



Evaluation of serum prostate specific antigen level in correlation with age, prostatic volume and International Prostate Symptom Score

KEYWORDS

prostate specific antigen, screening, international prostate symptom score, prostate cancer

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ABSTRACT *The aim of the study was to see if there is any correlation between serum prostate specific antigen (PSA) and prostate enlargements. This correlation was studied in order to establish whether elevated PSA levels could be a diagnosis for prostate cancer before the appearance of any specific symptoms. 313 male subjects from Mureş County (Romania) participated to the screening. The results from the PSA measurement and the prostate volume examination were compared. A positive correlation is present between the IPSS and the PSA serum concentration. Correlation was found between the PSA serum concentration and age. No correlation was found between serum PSA level and other laboratory parameters. PSA concentration compared with prostatic volume and residual urine volume were also more closely investigated. The corroboration of PSA level with information obtained by ultrasound and rectal examination, showed to be helpful in early diagnosis of prostate cancer and benign prostate hyperplasia (BPH).*

Introduction:

Determination of PSA (prostate specific antigen) is the most used marker for screening in patients above 50 years of age and its high values can be correlated especially with BHP (benign prostate hyperplasia), prostate cancer, prostatitis (1), (2), (4), (5), (9), (11), (13). Based on screenings made amongst males between 50-70 years of age, in 3-4% of the cases prostate cancer can be diagnosed 5 years before symptoms occur.

The screening procedure usually includes three methods: PSA determination, rectal examination and transrectal ultrasound.

The International Prostate Symptom Score (IPSS), created by the American Urologist Association, is an 8 question (7 symptom questions + 1 quality of life question) screening form used for rapidly diagnose, track the symptoms and suggest to manage the lower urinary tract symptoms of BPH (8), (12).

Patients with BPH 1) may need no treatment, just observation, because many patients situation stays the same or even improves over the years, or 2) many may need only medical treatment, a) either only with an alpha-1-adrenergic antagonist, b) with a 5-alpha reductase inhibitor as monotherapy or c) with an alpha-1-adrenergic antagonist plus a 5-alpha reductase inhibitor, depending on the severity of their symptoms, or 3) may need surgery (2), (4), (5), (7), (14).

Material and methods:

The study was performed on 313 male subjects from Tîrgu Mureş and the surrounding areas. The general practitioners evaluated their patients using a standard questionnaire, the IPSS (International Prostate Symptom Score) and they generally selected patients with over 12 score (n = 259) to participate to this screening. This threshold was proposed by the firm that offered the financial support for this study, to eliminate patients with very mild symptoms, unlikely to need medication (Avodart® is the product of the GSK firm designed for the treatment of patients presenting BPH). A part of the subjects (n = 54) were selected by an urologist based on their symptoms and clinical examination data cor-

roborated with the IPSS.

The patients selected to participate to the screening were between 50 and 90 years of age, averaged 64.31 years +/- 8.78 (SD), median 64.00 years and 52,7% of the patients were from rural areas.

The PSA (prostate specific antigen) level was determined by an Immulite 1000 analyzer using a chemiluminescence procedure. The normal range is between 0,1 – 4 ng/ml. Free PSA was determined in patients presenting PSA values between 4-10 ng/ml. The normal range for free PSA is 0,1 – 0,86 mg/l.

The prostatic volume was determined by ultrasound performed by urologist, followed by a rectal examination (10).

PSA density (PSAD), the amount of PSA expressed in nanograms for each cubic centimeter of the prostate volume, was determined using the formula: serum PSA/gland volume estimated by ultrasound.

All the results of the patients selected by the general practitioners were also reviewed by urologist who wrote a medical letter containing detailed information on the patient's further management.

The statistical analysis of our data was performed by the GraphPad InStat program, we used correlation analysis and unpaired Student t test, occasionally with Welch-correction (in case of significant difference between standard deviation). All data passed Kolmogorov and Smirnov normality test for Gaussian distribution. Numeric results show mean values followed by standard deviation (SD).

Results:

The average PSA level was 3.73 ng/ml +/- 11.21 (SD), minimum 0.1, maximum 150 ng/ml, median 1.53 ng/ml (n=313). 59 subjects presented elevated PSA serum concentration (18.85% of the studied patients), in 33 of the cases (10.5%) the urologists prescribed medication for prostatic disease.

We obtained a positive correlation between the IPSS and

the PSA serum concentration ($r = 0.1151$, the slope is significantly different from zero, $p = 0.0408$), and also a positive correlation between the age of the patients and their serum PSA level ($r = 0.1315$, the slope is significantly different from zero, $p = 0.0201$).

Figure 1. Correlation between serum PSA level and IPSS

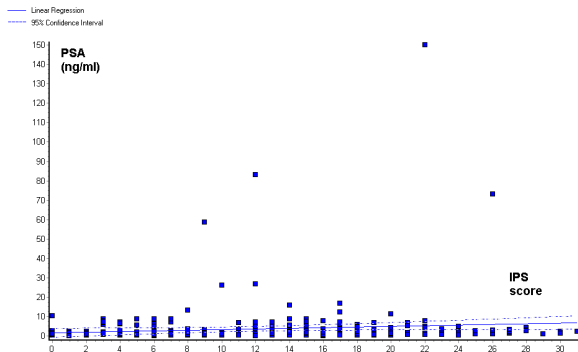
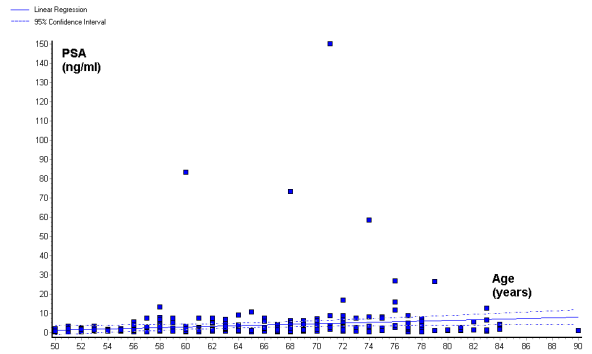


Figure 2. Correlation between serum PSA level and age

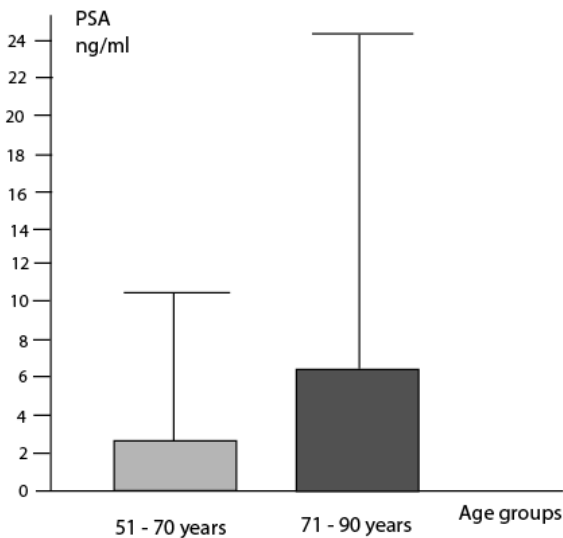


Separating the patients into different age groups and comparing PSA values in patients between 51-70 years and those between 71-90 years, the difference was at the limit of significance ($p = 0.0631$), using the Student t test, Welch corrected.

Table I. Comparison of PSA values and IPS score between patients of different age groups

Age group	Average age +/- SD	Average PSA value +/- SD Free PSA: 0.99 +/- 0.61 ng/ml	PSA range, median value	Average IPS score +/- SD	IPSS range, median value
51-70 years, 228 subjects	60,47 +/- 5.71 years	2,76 +/- 7.47 ng/ml	0.1 – 83.1 ng/ml, median: 1.33 ng/ml	10.83 +/- 7.29	0 – 30, median: 11.5
71-90 years, 85 subjects	75,84 +/- 3.96 years	6.58 +/- 17.82 ng/ml Free PSA: 1.72 +/- 1.07 ng/ml	0,1 – 150 ng/ml, median: 2.42 ng/ml	14.17 +/- 7.27	1 – 31, median: 13.5

Figure 3. Average PSA concentration in patients from different age groups



No significant difference ($p=0.2162$) was obtained comparing average PSA value (2.97 ± 7.16 ng/ml) for patients from rural areas (165 subjects) with that obtained in case of those from urban environment (4.55 ± 14.46 ng/ml, 148 subjects).

In some patients of our study-group ($n = 30$) we also determined other laboratory parameters to reveal possible correlations with the PSA value. These patients were those that came to the urologist working at our medical unit and were sent to the laboratory for these tests because of their other diseases. We studied these correlations because several articles mention dyslipidemia and metabolic syndrome as risk factors for BPH (3), (6). Several patients from distant rural ar-

reas didn't have any laboratory tests in their medical records, and one of the purposes of this study was to offer these patients with extremely poor financial background a possibility to participate to a proper screening programme regarding prostatic diseases.

The mean serum cholesterol level was 198.62 mg/dl ± 42.48 (SD), minimum 125.80 mg/dl, maximum 270.40 mg/dl, no correlation was found with serum PSA concentration ($r = -0.0303$, $p = 0.8738$). We considered the normal range for serum cholesterol level between $100 - 200$ mg/dl. 15 patients (50% of the subgroup) presented elevated serum cholesterol levels. Serum triglyceride mean concentration was 163.82 mg/dl ± 81.46 (SD), minimum 61.10 mg/dl, maximum 422.50 mg/dl, no correlation was found with serum PSA concentration ($r = -0.1274$, $p = 0.5353$). The normal range for triglycerides is considered $50 - 150$ mg/dl. 7 patients (23.3% of the subgroup) presented elevated serum triglyceride levels. Average glycaemic level was 101.34 mg/dl ± 22.24 (SD), minimum 70.40 mg/dl, maximum 149.90 mg/dl, no correlation was found with serum PSA concentration ($r = 0.09152$, $p = 0.7012$). The normal range for blood glucose level is $60 - 100$ mg/dl. 10 patients (one third of the subgroup) presented elevated glycaemia. Mean serum uric acid concentration was 5.96 mg/dl ± 1.86 (SD), minimum 2.90 ng/ml, maximum 9.60 mg/dl, no correlation was found with serum PSA concentration ($r = 0.04790$, $p = 0.8551$). The normal range for serum uric acid concentration is $3 - 7$ mg/dl. 5 patients (16.7% of the subgroup) presented elevated serum uric acid concentration.

Based on the fact that PSA density higher than 0.15 ng/cc should raise concerns about prostatic cancer, we determined this parameter in our patients (we could calculate PSAD in case of 191 subjects). The average value was 0.086 ng/cc ± 0.71 SD, maximum 9.77 , minimum 0 , median 0.016 ng/cc. We observed values exceeding 0.15 ng/cc in 7 patients (2.15%) and one of these patients was already diagnosed with prostatic cancer (PSA: 150 ng/ml), in case of the others firm prostate glands were found by rectal examination,

and prostate biopsy was then recommended. Overall 12 of the studied patients (3.7%) presented firm prostate glands at rectal examination.

The residual urine volume was minimal in case of 62 patients (19%), under 50 ml was in case of 15 patients (4.6%), between 50-100 ml was observed in 13 patients (4%), and over 100 ml in 5 patients (1.5%).

We could obtain information regarding associated diseases in 57 patients. Concerning associated diseases, we found diabetes mellitus in 12 of these patients (21.05%), documented cardiovascular diseases were present in case of 10 patients (17.54%), and malignancy was present in 5 patients (8.77%), while other urologic disorders besides benign prostate hyperplasia could be observed in 13 patients (22.81%).

Discussions

Comparing the data of our study with other scientific articles, the correlation of PSA level with age and IPSS is similar to that mentioned in the literature.

Several studies suggest that in any patient presenting BPH, the possible presence of type 2 diabetes, hypertension, obesity, high insulin level and low HDL-cholesterol levels should be considered, and in patients suffering from these conditions, the possibility of a clinically important BPH should be kept in mind (3), (6). Our study also underlines the close relationship between BHP, dyslipidemia and diabetes mellitus.

Besides the biochemical parameters determined in a subgroup of the studied patients, the measurement of serum LDL-cholesterol, HDL-cholesterol level and insulinaemia should be considered in a larger group of patients presenting BPH.

Conclusions:

Higher PSA levels were obtained in patients from elderly age groups compared to the younger subjects; we found a positive correlation between the age and the patients and their serum PSA level, but no significant difference could be noticed in PSA average levels between patients from rural and urban environment.

Positive correlation was obtained between IPSS and PSA concentration, which underlines the role of this standard questionnaire to select patients for similar studies.

Corroborating PSA level with information obtained by ultrasound and rectal examination helps the early diagnosis of prostate cancer and BPH.

No correlation was found between serum PSA level and other laboratory parameters, but this should be investigated in a larger group of patients.

Diabetes mellitus, cardiovascular pathology (hypertension, ischemic cardiopathy, stroke, arteriopathy, myocardial infarction) and urologic disorders (prostatitis, renal cyst, pyelonephritis, single kidney, nephrosclerosis, chronic renal insufficiency, varicocele) are the most common associated diseases in patients presenting benign prostate hyperplasia.

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