

# THE IMPORTANCE OF THE IMMUNOLOGICAL MARKERS IN PROSTATE CARCINOMA

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**Abstract:** *The biological markers are substances produced by tumour, observable in periphery blood, urine, tumour tissue, identifiable true radio – immunology laboratory methods. The most usually biomarkers from prostatic neoplasm with prognostic importance and predictive for diagnostic and treatment are the PSA and free-PSA*

**Keywords:** *prostatic carcinoma, the biological markers*

**Rezumat:** *Markerii imunologici sunt substanțe produse de tumoră evidențiable în sângele periferic, urină, țesut tumoral, identificabile prin mijloace de laborator radio-imunologice. Cei mai uzuali biomarkeri din neoplaziile prostatice cu rol prognostic și predictive al diagnosticului și tratamentului sunt PSA-ul și Free PSA.*

**Cuvinte cheie:** *cancer prostatic, biomarkeri*

## INTRODUCTION

Beginning with the 1980s the incidence of prostate carcinoma has risen spectacularly all over the world, in some countries (the USA, Sweden) being on the top of the illnesses, over-passing lung cancer. In 1990, in the European Community, 2.6 million new cases were registered, which represent 11% from all types of male cancer, with a death rate of 9% (3, 4). Prostate carcinoma is a national health problem, more important especially in the most developed countries, for which the incidence is of 15%, than in the developing countries, with an incidence of 4% (5).

The explanation of this phenomenon is the continuous growth of lifespan and the efficacious screening through insertion of PSA bio-marker (8). Last years researches showed a diversity of biological products – biological markers, which are, on one hand substances produced by the tumour itself observable in periphery blood, urine, tumour tissue; and on the other hand, are those biological phenomena intimately tied up to the presence of the tumour, identifiable through radio-immunology laboratory methods, with prognosis and predictive importance for the diagnosis.

The most important markers for prostate carcinoma are PSA and free-PSA.

PSA is a glyco-protein with a single proteic chain, produced by epithelial cells which line the acini and the ductiles in the prostate structure. High levels of PSA may be found in the blood of men who suffer of

benign prostate affection (prostatitis and benign prostate hyperplasia - BPH) or malignant. PSA values are useful in prostate carcinoma management. It can be used with diagnosis value, along with free-PSA and free-PSA report/total PSA.(7)

## OBJECTIVES AND RESEARCH METHOD

The present paper encircles itself between the papers which describe the male genital-urinary cancer, e. g. testicular and prostate carcinoma, and it desires to realize a preliminary prospective analysis over a 93 homogenous group of patients with testicular cancer in order to build up a clinical-therapeutically characterization and to identify theoretical possibilities of using the immunological markers when diagnose this type of cancer, the relapses of the illness, using them as prognosis and monitoring treatment factors.

Through this analysis we evaluated a series of clinical and para-clinical aspects collected from the patients with prostate carcinoma (the extension degree of the tumour, the stage of the illness, the moment of the local recurrence and the appearance of the metastasis), in order to show some possible connections between these and the value of the immunological markers.

**Observed markers:** for the prostate carcinoma – PSA. The normal PSA value is under 4.5ng/ml.

**Study inclusion criteria:** TNM stages; histopathological confirmation: information regarding the extension degree of the tumour and ganglionic infestation; patients with specific oncologic treatment; the value of the immunological markers at the beginning and during the treatment; objective documentation regarding the metastasis and the local recurrence.

## RESULTS AND DISCUSSION

The use of PSA as screening marker to detect prostate carcinoma (when the patients do not show symptoms) is uncertain. Rectal examination and PSA are recommended constantly in prostate carcinoma, at certain time intervals, when talking about men aged between 55-74 years old. So, the screening addresses itself to more than 50 years old men, with at least 10 years life expectation, or to over 40 years old men with high risk (meaning with prostate carcinoma precedents in the family). PSA is a part of the first rank diagnosis when

## CLINICAL ASPECTS

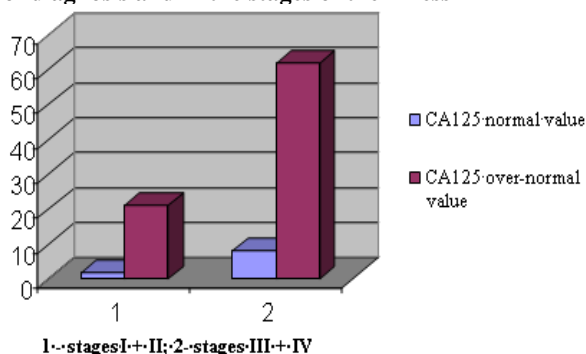
talking about prostate carcinoma. It is considered that a PSA value of 4-4.5ng/ml raises suspicions of a prostate carcinoma.

After applying the selection criteria shown above, we chose a group of 93 patients, aged between 45-88 years old, with an age average of 66.5 years.

From the 93 patients, 23 patients were in the 1<sup>st</sup> and the 2<sup>nd</sup> stages of the illness, and 70 patients in the 3<sup>rd</sup> and the 4<sup>th</sup> stages of the illness. One single patient (1.07%) suffered a complete operation, 34 patients (36.55%) were incomplete operated (orchiectomized +/-TUR) and 58 patients (62.36%) did not suffer any surgical intervention. For 58 patients the illness evolved in bony, lung, and liver metastasis or had a local recurrence; in the case of the other 35 patient (37.64%) the illness did not evolve. In the majority of cases, PSA values were registered at the beginning and at the end of every stage of the therapy.

From the total number of patients, PSA value in the moment of diagnosis was the following: over-normal value for 83 patients (89.24%), comparing with normal value for 10 patients (10.76%); these numbers show once more the importance of PSA high value in determining the diagnosis. When correlate the PSA value in the moment of diagnosis with the stages of the illness we noted that during advanced stages PSA value was high in 62 cases (66.66%); during initial stages PSA high value was registered in only 21 cases (22.58%); these numbers are statistically eloquent;  $p = 0.04$  (Picture no.1)

**Picture no. 1: Correlation between PSA in the moment of diagnosis and in the stages of the illness**



These results show that PSA values identified in the moment of diagnosis was of great importance in determining the final diagnosis (it may be an indicator of prostate carcinoma), over-normal value of the marker was always associated with advanced stages of the illness.

PSA values identified in the moment of diagnosis was of great importance in determining the final diagnosis

It was ascertained that in the case of the patients with abnormal PSA value during the first six months from the beginning of the treatment the prognosis is not sure. The patients with high PSA values in the moment of diagnosis will also have high values markers in case of relapse. PSA value may be a prognosis indicator, and the research show that PSA growth in the case of prostate

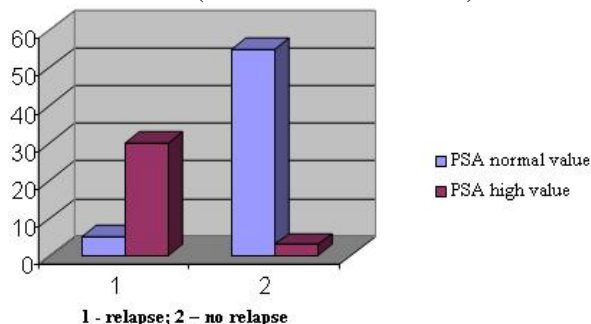
carcinoma patients may precede the symptoms of a relapse. Due to post-therapeutically PSA monitoring, patients benefit from the changing of treatment when exists the suspicion of a relapse, even if there are no symptoms, but the PSA values are high.

This is what the present paper states. Monitoring the therapy, was shown that PSA marker value during monitoring was of: normal value for 60 patients (64.52%) and high value for 33 patients (35.48%). Five patients (5.37%) from the total of 60 patients (64.52%) with normal value registered an evolution of the illness (metastasis or relapses), and the rest of 55 patients (59.14%) did not register an evolution of the illness. From those 33 patients with PSA high value, 30 patients (32.26%) registered an evolution in their illness, and 3 patients (3.22%) did not register an evolution of their illness. Table 1, Diagram 2)

**Table no. 1. PSA correlation with the evolution of the illness (metastasis or relapses)**

PSA evolution	Evolution	No evolution	Total
Normal value	5 (5.37%)	55 (59.14%)	60 (64.52%)
Over-normal value	30 (32.26%)	3 (3.22%)	33 (35.48%)
Total	35 (37.64%)	58 (62.36%)	93 (100%)

**Picture no. 2. PSA correlation in evolution with the disease evolution (metastasis or recurrence)**



It can be easily observed that 32.26% of the patients who registered an evolution in their illness registered also a PSA high value. **PSA value is proved to be an indicator for the negative prognosis of the illness.**

From the 93 patients studied, 35 patients (37.67%) registered an evolution in their illness: 6 (17.14%) were diagnosed in the initial stages (the 1<sup>st</sup> and the 2<sup>nd</sup>) of the illness, and the rest of 29 patients (82.85%) were diagnosed in the 3<sup>rd</sup> and the 4<sup>th</sup> stages.

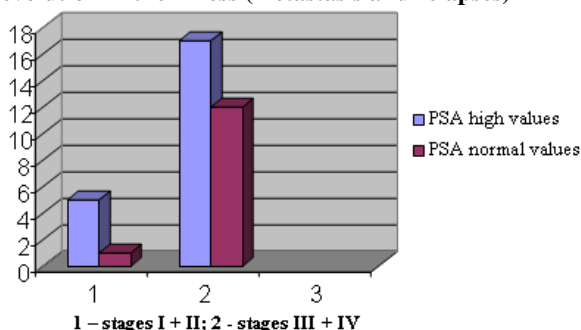
From the 6 patients diagnosed in the 1<sup>st</sup> and the 2<sup>nd</sup> stages and who registered an evolution in their illness, 5 patients (14.28 %) had high PSA value, and 1 patient (2.92 %) had normal PSA value; from those 29 patients diagnosed in the 3<sup>rd</sup> and 4<sup>th</sup> stages and who registered an evolution in their illness, 17 (48.57 %) had high PSA value, and 12 patients (34.28 %) normal PSA value.

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**Table no. 2. PSA value correlated with the stage of the illness and the moment when appeared an evolution in the illness (metastasis and relapses)**

Patients with relapse - stage	High PSA	Normal PSA value	Total
I + II	5 (14.28%)	1 (2.87%)	6 (17.15%)
III + IV	17 (48.57%)	12 (34.28%)	29 (82.85%)
Total	22 (62.85%)	13 (37.15%)	35 (100%)

**Picture no. 3. PSA value correlated with the stage of the illness and the moment when appeared an evolution in the illness (metastasis and relapses)**



Advanced illness stage correlated with high PSA marker value is indicators for a negative prognosis illness evolution, showing the failure of the therapeutic process through metastasis and relapse.

**Table no. 3. Correlation of PSA value in the moment of diagnosis, post-therapeutic values and the relapsed evolution in the illness**

Patients with relapse (metastasis)	PSA diagnosis	Post-therapy PSA	PSA evolution
normal	2	17	5
high	33 (94.28%)	18 (51.42%)	30 (85.71%)
total	35	35	35

The table above clearly shows us that from the 33 patients (94.28%) who had high PSA value in the moment of diagnosis, for 18 patients (51.42%) the PSA value did not normalized during the post-therapy stage (around 6 months from the beginning of the treatment: surgical intervention, hormonotherapy, radiotherapy, chemotherapy) and the prognosis regarding their illness was not sure, due to the evolution in their illness and in the fact that the marker value remained high for 30 patients (85.71%).

The high PSA marker value in the moment of diagnosis and most of all during post-therapy are indicators for a negative prognosis in illness evolution, showing the failure of the therapeutic process through metastasis and relapse.

### CONCLUSIONS

1. High PSA values are related to advanced stages of prostate neoplasia;
2. PSA values in the moment of diagnosis represent a

great help in determining the diagnosis of prostatic cancer;

3. PSA is useful in monitoring the treatment (it draws attention upon a treatment with reduced efficacy or the lack of response to a certain treatment, which imposes the change of that treatment);
4. PSA is a prognosis indicator.

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