng/ml. ***Int Urol Nephrol*** 2006; 38: 553-557.
3. Yeniyol CO, Bozkaya G, Cavusoglu A, Arslan M, Karaca B, Ayder AR. The relation of prostate biopsy results and ratio of free to total PSA in patients with a total PSA between 4-20 ng/mL. ***Int Urol Nephrol*** 2001; 33: 503-506.
4. Miller MC, O'Dowd GJ, Partin AW, Veltri RW. Contemporary use of complexed PSA and calculated percent free PSA for early detection of prostate cancer: impact of changing disease demographics. ***Urology*** 2001; 57: 1105-1111.
5. Zhong CY, Liu M, Deng SM, Zhang LQ, Zhang YG, Wan B, et al. Clinical significance of correlation factors on serum PSA concentration. Journal of Chinese Physician 2003; 5: 458-460.

6. Harvey P, Basuita A, Endersby D, Curtis B, Iacovidou A, Walker M. A systematic review of the diagnostic accuracy of prostate specific antigen. ***BMC Urol*** 2009; 9: 14.
7. Long R, Giri S, Diver S, Duddy L, McKeown D, Moran K. Effect of prostate manipulation on the serum levels of complexed prostate-specific antigen and total prostate-specific antigen. ***Int J Urol*** 2006; 13: 947-950.
8. Kravchick S, Bunkin I, Peled R, Yulish E, Ben-Dor D, Kravchenko Y, et al. Patients with elevated serum PSA and indwelling catheter after acute urinary retention: prospective study of 63 patients with 7-year follow-up. ***J Endourol*** 2007; 21: 1203-1206.
9. Erdogan K, Gurdal M, Tekin A, Kirecci S, Sengor F. The effect of urethral catheterisation on serum prostate-specific antigen levels in male patients with acute urinary retention. ***Yonsei Med J*** 2003; 44: 676-678.
10. DeCastro BJ, Baker KC. Effect of flexible cystoscopy on serum prostate-specific antigen values. ***Urology*** 2009; 73: 237-240.
11. Shariat SF, Scardino PT, Lilja H. Screening for prostate cancer: an update. ***Can J Urol*** 2008; 15: 4363-4374.
12. Shao Q, Song J, Zhou ZJ, Du LD. Differentiation of prostate cancer from benign prostatic disease by total prostate specific antigen dynamic profiles after transrectal prostate biopsy. ***Zhonghua Nan Ke Xue*** 2008;14: 597-601.
13. Wang Y, Sun G, Pan JG, Guo ZJ, Li T. Performance of tPSA and f/tPSA for prostate cancer in Chinese. A systematic review and meta-analysis. ***Prostate Cancer Prostatic Dis*** 2006; 9: 374-378.
14. Loeb S, Catalona WJ. Prostate-specific antigen in clinical practice. ***Cancer Lett*** 2007; 249: 30-39.
15. Oberpenning F, Schmid HP, Fuchs-Surdel W, Hertle L, Semjonow A. The impact of intraoperative manipulation of the prostate on total and free prostate-specific antigen. ***Int J Biol Markers*** 2002; 17: 154-160.
16. Fonseca RC, Gomes CM, Meireles EB, Freire GC, Srougi M. Prostate specific antigen levels following transurethral resection of the prostate. ***Int Braz J Urol*** 2008; 34: 41-48.

Related topics

Mosli HA, Abdel-Meguid TA, Al-Maghrabi JA, Kamal WK, Saadah HA, Farsi HM. The clinicopathologic patterns of prostatic diseases and prostate cancer in Saudi patients. ***Saudi Med J*** 2009; 30: 1439-1443.

Gazzaz FS, Mosli HA. Lack of detection of human papillomavirus infection by hybridization test in prostatic biopsies. ***Saudi Med J*** 2009; 30: 633-367.

Taha SA, Kamal BA. Screening program for prostate cancer at a university hospital in eastern Saudi Arabia. ***Saudi Med J*** 2005; 26: 1104-1106.