Significance of serum total prostate specific antigen and digital rectal examination in the diagnosis of prostate cancer

Abdelkarim A. Abdrabo, MSc, PhD, Adil I. Fadlalla, MCS, MD, Imad M. Fadl-Elmula, MD, PhD.

ABSTRACT

الأهداف: التعرف على أهمية مستوى المستضد الكلي الخاص بالبروستاتا والفحص اليدوي لغدة البروستاتا في تشخيص سرطان البروستاتا.

الطريقة: شملت هذه الدراسة 118 مريض مصاب بأعراض في المسالك البولية السفلية، وتراوحت مستويات المستضد الكلي الخاص بالبروستاتا لديهم ما بين 2.5 إلى 10 نانوغرام/مل. تردد المشاركين في الدراسة على عيادة المسالك البولية بمستشفى سوبا الجامعي، سوبا، السودان وذلك خلال الفترة من أغسطس 2008م إلى يناير 2010م. لقد تم قياس مستوى المستضد الكلي الخاص بالبروستاتا بطريقة القياس المناعي الإنزيمي، وعليه قُسم المرضى المشاركين في الدراسة إلى مجموعتين: الأولى التي تراوحت مستويات المستضد لديهم ما بين 2.5 إلى 4 نانوغرام/مل، والثانية ما بين 4.1 إلى 10 نانوغرام/مل. بعد ذلك أجرى فحص البروستاتا اليدوي وبناء عليه صُنف المرضى إلى مجموعة يشتبه إصابتها بسرطان البروستات ومجموعة لا يُشتبه بإصابتها. وقد أُخذت خزعات متعددة من البروستاتا عن طريق فتحة الشرج لإجراء التحليل النسيجي.

النتائج: لقد بلغت حساسية فحص المستضد لتشخيص السرطان لدى 118 مريض 91.6%، في حين بلغت مدى دقته 24%، والقيمة التنبؤية الإيجابية 34%. أما بالنسبة للفحص اليدوي للبروستاتا فقد بلغت الحساسية 63.8% والدقة 68%، والقيمة التنبؤية الإيجابية 46.9%. وهكذا عندما جُمع الاثنين بلغت الحساسية في تشخيص سرطان البروستاتا 100% والدقة 92% والقيمة التنبؤية الإيجابية 49%.

خاتمة: أثبتت الدراسة بأن الجمع بين المستضد الكلي الخاص بالبروستاتا والفحص اليدوي للبروستاتا يزيد من نسبة الحساسية، والدقة، والقيمة التنبؤية الإيجابية في الكشف عن سرطان البروستات.

Objectives: To assess the significance of serum total prostate specific antigen (tPSA) and digital rectal examination (DRE) in the diagnosis of prostate cancer (PC).

Methods: One hundred and eighteen patients with serum tPSA ranging between 2.5 and 10 ng/ml with lower urinary tract symptoms presented at the Urology Clinic of Soba University Hospital, Khartoum, Sudan from August 2008 and January 2010 were included in the study. Serum tPSA was measured using enzyme immunoassay method, and accordingly, the patients were classified into 2 groups: patients that had tPSA between 2.5-4.0 ng/ml; and patients that had tPSA between 4.1-10 ng/ml. The DRE was performed on all patients by a qualified urologist, and were recorded as a group with suspicion of PC, and a group with no suspicion of PC. All patients underwent transrectal sextant prostate biopsy.

Results: The DRE alone showed 63.8% sensitivity and 68% specificity with 46.9% positive predictive value (PPV) for the diagnosis of PC. The tPSA test revealed 91.6% sensitivity and 24% specificity with PPV of 34%. However, when combining DRE and tPSA, the sensitivity reached 100% and the specificity increased to 92% with PPV of 49%.

Conclusion: Combining DRE and tPSA test increases the sensitivity, specificity, and PPV of PC detection.

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From the Departments of Clinical Chemistry (Abdrabo), Pathology (Fadl-Elmula), Faculty of Medical Laboratory Sciences, Al Neelain University, and the Department of Urology (Fadlalla), Soba University Hospital, Faculty of Medicine, University of Khartoum, Khartoum, Sudan.

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Address correspondence and reprint request to: Dr. Abdelkarim A. Abdrabo, Department of Clinical Chemistry, Faculty of Medical Laboratory Sciences, Al Neelain University, PO Box 12702, Khartoum 11121, Sudan. Tel. +249 (91) 2905847. Fax. +249 (18) 3796532. E-mail: Abdrabokarim@hotmail.com

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The prostate remains one of the leading sites of internal malignancy, and the second most common cause of cancer death in men. Prostate cancer (PC) is the fourth most common male malignancy worldwide.[1] Studies have shown that early detection of PC reduces mortality, and improves the prognosis and quality of patient's life.[2] The measurement of prostate specific antigen (PSA) in serum and digital rectal examination (DRE) are the most widely used and efficient methods for the early detection of PC.[3] Prostate specific antigen is now a well established tumor marker that aids in the diagnosis, staging, and follow up of PC, and it was recommended to be superior to the previously used marker, the prostatic acid phosphatase.[4,5] The PSA function is not yet understood, but the well known accepted function, which is related to the activity of kallikreins is to dissolve the seminogelins and fibronectin formed in semen after ejaculation, and plays a role in the regulation of cell proliferation and apoptosis.[6] Although it is the most important tumor marker, PSA is organ-specific but not cancer-specific, so the presence of other prostate diseases such as benign prostatic hyperplasia (BPH), and prostatitis may influence its effectiveness for cancer detection.[4] The cutoff point of total PSA (tPSA) at which prostate biopsy should be taken was not identified in different geographical regions, and/or ethnic groups. Although the use of a baseline tPSA cutoff value 4 ng/mL for PC screening is well established in many different areas, many studies found men with PC having tPSA level less than 4.0 ng/ml.[7] In clinical practice, biopsies are generally performed only when the results of a PSA test or DRE is abnormal, which leads to misdiagnosis of most of the small PCs present in many older men. One of the approaches suggested to increase the sensitivity and specificity of tPSA to detect PC was to use it in combination with DRE.[8] The aim of this study is to assess the value of DRE and PSA determination in the detection of PC among patients presenting with lower urinary tract symptoms (LUTS).

Methods. Between August 2008 and January 2010, the tPSA of 540 patients referred to the Urology Clinic of Soba University Hospital, Khartoum, Sudan due to lower urinary tract symptoms was measured. The collection of blood samples took place between 08:00 and 11:00 before any manipulation that could alter PSA concentration. Those with tPSA value ranging between 2.5 and 10 ng/ml (118 patients) were included in the study. The patients were grouped according to: tPSA ranging between 2.5 and 4.0 ng/ml; and patients with tPSA ranging between 4.1 and 10 ng/ml. The DRE was performed by qualified urologist, and the 118 patients were classified, based on DRE in patients with suspicion of PC and patients with no suspicious PC. Multiple transrectal sextant biopsies were performed in all 118 patients, and based on histology results, patients were classified in patients with PC, and patients with BPH. The study was conducted according to the principles of the Helsinki Declaration, and was approved by the ethical committee of Al Neelain University. Each patient has signed a written informed consent.

Specimen collection and processing. Serum sample was used for the assay of tPSA, using automated immunoenzymometic automated system (Tosoh Corporation, Tokyo, Japan). Blood specimens collected were stored at 18-25ºC until a clot had formed (usually 15-45 minutes), then centrifuged to obtain the serum sample for assay. Samples were stored at 2-8ºC for up to 24 hours prior to analysis. If the analysis could not be carried out within 24 hours, the samples were stored frozen at -20ºC, or below for up to a suitable day (not more than 60 days).[9]

Data were analyzed using the Statistical Package for Social Sciences software version 17 for Windows®(SPSS Inc, Chicago, IL, USA). The data were expressed in mean ± standard deviation (SD). Sensitivity, specificity, and positive predictive values (PPV) were calculated, and the means were compared using independent sample t-test.

Results. Out of 118 elderly men presented with LUTS, 69.4% (82 men) were at last diagnosed with BPH, and 30.5% (36 men) with PC. The mean age in the study population (118 men) was 70 years (range; 56-83), the mean of tPSA was 6.4 ng/ml, 18.6% (23 men) have tPSA between 2.5-4.0 ng/ml, while 81.4% (95 men) have tPSA between 4.1-10 ng/ml. The DRE results revealed that 49 patients (41.5%) had abnormal DRE suggesting PC, while 69 patients (58.5%) had no suspicious PC. In the study group, DRE in the detection of PC has a sensitivity of 63.8%, and specificity of 68%, while the PPV was 46.9% (**Table 1**). The results of the study also showed that out of 82 men with BPH, 24% (20 men) have tPSA between 2.5-4.0 ng/ml, while 75% (62 men) have tPSA between 4.1-10 ng/ml in patients with PC, 8% (3 men) have tPSA between 2.5-4.0 ng/ml, while 92% (33 men) have tPSA between 4.1-10 ng/ml. The mean ± SD of tPSA level in BPH patients was 5.8 ± 2.1 ng/ml, while in PC it was 7.8 ± 2.0 ng/ml, and no significant differences were found between the 2 groups in this intermediate tPSA levels (2.5-10 ng/ml) (p=0.929). The biopsy results of patients with abnormal finding of DRE and low tPSA levels (2.5-4.0 ng/ml), showed none of them had PC, indicating that DRE is of low value in patients with low tPSA levels (**Table 2**). The sensitivity was 91.6%, and specificity was 24% of tPSA in the detection of PC, while the PPV was 34.7% (**Table 1**). The analyzed data also showed that the

Table 1 - Results of prostate specific antigen (PSA) and digital rectal examination (DRE) in prostate cancer (PC) detection of studied patients in Soba University Hospital, Khartoum, Sudan.

Tests	Biopsy results			Sensitivity and specificity
	BPH	PC	Total	
DRE, n				
No suspicious	56	13	69	Sensitivity=63.8% Specificity=68.0% PPV= 46.9%
Suspicious	26	23	49	
PSA, n				
2.5-4.0 ng/ml	20	3	23	Sensitivity=91.6% Specificity=24.0% PPV= 34.7%
4.1-10 ng/ml	62	33	95	

BPH - benign prostatic hyperplasia, PPV - positive predictive values

Table 2 - Results of prostate specific antigen (PSA) in patients with abnormal digital rectal examination of studied patients in Soba University Hospital, Khartoum, Sudan.

Test	Biopsy result			Specificity and PPV
	BPH	PC	Total	
PSA, n				
2.5-4.0 ng/ml	2	0	2	Sensitivity=100% PPV=49%
4.1-10 ng/ml	24	23	47	

BPH - benign prostatic hyperplasia, PC - prostate cancer, PPV - positive predictive values

combination of the 2 results: tPSA and DRE improved the PPV to 49% and sensitivity to 100% (**Table 2**).

Discussion. The use of serum tPSA levels and the DRE improved the early detection rate for PC however, the use of either of these tests may result in misdiagnosis and a low prediction of PC. In the present study, we enrolled 118 men with tPSA levels of 2.5-10.0 ng/ml, and with or with no suspicious DRE, and to evaluate the efficacy of tPSA and DRE in PC detection at low and intermediate tPSA levels. The recent study indicated that the sensitivity of DRE to detect PC was 68%, while the specificity was 63.3%, and the PPV was 47%, and this finding is in agreement with the results reported by Galic et al[10] who observed a PPV of 49%, and higher than that reported by Seo et al (22.3%)[11] and Ng et al (37%),[12] while in another study carried out by Cooner et al[13] revealed that the PPV was 36% for cancer detection using DRE. The results of the recent study showed that PPV of tPSA in cancer detection was 34.7%, and this result was higher than that reported in 2 previous studies by Seo et al in 2007 (PPV=31%),[11] and Manyahi et al in 2009 (PPV=16%),[8] and lower than that reported by Ng et al in 2005[12] who reported that the PPV of tPSA is 67% in patients with abnormal finding of DRE, and this is may be due to the small sample size of this study.

The positive predictive value of tPSA in patients with abnormal findings of DRE was 49%, and this indicates that the combination of the 2 detection methods (tPSA and DRE) showed better detection rate, and pointed towards PC with sensitivity of 100%, and a PPV of 49%. Our results is in complete accordance with previous literature.[10] The recent study indicated that in most patients with cancer their tPSA levels was >4.0 ng/ml, showing that it is rare to find patient with cancer having tPSA <4.0 ng/ml, however, we have to take into consideration the sample size of the current study as the previously reported results by Ng et al in 2005,[12] and Thompson et al in 2004[7] indicated that patients with cancer having tPSA level <4.0 ng/ml is not rare.

One of the limitations in this study is its small sample size. Although Sudanese patients with prostate problems are not rare, most of the participants had not met our inclusion criteria. The other limitation was the lack of tumor characteristics, thus, other studies should include a larger number of participants and data with tumor characteristics that should be made available.

In conclusion, although tPSA determination detected a considerable proportion of tumors, urologists should take the results of the diagnostic tools (tPSA and DRE) at the same time for diagnosis of PC in men with lower urinary tract symptoms.

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References

1. Penson DF, Chan JM. Prostate cancer. ***J Urol*** 2007; 177: 2020-2029.
2. Botchorishvili G, Matikainen MP, Lilja H. Early prostate-specific antigen changes and the diagnosis and prognosis of prostate cancer. ***Curr Opin Urol*** 2009; 19: 221-226.
3. Miles BJ, Shalev M, Aguilar-Cordova E, Timme TL, Lee HM, Yang G, et al. Prostate-specific antigen response and systemic T cell activation after in situ gene therapy in prostate cancer patients failing radiotherapy. ***Hum Gene Ther*** 2001; 12: 1955-1967.
4. Brett T. Prostate specific antigen. ***Aust Fam Physician*** 2011; 40: 497-500.
5. Jain S, Bhojwani AG, Mellon JK. Improving the utility of prostate specific antigen (PSA) in the diagnosis of prostate cancer: the use of PSA derivatives and novel markers. ***Postgrad Med J*** 2002; 78: 646-650.
6. Diamandis EP. Prostate-specific antigen: a cancer fighter and a valuable messenger? ***Clin Chem*** 2000; 46: 896-900.
7. Thompson IM, Pauler DK, Goodman PJ, Tangen CM, Lucia MS, Parnes HL, et al. Prevalence of prostate cancer among men with a prostate-specific antigen level < or =4.0 ng per milliliter. ***N Engl J Med*** 2004; 350: 2239-2246.

8. Manyahi JP, Musau P, Mteta AK. Diagnostic values of digital rectal examination, prostate specific antigen and trans-rectal ultrasound in men with prostatism. ***East Afr Med J*** 2009; 86: 450-453.
9. Burtis CA, Ashwood ER, Bruns DE, editors. Introduction to Principle of laboratory analysis and safety. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 4th ed. Philadelphia (PA): Elsevier Saunders; 2006. p. 3-39.
10. Galic J, Karner I, Cenan L, Tucak A, Hegedus I, Pasini J, et al. Comparison of digital rectal examination and prostate specific antigen in early detection of prostate cancer. ***Coll Antropol*** 2003; 27 (Suppl 1): 61-66.
11. Seo HK, Chung MK, Ryu SB, Lee KH, Korean Urological Oncologic Society Prostate Cancer Study Group. Detection rate of prostate cancer according to prostate-specific antigen and digital rectal examination in Korean men: a nationwide multicenter study. ***Urology*** 2007; 70: 1109-1112.
12. Ng TK, Vasilareas D, Mitterdorfer AJ, Maher PO, Lalak A. Prostate cancer detection with digital rectal examination, prostate-specific antigen, transrectal ultrasonography and biopsy in clinical urological practice. ***BJU Int*** 2005; 95: 545-548.
13. Cooner WH, Mosley BR, Rutherford CL Jr, Beard JH, Pond HS, Terry WJ, et al. Prostate cancer detection in a clinical urological practice by ultrasonography, digital rectal examination and prostate specific antigen. 1990. ***J Urol*** 2002; 167: 966-973.

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Abdrabo AA, Fadlalla AI, Fadl-Elmula IM. Age-specific reference range for serum prostate-specific antigen in Sudanese men. ***Saudi Med J*** 2011; 32: 930-932.

Zhao Y, Chen J, Wang M, Sun P, Li L, Zhang H, Jin X. Photoselective vaporization combined with bipolar transurethral resection for the treatment of large prostate adenoma in high-risk patients. ***Saudi Med J*** 2010; 31: 1320-1325.

Arafa MA, Rabah DM, Abdel-Gawad E, Ibrahim FK. Association of physicians' knowledge and behavior with prostate cancer counseling and screening in Saudi Arabia. ***Saudi Med J*** 2010; 31: 1245-12450.

Lin YH, Jiang YG, Li MC, Luo Y, Wang JS. Effects of prostate manipulation on serum total and free prostate specific antigen, and free-to-total prostate specific antigen ratio. ***Saudi Med J*** 2010; 31: 999-1004.