Original Article

# Do the values of prostate specific antigen obtained from fresh and dried urine reflect the serum measurements?

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## Abstract

**Aim:** To investigate if free PSA (fPSA) and total PSA (tPSA) values obtained from simultaneously collected urine, fresh and dried on filter paper, reflect the serum free and total PSA.

**Materials and Methods:** The sera and 20 cc first voided urine from 33 consecutive men aged between 40 and 84 (mean 61 ± 12), were collected in the morning and delivered to the laboratory. Three different aliquots of 100 microgram urine were taken with automatic pipette and dropped on 3 certain areas of a filter paper and allowed to dry for each patient. On each paper, borders of dried urine were marked. PSA values were obtained from the sera and fresh urine samples and recorded. Later on particular days dried urine samples were dissolved and eventually PSA values were derived and recorded again. The results were compared to each other. Correlations were evaluated by using an SPSS statistics program.

**Results:** Serum PSA values correlated weakly ($r < 0.24$) with fresh and dried urine PSA values. While PSA in fresh and dried urine samples showed strong correlation ($0.5 < r < 0.74$), a very strong correlation ($r > 0.75$) among PSA values of dried urine samples of 1-day, 7- and 28-days, were seen.

**Conclusions:** We conclude that PSA values obtained from fresh and dried urine could not reflect serum PSA values. But, because dried urine on a filter paper can be stable for years, it could be used for forensic purposes.

**Key Words:** Determination, paper, prostate-specific antigen, urine

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## INTRODUCTION

However, serum PSA values have some limitations for early detection of prostate cancer, it has been used for diagnosis; follow-up of treatment and screening the disease.[1-3] Serum PSA, produced mainly by the prostatic epithelial cells and the periurethral glands, can be found in various body fluids.[4,5] Urine, as a rich pool of waste materials produced by metabolic processes in the body, contains large amounts of PSA.[6] It can also provide a non-invasive sample collection, more comfortable storage and delivery opportunity of convenience for prostate cancer diagnosis, follow-up and screening programs in especially rural area. For this reason, PSA levels in the serum and urine have been used for screening and follow-up of prostate cancer.[7] Dried urine on filter paper has been used by dissolving it later, in forensic medicine.[8]

In this study we have tried to investigate if PSA values obtained from fresh and dried urine could reflect the serum PSA values.

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## MATERIALS AND METHODS

After obtaining a permission from the local ethics committee, 41 consecutive male patients aged 40 and over (40-84, mean

61 ± 12) were included in the study. Nineteen of those patients were under medication due to BPH symptoms for at least 3 months. Four of the 19 participants were also taking a 5-alpha reductase inhibitor additionally.

Having a diagnosis of prostate cancer or being under a treatment of prostate cancer, a history of biopsy of the prostate, an indwelling urethral catheter, any surgical manipulation for the lower urinary system in the last month, an active infection with or without antibiotic treatment, the liver and the renal function abnormalities were taken as exclusion criteria.

When the blood was taken for PSA in the morning, first voided 20 cc of urine samples were also collected from the patients. Blood serum and fresh urine samples were delivered to the laboratory without delay. At the same time, both serum and urine PSA levels were measured by Architect I 2000 SR® chemiluminescence method (Kemiflex®, Abbott Diagnostics, Illinois, USA). Eight patients suspected of prostate cancer by the results were excluded.

Three aliquots of 100 microgram of urine were taken with automatic pipette and dropped on 3 different areas of the filter paper keeping each at a distance not to touch the other and the borders of dried urine were marked with a needle puncture then allowed to dry at room temperature, for each patient. Dried urine samples were dissolved in 1 cc of serum physiologic later in days of 1, 7 and 28. PSA values were obtained from these solutions with the same method as used for the sera and the urine samples. The results were calculated by multiplying the measured values by ×10 as dilution factor and were recorded.

All analyses were performed by using commercially available statistics program software (SPSS, ver. 18, 2009, Chicago, IL, USA). For statistical analysis Kolmogrow Smirnov test was used to understand the properties of distribution of the data. Then a nonparametric test of correlation, Spearman's rho test, was used to see the associations of the groups. All results were compared with each other; relationships were evaluated statistically by using Spearman's correlation analysis. As power of correlation, the range between 0.00 and 0.24 was taken as weak correlation ($r \leq 0.24$); 0.25-0.49 as moderate ($0.25 \leq r \leq 0.49$); 0.50-0.74 as strong ($0.50 \leq r \leq 0.74$) and 0.75-1.00 as very strong ($0.75 \leq r \leq 1.00$), according to the correlation coefficient.

## RESULTS

Serum, fresh and dried urine PSA values are shown in Table 1. Serum tPSA values correlated weakly with tPSA values obtained from fresh and all 3 dried urine samples (r = 0.09; 0.06; 0.18 and 0.09 between serum and fresh urine, 1-day, 7-day, 28-day values, respectively). Serum fPSA also correlated weakly resembling the tPSA. Fresh urine PSA values correlated strongly with dried urine PSA values of 1-, 7- and 28-day (for tPSA r = 0.65; 0.57; 0.62 and for fPSA r = 0.61; 0.57 and 0.60, respectively). tPSA values of all 3 dried urine samples were correlated very strongly among them (r = 0.91 between days 1 and 7, r = 0.97 between 1 and 28-day resembling fPSA as 0.92 and 0.98, respectively). Fresh and dried urine associations are shown in Table 2.

## DISCUSSION

PSA measurements in urine could be used for diagnosis, treatment and follow-up of prostate cancer.[9-12] PSA is not lost in dried urine on filter paper up to 3 years and could be measured after dissolved.[8] Filter paper has been used for decades extensively to collect, store and transfer heel blood for screening the disease phenylketonuria.[13] Similarly, it was established that blood dried on filter paper could keep PSA stable and if the blood dissolved conveniently PSA could be measured and this method might be of value in prostate cancer screening programs.[14] Collecting urine on filter paper provides some important advantages compared to venous blood draw. First of all, collecting urine is not an invasive method as venipuncture and does not require health providers, special instruments and proper environment. It is affordable and has also a convenience of storage and transport of the biomarker. As a negative aspect, standardization of obtaining and storing

**Table 1: Mean results of fPSA and tPSA of each group**

| | fPSA (ng/ml) | tPSA (ng/ml) |
|---|---|---|
| Serum | 0.305±0.372 | 1.180±1.140 |
| Fresh urine | 186.660±109.437 | 295.444±298.223 |
| Dried urine, 1. day | 53.548±78.336 | 57.316±90.427 |
| Dried urine, 7. day | 53.318±78.987 | 67.017±131.861 |
| Dried urine, 28. day | 47.216±75.517 | 58.421±134.631 |

**Table 2: Fresh and dried urine samples correlations**

| Spearman's rho | UPSA | dPSA | wPSA | mPSA |
|---|---|---|---|---|
| UPSA | | | | |
| Correlation coefficient | 1.000 | 0.711** | 0.674** | 0.614** |
| Sig. (2-tailed) | | 0.000 | 0.000 | 0.000 |
| *N* | 41 | 41 | 41 | 41 |
| dPSA | | | | |
| Correlation coefficient | 0.711** | 1.000 | 0.955** | 0.927** |
| Sig. (2-tailed) | 0.000 | . | 0.000 | 0.000 |
| *N* | 41 | 41 | 41 | 41 |
| wPSA | | | | |
| Correlation coefficient | 0.674** | 0.955** | 1.000 | 0.982** |
| Sig. (2-tailed) | 0.000 | 0.000 | . | 0.000 |
| *N* | 41 | 41 | 41 | 41 |
| mPSA | | | | |
| Correlation coefficient | 0.614** | 0.927** | 0.982** | 1.000 |
| Sig. (2-tailed) | 0.000 | 0.000 | 0.000 | |
| *N* | 41 | 41 | 41 | 41 |

**Correlation is significant at the 0.01 level (2-tailed), UPSA: Fresh urine PSA, dPSA: 1-day PSA, wPSA: 7-day PSA, mPSA: 28-day PSA

the sample is one of the most important challenges. Results derived from fresh and dried urine samples need to be corrected. We have chosen the days 1, 7 and 28 to see what would happen 1 day, 1 week and 1 month later if urine containing PSA dried. We have seen a significant difference in PSA content of urine when it dried but persisted along a month stable. Laboratory standard protocols require serum or plasma samples, so the remaining biomarkers may require specific protocols validated for clinical use.[15]

As observed between the serum and the urine values of PSA, the serum fPSA and tPSA values also did not correlate strongly with the fPSA and tPSA values obtained from dried urine on filter paper by dissolving it periodically. This denotes that PSA values obtained from dried urine could not represent the serum values. Meanwhile among the three urine samples derived by dissolving from the filter papers PSA values correlated very strongly. But PSA values of fresh urine and dried urine correlated only strongly. Eventually, PSA values obtained from fresh and dried urine couldn't reflect the serum values even though they have strong or very strong correlations among them. No literature has been encountered exhibiting any correlation between the serum and dried urine PSA values. But Sato stated that semen and urine samples those containing PSA could be kept stable on filter paper for 3 years for forensic purposes but he didn't state if there was any correlation between the PSA values of such biomarkers and the serum.[8]

It has been suggested that free and complex PSA (cPSA) were metabolized by the liver but fPSA had an additional elimination pathway such as glomerular filtration resulting in a shorter duration of half life.[16,17] When cPSA suggested to be secreted by the periurethral glands, fPSA could be expected as the main PSA fraction in the urine.[4] In accordance with this, free/total PSA ratios derived from fresh and dried urine were calculated as higher when compared to the serum free/total PSA ratios (63.1% fresh and 93.4% one-day versus 25.8% serum).

Bolduc *et al.* stated that if urine tPSA was more than 150 mg/dl when the serum tPSA was between 2, 50 and 10,00 ng/ml, it would be an indicative of a benign condition.[18] On the other hand Pejcic stated that urinary PSA itself could not differentiate between malignant and benign lesions but with serum PSA, it could be beneficial in staging and follow-up of the patients underwent hormonal therapy.[19] We also estimate that PSA values obtained from the fresh and dried urine samples could not be a diagnostic tool for this purpose. For urinary PSA could reflect any PSA increment in the body earlier, fresh and dried urine PSA values could be valuable in staging and follow-up of the patients but these values need to be showed to correlate with such conditions.

PSA values obtained from fresh and dried urine samples did not correlate strongly with simultaneously obtained serum PSA values. So, we conclude that PSA values derived from fresh and dried urine samples could not reflect serum PSA values. Therefore PSA values obtained from fresh and dried urine samples could not be a diagnostic tool but need to be showed how strongly correlated with changes of benign or malignant events of the prostate to follow-up outcomes of prostatic diseases. But, because dried urine on a filter paper can be stable for years, it could be used for forensic purposes.

## REFERENCES


1. Pelzer AE, Volgger H, Bektic J, Berger AP, Rehder P, Bartsch G, *et al.* The effect of percentage free prostate-specific antigen (PSA) level on the prostate cancer detection rate in a screening population with low PSA levels. BJU Int 2005;96:995-8.
2. Sirovich BE, Schwartz LM, Woloshin S. Screening men for prostate and colorectal cancer in the United States: Does practice reflect the evidence? JAMA 2003;289:1414-20.
3. Seo HS, Lee NK. Predictors of PSA screening among men over 40 years of age who had ever heard about PSA. Korean J Urol 2010;51:391-7.
4. Irani J, Millet C, Levillain P, Doré B, Begon F, Aubert J. Serum-to-urinary prostate specific antigen ratio: its impact in distinguishing prostate cancer when serum prostate specific antigen level is 4 to 10 ng./ml. J Urol 1997;157:185-8.
5. Lövgren J, Valtonen-André C, Marsal K, Lilja H, Lundwall A. Measurement of prostate-specific antigen and human glandular kallikrein 2 in different body fluids. J Androl 1999;20:348-55.
6. Murthy A, Rajendiran TM, Poisson LM, Siddiqui J, Lonigro1 RJ, Alexander DC *et al.* alternative screening tool for prostate adenocarcinoma: Biomarker discovery. MURJ 2010;19:71.
7. Hillenbrand M, Bastian M, Steiner M, Zingler C, Müller M, Wolff JM, *et al.* Serum-to-urinary prostate-specific antigen ratio in patients with benign prostatic hyperplasia and prostate cancer. Anticancer Res 2000;20:4995-6.
8. Sato I, Sagi M, Ishiwari A, Nishijima H, Ito E, Mukai T. Use of the "SMITEST" PSA card to identify the presence of prostate-specific antigen in semen and male urine. Forensic Sci Int 2002;127:71-4.
9. Haroun AA, Hadidy AS, Awwad ZM, Nimri CF, Mahafza WS, Tarawneh ES. Utility of free prostate specific antigen serum level and its related parameters in the diagnosis of prostate cancer. Saudi J Kidney Dis Transpl 2011;22:291-7.
10. Breul J, Pickl U, Hartung R. Prostate-specific antigen in urine. Eur Urol 1994;26:18-21.
11. Pejcić T, Hadzi-Djokić J, Marković B, Dragićević D, Glisić B, Lalić N, *et al.* Urinary PSA level and relative tumor volume after prostate biopsy. Acta Chir Iugosl 2009;56:17-21.
12. Irani J, Salomon L, Soulié M, Zlotta A, de la Taille A, Doré B, *et al.* Urinary/serum prostate-specific antigen ratio: comparison with free/total serum prostate-specific antigen ratio in improving prostate cancer detection. Urology 2005;65:533-7.
13. Berry HK. Procedures for testing urine specimens dried on filter paper. Clin Chem 1959;5:603-8.
14. Hoffman BR, Yu H, Diamandis EP. Assay of prostate-specific antigen from whole blood spotted on fitler paper and application to prostate cancer screening. Clin Chem 1996;42:536-44.
15. McDade TW, Williams S, Snodgrass JJ. What a drop can do: Dried blood spots as a minimally invasive method for integrating biomarkers into population-based research. Demography 2007;44:899-925.
16. Bruun L, Savage C, Cronin AM, Hugosson J, Lilja H, Christensson A. Increase in percent free prostate-specific antigen in men with chronic kidney disease. Nephrol Dial Transplant 2009;24:1238-41.

17. Kilic S, Yalcinkaya S, Guntekin E, Kukul E, Deger N, Sevuk M. Determination of the site of metabolism of total, free, and complexed prostate-specific antigen. Urology 1998;52:470-3.
18. Bolduc S, Lacombe L, Naud A, Grégoire M, Fradet Y, Tremblay RR. Urinary PSA: A potential useful marker when serum PSA is between 2.5 ng/mL and 10 ng/mL. Can Urol Assoc J 2007;1:377-81.
19. Pejcic T, Hadzi-Djokic J, Acimovic M, Topuzovic C, Milkovic B, Janjic A. Urinary prostate specific antigen: is the clinical use likely? Acta Chir Iugosl 2005;52:69-74.

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