



PSA DENSITY - A MARKER FOR POORLY-DIFFERENTIATED PROSTATE CANCER

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ABSTRACT

Purpose: The present study examines the relationship between Prostate-Specific Antigen Density (PSAD) and the degree of differentiation of prostate cancer, as determined by the Gleason score.

Material/Methods: A single-center study was conducted. We analyzed 155 patients who had had surgeries at the Urology Clinic of Saint Anna Hospital in Varna.

Results: We found that an elevated PSAD - especially above 0.15 ng/ml^2 - increases the probability of detecting a poorly-differentiated cancer (with a high Gleason score) with unfavorable features from the pathological report after the radical prostatectomy (seminal vesicle involvement, lymph node metastases and extraprostatic tumor extension).

Conclusions: PSAD is a valid tool which correctly predicts the unfavorable pathology of the removed specimen.

Keywords: Prostate-specific antigen, prostate volume, Gleason score,

INTRODUCTION

The discovery of prostate-specific antigen (PSA) as a tumor marker for prostate cancer (PCa) led to a real revolution in the diagnosis of this disease [1]. However PSA is organ-specific, not tumor-specific, and can be elevated in other conditions, the most common of which is benign prostatic hyperplasia [2, 3]. An attempt to solve some of the problems associated with PSA is the use of PSAD (Prostate-Specific Antigen Density). In it, the PSA is divided by the volume of the prostate to determine the amount of tumor marker secreted per unit of prostate volume - thus eliminating the prostate size factor, where large prostates give an unrealistically high PSA. In the subsequent analysis, we studied the relationship between PSAD and Gleason score (GS) to see if a higher PSAD means a more malignant PCa (with a higher GS).

MATERIALS AND METHODS

The object of the study are 155 patients who underwent radical prostatectomy (RP) at the Urology Clinic of the St. Anna Hospital - Varna. Patients who were operated between January 2013 and December 2020, for whom GS from the biopsy and RP, as well as PSAD are known, were included. In some patients, the prostate biopsy (and the pathological analysis, respectively) was performed in another medical institution. Data were analyzed with IBM SPSS, version 23.

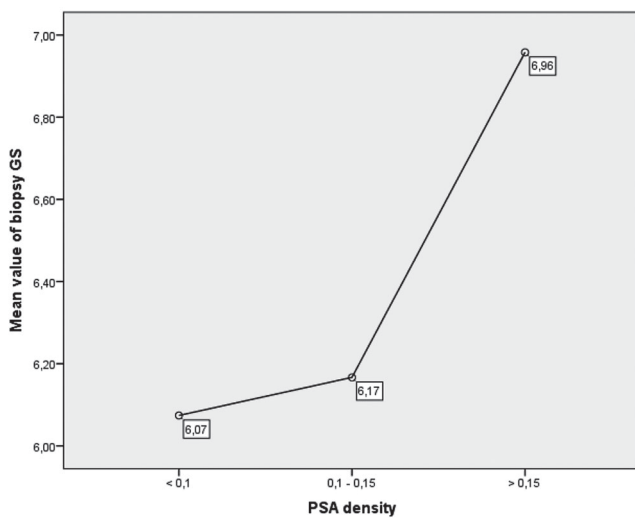
RESULTS

The mean age of the operated patients was 67.6 years, their mean PSA was 15.5 ng/ml , the mean prostate size was 65.34 ml , and the mean PSAD for the entire group was 0.29 ng/ml^2 .

A statistically significant relationship was found between PSAD and GS after prostate biopsy

(Kruskal Wallis test, $X^2 = 16.488$; $p = .021$). For the purpose of the analysis, PSAD values were divided into three groups (below 0.1; between 0.1 and 0.15 and above 0.15). The group with PSAD < 0.1 included 27 (17.2% of all) patients with an average value of GS = 6.07. The group with PSAD 0.1 - 0.15 included 36 (22.9%) patients with an average value of GS = 6.16. The group with PSAD > 0.15 included 94 (59.9%) patients with an average value of GS = 7.03. For graphical representation, the mean values of GS were used (Figure 1).

Fig. 1. Mean GS values after prostate biopsy for the three PSAD groups



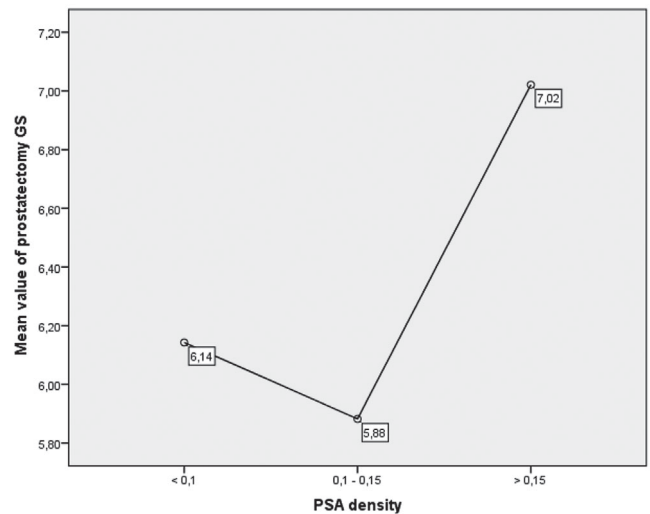
A statistically significant difference in biopsy-GSs was found between the groups with PSAD values < 0.1 and > 0.15 (Mann-Whitney U test, MWU = 864,000; $p = .007$). GS values were statistically significantly higher in the group with PSAD > 0.15 . Also, a statistically significant difference was found in GS values after biopsy between the groups with PSAD values 0.1 - 0.15 and > 0.15 (Mann-Whitney U test, MWU = 1177.500; $p = .004$). GS values were statistically significantly higher in the group with PSAD > 0.15 . No statistically significant difference was found between the groups with PSAD values < 0.1 and 0.1 - 0.15 (Mann-Whitney U test, MWU = 470,000; $p = .817$).

When dividing GS into two groups (≥ 7 and < 7), a statistically significant relationship was also found between GS and PSAD ($X^2 = 8.956$; $p = .011$). The probability of a patient with a PSAD $>$

0.15 to have a GS ≥ 7 was 1.3 times higher compared to a patient whose PSAD was between 0.1 and 0.15 (OR = 1.291; 95%CI = 1.006 - 1.656 ; $p = .028$). The probability of a patient with a PSAD > 0.15 to have a GS ≥ 7 was 1.3 times higher compared to a patient whose PSAD was < 0.1 (OR = 1.308; 95%CI = 1.039 - 1.648; $p = .010$).

The results were similar when comparing PSAD and GS after RP (Kruskal Wallis test, $X^2 = 17.223$; $p = .028$) - here again in the analysis, PSAD values were divided into three groups (below 0.1; between 0.1 and 0.15 and above 0.15). The group with PSAD < 0.1 included 21 (14%) patients with an average value of GS = 6.14. The group with PSAD 0.1 - 0.15 included 34 (22.7%) patients with an average value of GS = 5.88. The group with PSAD > 0.15 included 95 (63.3%) patients with an average value of GS = 7.02. For graphical representation, the mean values of GS were used (Figure 2).

Fig. 2. Mean GS values after radical prostatectomy for the three PSAD groups



A statistically significant difference was found in post-RP GS values between the groups with PSAD < 0.1 and > 0.15 (Mann-Whitney U test, MWU = 721,000; $p = .040$). GS values were statistically significantly higher in the group with PSAD > 0.15 . A statistically significant difference was found in post-RP GS values between the groups with PSAD 0.1 - 0.15 and > 0.15 (Mann-Whitney U test, MWU = 1003.500; $p = .001$). GS values were statistically significantly higher in the group with PSAD > 0.15 . No statistically signifi-

cant difference was found between groups with PSAD < 0.1 and 0.1 – 0.15 (Mann-Whitney U test, MWU = 330,500; p = .633).

When dividing GS into two groups (≥ 7 and < 7), a statistically significant relationship was also found between GS and PSAD ($X^2 = 11.780$; p = .003). The probability of a patient with a PSAD > 0.15 to have a GS ≥ 7 was 1.4 times higher compared to a patient whose PSAD was between 0.1 and 0.15 (OR = 1.396; 95%CI = 1.101 – 1.771; p = .002). The probability of a patient with PSAD > 0.15 to have a GS ≥ 7 was 1.2 times higher compared to a patient whose PSAD was < 0.1 (OR = 1.235; 95%CI = 1.011 – 1.508; p = .021).

DISCUSSION

PCa can be treated in many ways – including hormonal therapy, prostate surgery and radiotherapy. Accurate treatment depends on the correct initial diagnosis, which is why detecting possible signs of poorly-differentiated PCa is so important. As GS after the prostate biopsy is sometimes different from that after RP [4, 5], we have analyzed both scenarios - the association of PSAD with GS from biopsy and the association of PSAD with GS after RP; it appears that there is no significant difference between the two approaches. In both cases, with PSAD > 0.15 ng/ml², the probability of detecting PCa with higher GS increases. Similar results are also found in other studies [6, 7]. At the same time, attempts have recently been made to include PSAD in the overall algorithm for the diagnosis of PCa [8, 9]. Patients with PSAD < 0.09 ng/ml² are likely to be at low risk for PCa and do not require prostate biopsy. Conversely, patients

with PSA > 0.15 ng/ml² and PI-RADS 3 (grey zone on MRI) are at high risk of PCa and should be biopsied. However, not all authors agree that PSAD adds new information to the already performed MRI [10].

In support of the above-mentioned data on the adverse influence of elevated PSAD, we can also add some data from the pathological report after RP [11]: we had 20 patients with an involved seminal vesicle (stage pT3b), of them, only one with PSAD < 0.1, two with PSAD between 0, 1 and 0.15, and all the others (17 patients) had PSAD > 0.15. There were 4 patients with lymph node metastases (stage pN1), of which only one had PSAD < 0.1, and the other three had PSAD > 0.15. There were 43 patients with extraprostatic tumor extension (stage pT3a), of which four had PSAD < 0.1, nine had PSAD between 0.1 and 0.15, and all the rest (30 patients) had PSAD > 0.15. The number of patients is not enough for accurate statistical analysis, but there also seems to be an increased risk of detecting PCa with unfavorable characteristics from the pathological report after RP.

CONCLUSION

The analysis shows that an elevated PSAD - especially above 0.15 ng/ml² – increases the probability of detecting a poorly-differentiated PCa (with higher GS both from the biopsy of the prostate and from the RP). Probably also increased is the risk of detecting PCa with unfavorable characteristics from the pathological report after RP – with seminal vesicle involvement, lymph node metastases and extraprostatic tumor extension.

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