

## Original Research Article

# The role of preoperative PSA level in prostate cancer

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### ABSTRACT

**Background:** PSA levels between 0-4 ng/ml is generally accepted as normal range, there is no world widely accepted cut-off value. PSA level is most commonly used for determining patients to whom needle biopsy should be performed. Authors aimed to investigate the relationship between preoperative PSA level and histopathological features.

**Methods:** Ninety prostatic adenocarcinoma cases diagnosed between January 2013 and January 2018 and treated by RP were included. Patients had no measurement of PSA before the operation were excluded from the study. Patients were grouped according to preoperative PSA as low-risk (<10 ng/ml), medium-risk (10-20 ng/ml) and high-risk (>20 ng/ml). The relations between all of the histopathological parameters were analyzed in addition to the preoperative PSA levels.

**Results:** The mean age and preoperative PSA level was found as 64.16, and 12.33, respectively. The presence of EPE and tumour positive base margin showed significant relation among PSA groups as well as the presence of lymphovascular invasion and the involvement of the seminal vesicles. Intracytoplasmic mucin and foamy cytoplasm was more common in low-risk PSA group and the difference was significant.

**Conclusions:** PSA level is one of the most commonly used marker for predicting high risk patients before the operation however it may also show relation with various histopathological factors that have effect on the prognosis of prostatic adenocarcinoma.

**Keywords:** Histopathology, Prostate cancer, Prostate specific antigen

## INTRODUCTION

Prostate cancer is the most common cancer in men and also the second most common reason of cancer related deaths.<sup>1</sup> Among many diagnostic tests routine measurements of prostate specific antigen (PSA) has an important role in diagnosis.<sup>2</sup> Even though PSA levels between 0-4 ng/ml is generally accepted as normal range, there is no world widely accepted cut-off value. Different grouping scales were defined for preoperative PSA levels. But the most commonly used one is low-risk (PSA<10 ng/ml), medium-risk (PSA 10-20 ng/ml) and

high risk (PSA>20 ng/ml).<sup>3</sup> PSA level is most commonly used for determining patients to whom needle biopsy should be performed. However, many studies point out the PSA level may also correlate with the biological aggressiveness of the tumor.

Many histological parameters such as Gleason score, extra prostatic extension, involvement of vesiculoseminalis, status of lymph nodes and surgical margins can be essential for predicting prognosis in addition to preoperative PSA levels.<sup>4</sup> In this study, authors aimed to investigate the relationship between preoperative PSA level, Gleason score, tumor volume,

surgical margin status, extra prostatic extension and histopathological features in prostate cancer cases treated with RP.

## METHODS

A total number of 90 cases diagnosed with prostatic adenocarcinoma between January 2013 and January 2018 and treated by RP were included in this study. Patients had no measurement of PSA before the operation were excluded from the study. All of the specimens were evaluated with same procedure as all surgical margins were inked and all of the specimens were submitted for microscopic evaluation totally. The presence of histopathological features was noted for each case. Gleason score was used as grade grouping which was accepted by WHO in 2016.<sup>5,6</sup> The presence of high grade prostatic intraepithelial neoplasia, intraluminal mucin and foamy cytoplasm were estimated as positive even seen in a single gland.

The relations between all of the histopathological parameters such as Gleason score, extra prostatic extension, perineural invasion, vascular invasion, ganglion involvement, tumor positive surgical margins, necrosis, vesiculoseminalis involvement, HGPIN, intraluminal mucin, and foamy cytoplasm were studied in addition to the preoperative PSA levels.

Patients were grouped according to preoperative PSA as low-risk (<10 ng/ml), medium-risk (10-20 ng/ml) and high-risk (>20 ng/ml). These groups were then compared for differences among histopathological features. ANOVA test was used for continuous variables, chi-square test and Kruskal-Wallis test were used for categorical variables. The statistical analysis was done by SPSS v22.0 (SPSS Inc, Chicago, IL, USA) and a  $p$  value <0.05 was accepted as significant.

## RESULTS

The mean age and preoperative PSA level was found as 64.16, and 12.33, respectively. Nine cases (10%) were located in the right lobe, 11 (12.2%) were in the left lobe and in 70 cases (77.8%) both lobes of the prostate were involved by the tumor. Nineteen (21.1%) of the tumors were orientated in anterior part of the prostate, whereas 71 of them (78.9%) in the posterior part. All of the cases were alive except only one patient (1.1%). The distribution of the Gleason grade groups were as follows; 34 cases (37.8%) grade group 1, 37 cases (41.1%) grade group 2, 10 cases (11.1%) grade group 3, 4 cases (4.4%) grade group 4 and 5 cases (5.6%) grade group 5.

Authors could not reach the preoperative PSA level of two cases. According to the preoperative PSA levels 50 of the cases were in the low-risk group (PSA<10ng/ml), 25 were in the intermediate-risk group (PSA 10-20 ng/ml) and 13 were in the high-risk group (PSA >20 ng/ml).

According to PSA level groups, the mean ages of the low-risk, intermediate-risk and high-risk groups were found as 63.5, 65 and 64, respectively, but the difference was not significant.

Extra prostatic extension (EPE) was observed in 35 cases (38.9%). Tumor positive surgical margins were detected in the apex in 18 cases (20%), in the base in 11 cases (12.2%) and in the lateral margins in 47 cases (52.2%). The presence of EPE and tumor positive base margin showed significant relation among PSA groups ( $p=0.002$  versus  $p=0.009$ , respectively)

Among all cases; 22 cases (24.4%) showed lymphovascular invasion, 67 cases showed (74.4%) perineural invasion, 49 cases (54.4%) showed ganglionic involvement, 3 cases (3.3%) had metastasized to regional (obturator) lymph nodes, and 11 cases (12.2%) involved seminal vesicles. The presence of lymphovascular invasion and the involvement of the seminal vesicles showed significant relation among the PSA groups ( $p=0.019$  versus  $p=0.002$ , respectively). No significant relation was observed between PSA groups and perineural invasion, ganglionic involvement and lymph node metastasis.

High grade prostatic intraepithelial neoplasia near tumoral glands was seen in 71 cases (78.9%). Other histopathological features such as intracytoplasmic mucin and foamy cytoplasm were observed in 36 (40%) and 26 cases (28.9%) respectively. Intracytoplasmic mucin and foamy cytoplasm was more common in low-risk PSA group and the difference was significant ( $p=0.008$  and  $p=0.002$ , respectively).

## DISCUSSION

Preoperative PSA level is one of the most widely used measurement for determining patients risky for prostate cancer. Although the cut-off values of PSA may change between different centers the general approach is to biopsy patients with a minimum PSA level of 4 ng/ml. The most common subclassification of PSA groups were divided into 3 categories for cancer risk as low- risk, intermediate-risk and high-risk levels.<sup>3</sup> This was the main point of present study.

Various researches can be found in the literature focusing on the prognostic effect of the age in prostate cancer. However, it is still controversial that if age is a major prognostic factor or not.<sup>7</sup> Some studies supported younger patients had a better outcome than older patients.<sup>8</sup> In present study, authors found no significant relation between age among PSA groups.

Gleason grading is the most commonly used grading system for prostate cancer which is revised by WHO in 2016.<sup>5,6</sup> The revised system defines grade grouping from 1 to 5. This grade grouping is strongly correlated with prognosis similar with classical Gleason grading. As most

of present patients were alive (98.9%) authors could not make a realistic comment on the role of grade grouping on PSA risk groups.

On histopathological evaluation of RP specimens many different features were assessed. Among these parameters, vascular invasion (lymphatic or venous) has no role in pathological staging. Even though, lymphovascular invasion is generally seen in advanced tumors, isolated effect of vascular invasion on prognosis remains a mystery.<sup>9</sup> In present study, vascular invasion was observed in 22 cases. Six of these cases had high-risk PSA level and there was a significant relation between PSA risk groups and lymphovascular invasion ( $p=0.019$ ). Similar to this, perineural invasion was detected in 67 cases but authors found no significant relation for the presence of perineural invasion among PSA groups ( $p=0.103$ ).

Extraprostatic extension (EPE) is defined as the direct extension of tumor cells beyond the confines of the prostatic capsule into periprostatic adipose tissue. EPE is one of the most important prognostic factor as it also changes the tumor stage to a T3 lesion, locally advanced disease.<sup>5</sup> Also it is very important not to misdiagnose involvement of skeletal muscle, ganglions, or individual nerves by tumor cells as EPE. Similar with the literature the presence of EPE showed significant relation among PSA groups ( $p=0.002$ ) which can point out that higher PSA levels may indicate advanced stages.

Involvement of the seminal vesicles is another important factor which associates with T3 disease (WHO 2016).<sup>2</sup> Seminal vesicle involvement is hard to define as the epithelial cells of the seminal vesicles are characterized by the presence of hyperchromatic and pleomorphic nuclei, but the presence of lipofuscin pigment may help to distinguish normal seminal vesicles. Thus, the involvement of the seminal vesicles should be interpreted cautiously. Similar with EPE, the involvement of the seminal vesicles showed significant relation among PSA groups ( $p=0.002$ ) pointing out the advanced stage patients generally have higher PSA levels.

Surgical margin positivity is one of the most important prognostic factors in many tumors as well as prostate cancer. In RP specimens three different surgical margins were described as the apex, the base and the lateral margins of the prostate. Authors assessed these three margins among PSA groups, but only base margin positivity showed significant relation among PSA groups. However, authors observed margin positivity in mostly intermediate and high-risk groups. This might be explained as the larger tumor size may cause higher PSA levels.

In addition to the known classical prognostic histopathological factors such as Gleason score, extra prostatic extension, vascular invasion, perineural invasion, positive surgical margins, authors also

investigated the prognostic role of the presence of intraluminal mucin and tumoral cells with foamy cytoplasm. Intraluminal mucin can be seen as amorphous basophilic secretions in the lumina of carcinomatous glands.<sup>7</sup> Some tumor cells contain vacuolated or abundant foamy cytoplasm. These tumors are known as foamy gland carcinomas and graded by Gleason system.<sup>10-12</sup> The two histological features mentioned above are known to be associated with prostatic adenocarcinoma, however their effect on prognosis remains a mystery.<sup>7</sup> In present study, these histological features were found to be significantly related to PSA groups as they were detected more commonly in low-risk PSA group.

## CONCLUSION

In conclusion, PSA level may not just show the risk category of the prostate cancer but also may be associated with some histopathological prognostic factors. These results have to be confirmed by wider studies with larger number of cases.

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## REFERENCES

1. Greenlee RT, Hill-Harmon MB, Murray T, Thun M. Cancer statistics, 2001. *CA Cancer J Clin*. 2001;51(1):15-36.
2. Buhmeida A, Pyrhönen S, Laato M, Collan Y. Prognostic factors in prostate cancer. *Diag Path*. 2006;1:4.
3. Cooperberg MR, Pasta DJ, Elkin EP, Litwin MS, Latini DM, Du Chane J, et al. The University of California, San Francisco Cancer of the prostate risk assessment score: a straightforward and reliable preoperative indicator of disease recurrence after radical prostatectomy. *J Urol*. 2005;173(6):1938-42.
4. Björk T, Lilja H, Christensson A. The prognostic value of different forms of prostate specific antigen and their ratios in patients with prostate cancer. *BJU Int*. 1999;84:1021-7.
5. Humphrey PA, Egevad L, Netto G, Amin MB, Epstein JI, Rubin MA, et al. Acinar adenocarcinoma, Tumors of the prostate. In: Moch H, Humphrey PA, Ulbright TM, Reuter VE, eds. *WHO classification of tumours of the urinary system and male genital organs*. 4<sup>th</sup> ed. IARC, Lyon; 2016;3:138-162.
6. Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR, Humphrey PA, the grading committee. The 2014 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma definition of grading patterns and proposal for a new grading system. *Am J of Surg Pathol*. 2016;40(2):244-52.

7. Noiwan S, Rattanaapee S. Mucin production in prostatic adenocarcinoma: a retrospective study of 190 radical prostatectomy and/or core biopsy specimens in department of pathology, Siri raj Hospital, Mahidol University, Thailand. *J Med Assoc Thailand= Chotmaihet thangphaet*. 2011 Feb;94(2):224-30.
8. Freedland SJ, Presti JC, Kane CJ, Aronson WJ, Terris MK, Dorey F, et al. Do younger men have better biochemical outcomes after radical prostatectomy? *Urol*. 2004;63(3):518-22.
9. Ito K, Nakashima J, Mukai M, Asakura H, Ohigashi T, Saito S, et al. Prognostic implication of microvascular invasion in biochemical failure in patients treated with radical prostatectomy. *Urologia Internationalis*. 2003;70(4):297-302.
10. Dema A, Taban S, Lazar E, Borda A, Lazureanu C, Herman D, et al. Pseudo benign prostate carcinomas: causes of false-negative biopsy results. *Rom J Morphol Embryol*. 2011;52(3 Suppl):963-74.
11. Warrick JI, Humphrey PA. Foamy gland carcinoma of the prostate in needle biopsy: incidence, gleason grade, and comparative a-methylacyl-coa racemase vs. ERG expression. *Am J Surg Pathol*. 2013;37(11):1709-14.
12. Berman DM, Yang J, Epstein JI. Foamy gland high-grade prostatic intraepithelial neoplasia. *Am J Surg Pathol*. 2000;24(1):140-4.

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