Efficacy of plasma atherogenic index in predicting malignancy in the presence of Prostate Imaging-Reporting and Data System 3 (PI-RADS 3) prostate lesions

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Research Article

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Abstract

Purpose: The prevalence of the clinically significant prostate cancer (csPCa) among the Prostate Imaging-Reporting and Data System (PI-RADS) 3 cases is estimated to be 16%, which suggests that the indication for biopsy by the combined method may be further refined. Plasma atherogenic index (PAI) was shown to be positively correlated with the presence of malignity in patients with suspicious findings for renal cell cancer and colon cancer in reported studies. In this study, we aimed to evaluate whether there is an association with the presence of malignity in a patient with magnetic resonance imaging (MRI)-visible lesions, classified as PI-RADS 3 and PAI.

Methods: This retrospective study reviewed the data of 139 patients who underwent transrectal ultrasonography (TRUS)-guided systematic and cognitive fusion prostate biopsy for PI-RADS 3 lesions in multiparametric MRI (mpMRI). The patients were divided to two groups as malign (n=33) and benign (n=106) according to pathology results. The association between age, body mass index [BMI], comorbidities, smoking status, prostate specific antigen [PSA], PSA density [PSAD], free/total PSA, prostate weight, lesion diameter, triglyceride value, high density lipoprotein (HDL)-Cholesterol value, PAI value data and presence of malignity were investigated by descriptive and multivariate analysis. Receiver operating characteristic (ROC) curves were created to evaluate the predictive role of the parameters and cut-off values were found.

Results: PSA, PSAD, lesion diameter and PAI value were statistically significantly higher in the malignant group compared to the benign group, the free/total PSA ratio was lower (p<0.001, p<0.001, p=0.001, p=0.025, p<0.001, respectively). In multivariate logistic regression analysis, PSA > 9.9 ng/ml (OR=4.579; 95% CI=1.455-14.413; p=0.009), free/total PSA < 12.1% (OR=5.851; 95% CI=1.752-9.442; p <0.001), lesion diameter > 13.5 mm (OR=5.695; 95% CI=1.694-19.146; p=0.005) and PAI > 0.13 (OR=3.821; 95% CI=1.208-12084; p=0.022) were identified as independent risk factors for presence of prostate malignancy.

Conclusion: PAI demonstrated a strong association with PCa and additionally proved to be predictive in the discrimination between malignity positive and negative PI-RADS 3 lesions and it may be used as a predictive parameter in the decision of biopsy in patients with PI-RADS 3 lesions.

Introduction

Prostate cancer (PCa) represents the second most frequently diagnosed cancer and the sixth leading cause of cancer death among men. Its incidence is estimated up to 1.4 million cases in 2020, while it is expected to exceed the number of 2.3 million cases by 2040. The highest estimated incidence rates are found in Australia, Northern America, Western and Northern Europe, while the highest estimated mortality rates are found in the Caribbean, sub-Saharan Africa, and Eastern Europe. During the last years, PCa incidence and mortality have stabilized, or been on the decline, after a period of increase, which possibly reflects a decrease in prostate specific antigen (PSA) testing and elongation of patient survival (Culp et al. 2020).
Regarding the PCa screening, only recently PSA testing has proved its contribution to PCa mortality reduction, which was shown after a long follow-up period. Subsequently, the latest European Association of Urology (EAU) Guidelines recommended the PSA testing only after counseling patients with a minimal life expectancy of 10-15 years. The addition of multiparametric magnetic resonance imaging (mpMRI) in the diagnostic procedure seems to further improve the accuracy of diagnosis of the clinically significant PCa (csPCa) and is strongly recommended by EAU Guidelines (EAU Guidelines 2022). Indeed, the increased sensitivity of the combined approach has been confirmed from the available data (Barkovich et al. 2019). Another advantage is the reduction in the detection of clinically insignificant cancer, which diminishes the frequency of overtreatment (Eklund et al. 2021). Interestingly, MRI findings have been associated with molecular features of PCa, which are indicative of an aggressive disease (Houlahan et al. 2019). For the above reasons, the perspective of the application of MRI as the initial screening tool seems attractive and is supported by prospective data, but its wide adoption would increase strongly the financial burden of PCa diagnosis (Eldred-Evans et al. 2021).

According to the latest EAU Guidelines, a combined, namely systematic and targeted to MRI-visible lesion, prostate biopsy should be performed in case of finding lesions of Prostate Imaging-Reporting and Data System (PI-RADS) ≥ 3 (EAU Guidelines 2022). However, the prevalence of csPCa among the PI-RADS 3 cases is estimated to be 16%, which suggests that the indication for biopsy by the combined method may be further refined. According to a meta-analysis pooling the available data on this topic, the decision to perform a biopsy can be based additionally on the PSA density (PSAD). A low PSAD value (<0.10 ng/ml²) suggests that the biopsy can be safely omitted, while a value > 0.15 ng/ml² should be considered as an indication for biopsy (Schoots et al. 2021). The results of the above meta-analysis are also adopted by the EAU Guidelines. Another report on the detection of csPSA among PI-RADS 3 lesions concluded that an elevated PSAD value, older age, and biopsy-naïve status retain an independent predictive value in the multivariate analysis of the study (Fang et al. 2022). Lesion volume comprises another factor that can discriminate the significant PI-RADS 3 lesions. According to a study, PI-RADS 3 can be subdivided into 3a and 3b lesions, with the latest having a volume >0.5 ml. Performing biopsy in cases with high PSAD and 3b lesion demonstrated the maximum specificity and positive predictive value (PPV) for csPCa, avoiding 83.8% of the biopsies (Rico et al. 2021). Another approach suggests the use of biomarkers to subclassify the PI-RADS 3 lesions. According to a report, the application of MyProstateScore (MPS), which was based on measurement of serum PSA, urinary prostate cancer gene 2 (PCA3), and TMPRSS2:ERG, outperformed PSAD in ruling out csPCa among PI-RADS 3 lesions, demonstrating a complementary role in the respective patients (Tosoian et al. 2022). Preselection of patients for subsequent MRI examination and combined biopsy by application of biomarkers represents another strategy to reduce the rate of insignificant cancers, which is more important for PI-RADS 3 lesions. Kim et al. proposed performing the Phi test as a triaging method to reduce mpMRI and biopsies while retaining the rates of csPCa detection (Kim et al. 2020). Radiologic features offer another option to subclassify PI-RADS 3 lesions. Giambelluca et al. proposed two texture analysis-based models with a significant discriminating ability (Area Under Curve, AUC= 0.744- 0.817) in unveiling the clinically significant cases among the PI-RADS 3 lesions (Giambelluca et al. 2021).
Regarding the metabolic background of PCa, very little data are available about the effect of various metabolic components on the risk for PCa and csPCa. Relating to the effect of metabolic syndrome (MetS), a meta-analysis found an overall weak and non-significant association with PCa risk (Esposito et al. 2013). The included studies presented non-homogenous results, with some European reports demonstrating a significant association with PCa. Among the single components of the MetS, only hypertension and increased waist circumference were significantly associated with PCa risk. Blanc-Lapierre et al. studied the relationship of MetS to PCa risk and concluded that the existence of more than three components of MetS was associated with reduced PCa risk (Blanc-Lapierre et al. 2015). This negative association was more pronounced in the patients of young age and did not include a reduction in csPCa risk. Regarding obesity, an independent negative and positive association was discovered for low and high-grade PCa respectively (Vidal et al. 2014). Based on the same patient cohort, another study investigated the possible association of lipid profile-modifying medication with PCa risk. The report concluded that there is no association between regular statin therapy with PCa or aggressive PCa (Freedland et al. 2013).

Despite the negative results in associating metabolic components with PCa, the evidence for a relation of carcinogenesis with metabolic abnormalities are strong. According to a review, aberrant blood lipoprotein levels are associated with cancer risk and oncologic outcomes in patients with various cancer forms. On the other side, the authors of the study state that various types of cancers may be benefited from different lipid profiles so that the relation of cancer with lipid aberrations is not homogenous (Munir et al. 2014). Another review investigated the association of high-density lipoprotein (HDL) concentration with cancer risk (Pirro et al. 2018). Interestingly, the study confirms the inverse association between the above factors and additionally suggests an inverse causality, namely, that this association is not HDL-driven with an effect on cancer risk, but it is cancer-related with an effect on HDL concentration.

More recent studies are investigating the association of composite measures of lipid profile with cancer risk and prognosis. One of the more frequently used is plasma atherogenic index (PAI), which is calculated as the logarithm of the triglycerides concentration divided by HDL concentration, namely Log(Triglycerides/HDL), and represents an established predictive biomarker for cardiovascular diseases (Fernández-Macías et al. 2019). Interestingly, PAI seems to be positively correlated with the presence of malignity in patients with suspicious findings for another urological cancer, namely, renal cell cancer (RCC) (Karabay et al. 2019). According to the above report, PAI showed an independent predictive value for RCC in the patient cohort with a renal mass of unknown pathology. The authors concluded that PAI may be used as a predictive tool in such cases. Similarly, another study investigated the association of PAI with colon cancer (Gundogdu et al. 2021). The authors concluded that PAI was significantly higher in colon cancer patients, and may be used to define a high-risk group, which should be screened more frequently, in order to reduce the respective mortality rates.

To elucidate the possible relation of PAI to PCa, we investigated its association with the presence of malignity in a patient cohort with MRI-visible lesions, classified as PI-RADS 3. With the above study
design, we intended not only to associate PAI with the prostate histology but also with PI-RADS 3 category, which represents a gray zone in the classification of MRI-visible lesions.

**Materials And Methods**

The data of 1086 patients who had multiparametric prostate mpMRI due to elevated PSA or suspected digital rectal examination in our clinic between May 2019-June 2022 were analyzed retrospectively. Among these patients, 263 patients who were detected to have with PI-RADS 3 lesions in the prostate as a result of multiparametric prostate MRI and underwent transrectal ultrasonography (TRUS) guided systematic and cognitive fusion prostate biopsy were evaluated. Patients who were under active surveillance, were diagnosed with atypical small acinar proliferation (ASAP) or high-grade prostatic intraepithelial neoplasia (HGPIN) as a result of the biopsy pathology, were taking lipid-lowering medicine, and had insufficient data were excluded from the study. As a result, a total of 139 patients were included in the study. This study was approved by the Institutional Review Board of Ankara City Hospital (E2-22-2393).

Demographic (age, body mass index [BMI], comorbidities, smoking status), clinical (PSA, PSAD), free/total PSA, prostate weight) and pathological (biopsy international society of urological pathology [ISUP] grade, final ISUP grade, pathologic T stage, lesion diameter) and lipid profile (triglyceride value, HDL-Cholesterol value, PAI value) data of all patients were evaluated. According to the biopsy pathology results, the patients were assigned to two groups as malignant and benign.

*MpMRI and PI-RADS scoring*: MpMRI was performed using the 3.0-T MR system. The Prostate Imaging Reporting and Data System (PI-RADS) version 2 guidelines were followed to assess MR images (Weinreb et al. 2016). Suspicious lesions were defined according to PI-RADS version 2. The location and maximum diameter of the PI-RADS 3 lesions were recorded.

*TRUS-guided systematic and cognitive fusion prostate biopsy method*: Oral cefixime of 400 mg antibiotic prophylaxis was administered to all patients for 3 days, starting 24 hours before the procedure, and rectal cleansing was carried out using povidone iodine. Before starting the procedure, mpMRI images and reports for the cognitive fusion procedure were reviewed by two experienced urologist (E.O. and K.C.). All procedures were performed in the left lateral decubitus knee-chest position. TRUS evaluation was performed with a 6.5 MHz biplane transrectal probe using an ultrasonography device (Hitachi EUB-400). Based on the distance and anatomical landmarks (ejaculatory duct, cyst, calcification, etc.) measured in mpMRI, suspicious areas were marked with a 5-mm diameter circle on transection and sagittal TRUS images. Periprostatic blockade was performed with 5 ml of 1% lidocaine HCL (10 ml in total) using a 22G 25cm chiba needle (Geotek) starting from the base of the seminal vesicle to the apex of the prostate along the vascular nerve bundle in the posterolateral part of the prostate for each side. An 18G, 25 cm biopsy needle (Geotek) was used for prostate biopsy. A total of 12 core systematic biopsies were taken from the apex to the base primarily in the peripheral zone, as posterior and lateral as possible.
Then, additional 3-5 core cognitive prostate biopsies were performed from each suspicious area marked in mpMRI. Prostate biopsy procedures were performed by the experienced urologist (K.C.).

**Statistical analysis:** Data coding and statistical analyses were carried out on the computer using the SPSS 22 software (IBM SPSS Statistics, IBM Corporation, Chicago, IL). The conformity of the variables to the normal distribution was analyzed using the Shapiro-Wilk tests. Student’s T test and Mann-Whitney U test were employed to compare non-categorical parameters between groups. Chi-square test was used for categorical variables. Receiver operating characteristic (ROC) curves were created to evaluate the predictive role of the parameters, in which there was a significant difference between the two groups, for malignancy. Cut-off values were determined for each parameter. Multivariate analysis and the Backward LR method were used to assess whether the possible risk factors for malignancy were independent risk factors. A p value of < 0.05 was accepted as statistically significant.

**Results**

The mean age of 139 patients included in the study was 65.6±6.2 years and their BMI was 26.4±2.5 kg/m². The median PSA level was 6.5 (2-48.1) ng/ml. 33 (23.7%) of the patients constituted the malignant group. The prostate biopsy result of 24 (72.7%) of these patients was reported as ISUP grade 1. After radical prostatectomy, the pathology result of 17 (51.5%) patients was ISUP grade 1. The two groups were similar in terms of age, BMI, comorbidities, smoking status, prostate weight, triglyceride value and HDL-cholesterol value. While PSA, PSAD, lesion diameter and PAI value were statistically significantly higher in the malignant group compared to the benign group, the free/total PSA ratio was lower (p<0.001, p<0.001, p=0.001, p=0.025, p<0.001, respectively). Table 1 shows demographic, clinical and pathologic data of the patients.

In the present study, ROC curves with 95% confidence interval were created and cut-off values were determined for whether PSA, PSAD, free/total PSA, lesion diameter and PAI value were determining factors for malignancy (Figure 1 and Table 2). Then, risk factors for prostate malignancy were revealed in patients with PI-RADS 3 lesions in mpMRI through multivariate logistic regression analyses using the determined cut-off points. In multivariate logistic regression analysis, PSA > 9.9 ng/ml (OR=4.579; 95% CI=1.455-14.413; p=0.009), free/total PSA < 12.1% (OR=5.851; 95% CI=1.752-9.442; p <0.001), lesion diameter > 13.5 mm (OR=5.695; 95% CI=1.694-19.146; p=0.005) and PAI > 0.13 (OR=3.821; 95% CI=1.208-12084; p=0.022) were identified as independent risk factors (Table 3).

**Discussion**

The relation of cancer to the lipid profile of the patients comprises an intriguing topic since specific aberrations are observed frequently in different forms of the disease. The exact pathophysiologic mechanism and the direction of causality of the above alterations remain to be defined. Regarding the relation of PCa to lipid profile alterations, the current study showed a number of significant associations. For the purposes of the study, we compared two groups, which were not different in terms of
demographic data and medical history. Moreover, the lesion image of all patients was classified as PI-RADS 3 according to the respective classification system. The patient group had significantly higher PSA, PSAD and free/total PSA compared to the participants without PCa. Moreover, the lesion size of patients was significantly larger. Interestingly, the PAI value was significantly higher in the patient group, while its separate elements, namely triglycerides and HDL concentration, were not different between the comparing groups. By applying univariate logistic regression with optimized cut-off, PSA, PSAD, free/total PSA, lesion size, and PAI value demonstrated a significant predicting ability in discriminating PCa cases. More interestingly, the multivariate analysis showed that PSA, free PSA ratio, lesion size, and PAI retained an independent predictive value after adjustment for all other factors included in the model.

To the best of our knowledge, this is the first report associating the PAI value with the malignity in the suspicious cases for PCa. Especially intriguing is the above finding under the fact, that separate lipid components were not different between patients and participants with benign pathology. This constellation suggests that simple measures of lipid profile may be inadequate to describe the clinically relevant lipid profile alterations.

Regarding the available data on the relation of PCa with the lipid profile of the patients, our literature search revealed a limited number of reports. Wang et al. compared two groups of different disease risk category and found that high-risk PCa patients had significantly higher lipoprotein (a) concentration compared to low-risk patients, which retained its independent predictive value in the multivariate analysis (Wang et al. 2019). A review on the relation of HDL concentration with PCa summarized the available findings, concluding that low HDL levels comprise a risk and prognostic factor for PCa (Kotani et al. 2013). On the contrary, a recent study investigating the relation of the cholesterol components with PCa found that a high concentration of HDL and total cholesterol is associated with an increased risk of high-grade disease, while no association was found for low-density lipoprotein (LDL) (Jamnagerwalla et al. 2018). Wolny-Rokicka et al. investigated the lipid alterations across the progression stages of PCa and found that patients with locoregional disease had significantly higher HDL/cholesterol ratio and similar triglycerides/HDL ratio compared to metastatic patients (Wolny-Rokicka et al. 2017). Oxidized LDL (OxLDL), which comprises a risk factor for cardiovascular disease and biomarker indicative of oxidative stress, was found to be significantly correlated with PCa extension to the lymph nodes, while OxLDL stimulated PCa proliferation, migration, and invasion of cancer cells in vitro (Wan et al. 2015).

In our opinion, the relation of lipid profile to PCa is complicated similarly to the cardiovascular disease, where emerging findings are changing continuously the theoretical basis and strategy of the respective therapies. The results of our report give clear proof of the association between a composite lipid measure and the presence of malignity in suspicious cases, but the underlying mechanism remains to be elucidated. Moreover, the study design of the current report suggests that the above result can be applied in the subclassification of the PI-RADS 3 category, which represents a gray zone regarding the indication for performing a prostate biopsy. As the investigation for the further refinement of MRI imaging regarding the detection of csPCa goes on, we support the opinion that such predictors relating to the metabolic
background of the patients can contribute equally to the precise characterization of the visible-through-imaging findings and the maximal avoidance of unnecessary biopsies.

**Conclusion**

The addition of MRI imaging in the diagnostic procedure of PCa has contributed significantly to the improvement of oncological outcomes and the reduction of overtreatment, but further refinement of the above strategy is possible. This refinement refers mostly to PI-RADS 3 lesions, which harbor PCa in about 16% of the cases. Components of the metabolic background of the patients may play a role in carcinogenesis and can be applied to enhance the accuracy of the existing diagnostic methods. In the current study, PAI demonstrated a strong association with PCa and additionally proved to be predictive in the discrimination between malignity positive and negative PI-RADS 3 lesions.

**Declarations**

**Acknowledgements**

Authors’ contributions: Conception and design: SS, AK; Data acquisition: KC, EU; Data analysis and interpretation: SS, YK; Drafting the manuscript: SS, AK; Critical revision of the manuscript for scientific and factual content: ST, EO; Statistical analysis: SS, MEP; Supervision: EO

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**Availability of data and material:** The datasets generated and/or analysed during the current study are available in Figshare Repository at https://figshare.com/s/1b5021c69e26f68be453

**Conflicts of Interest:** The authors report no conflicts of interest.

**Ethics Approval:** The present study protocol was reviewed and approved by the Institutional Review Board of Ankara City Hospital (approval number: E2-22-2396)

**Consent to participate:** All patients previously consented to use their medical data for research purposes.

**Consent for publication:** Not applicable

**References**


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Prostate Cancer in the REDUCE Study. Cancer Epidemiology, Biomarkers & Prevention 23:2936-42. http://doi.org/10.1158/1055-9965.EPI-14-0795


Tables

Table 1. Demographic, clinical and pathologic characteristics of patients
<table>
<thead>
<tr>
<th></th>
<th>Total (n=139)</th>
<th>Malign (n=33, 23.7%)</th>
<th>Benign (n=106, 76.3%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (mean±SD)</td>
<td>65.6±6.2</td>
<td>67.4±6.4</td>
<td>65±6</td>
<td>0.673 t</td>
</tr>
<tr>
<td>BMI (kg/m²) (mean±SD)</td>
<td>26.4±2.5</td>
<td>25.9±2.8</td>
<td>26.5±2.4</td>
<td>0.411 m</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM, n (%)</td>
<td>21 (15.1)</td>
<td>7 (21.2)</td>
<td>19 (17.9)</td>
<td>0.672 c</td>
</tr>
<tr>
<td>HT, n (%)</td>
<td>55 (39.6)</td>
<td>17 (51.5)</td>
<td>46 (43.4)</td>
<td>0.413 c</td>
</tr>
<tr>
<td>CAD, n (%)</td>
<td>21 (15.1)</td>
<td>11 (33.3)</td>
<td>22 (20.8)</td>
<td>0.138 c</td>
</tr>
<tr>
<td><strong>Smoking Status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes, n (%)</td>
<td>31 (22.3)</td>
<td>9 (27.3)</td>
<td>22 (20.8)</td>
<td>0.432 c</td>
</tr>
<tr>
<td>No, n (%)</td>
<td>108 (77.7)</td>
<td>24 (72.7)</td>
<td>84 (79.2)</td>
<td></td>
</tr>
<tr>
<td>PSA (ng/ml) (median [min-max])</td>
<td>6.5 (2-48.1)</td>
<td>10.5 (3.7-48.1)</td>
<td>6 (2-18)</td>
<td>&lt;0.001 m</td>
</tr>
<tr>
<td>PSAD (%) (median [min-max])</td>
<td>11 (2-69)</td>
<td>13 (4-69)</td>
<td>9 (2-42)</td>
<td>&lt;0.001 m</td>
</tr>
<tr>
<td>Free/total PSA (%) (median [min-max])</td>
<td>23.2 (5-50)</td>
<td>11 (5-50)</td>
<td>24.5 (10.4-44.1)</td>
<td></td>
</tr>
<tr>
<td>Prostate weight (gr) (median [min-max])</td>
<td>69 (22-256)</td>
<td>65 (22-128)</td>
<td>69 (26-256)</td>
<td>0.718 m</td>
</tr>
<tr>
<td><strong>Biopsy ISUP grade</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1, n (%)</td>
<td>24 (72.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2, n (%)</td>
<td>5 (15.2)</td>
<td></td>
<td></td>
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<tr>
<td>3, n (%)</td>
<td>3 (9.1)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>4, n (%)</td>
<td>1 (3)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Final ISUP grade</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1, n (%)</td>
<td>17 (51.5)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>2, n (%)</td>
<td>9 (27.3)</td>
<td></td>
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<tr>
<td>3, n (%)</td>
<td>6 (18.2)</td>
<td></td>
<td></td>
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<tr>
<td>4, n (%)</td>
<td>1 (3)</td>
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<tr>
<td>pT stage</td>
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</table>

**Total (n=139)**

- Malign (n=33, 23.7%)
- Benign (n=106, 76.3%)

**p**

- 0.673 t
- 0.411 m
- 0.672 c
- 0.413 c
- 0.138 c
- 0.432 c
- <0.001 m
- <0.001 m
- 0.718 m
Table 2. The best cut off points for PSA, PSAD, free/total PSA, lesion diameter and PAI distinguishing the malignant group from the benign group with 95% confidence according to the area under the ROC curve.

<table>
<thead>
<tr>
<th></th>
<th>PSA (ng/ml)</th>
<th>PSAD (%)</th>
<th>Free/total PSA (%)</th>
<th>Lesion Diameter</th>
<th>PAI</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC</td>
<td>0.724</td>
<td>0.711</td>
<td>0.756</td>
<td>0.699</td>
<td>0.629</td>
</tr>
<tr>
<td>95 % Cl</td>
<td>0.632-0.816</td>
<td>0.615-0.807</td>
<td>0.638-0.875</td>
<td>0.598-0.8</td>
<td>0.514-0.744</td>
</tr>
<tr>
<td>p value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.025</td>
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<tr>
<td>Cut off point</td>
<td>9.9</td>
<td>9.5</td>
<td>12.1</td>
<td>13.5</td>
<td>0.13</td>
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<tr>
<td>Sensitivity</td>
<td>0.545</td>
<td>0.818</td>
<td>0.545</td>
<td>0.515</td>
<td>0.576</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.811</td>
<td>0.509</td>
<td>0.981</td>
<td>0.849</td>
<td>0.698</td>
</tr>
</tbody>
</table>

**PSA**: Prostate Specific Antigen, **PSAD**: Prostate Specific Antigen Density, **PAI**: Plasma Atherogenic Index, **CI**: Confidence Interval, **ROC**: Receiver Operating Characteristic.
Table 3. Determination of risk factors for malignity in patients with PIRADS 3 prostate lesion in multiparametric prostate magnetic resonance imaging

<table>
<thead>
<tr>
<th>Parameters</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>PSA &gt; 9.9 ng/ml</td>
<td>4.579 (1.455-14.413)</td>
<td>0.009</td>
</tr>
<tr>
<td>PSAD &gt; 9.5%</td>
<td>3.077 (0.742-12.763)</td>
<td>0.122</td>
</tr>
<tr>
<td>Free/total PSA &lt; 12.1%</td>
<td>5.851 (1.752-9.442)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lesion diameter &gt; 13.5 mm</td>
<td>5.695 (1.694-19.146)</td>
<td>0.005</td>
</tr>
<tr>
<td>PAI &gt; 0.13</td>
<td>3.821 (1.208-12.084)</td>
<td>0.022</td>
</tr>
</tbody>
</table>

CI: Confidence Interval, PSA: Prostate Specific Antigen, PSAD: Prostate Specific Antigen Density, PAI: Plasma Atherogenic Index

Figures

Figure 1
ROC curve of PSA, PSAD, free/total PSA, lesion diamater and PAI in predicting malignity