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Analysis of incidental prostate acinar adenocarcinoma: a single-center retrospective study

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ABSTRACT

Objectives: Our study was conducted in a single center to evaluate the characteristics of prostate acinar adenocarcinoma.

Methods: A retrospective archive search was conducted between January 1, 2018 and September 1, 2024, and 900 prostate transurethral resection (TUR) and 127 open prostatectomy materials were examined. A total of 43 TUR and 9 open prostatectomy materials were found to have prostatic acinar adenocarcinoma.

Results: The ages of the patients were between 51-90. Gleason scores ranged from 3+3:6 to 5+5:10. In immunohistochemical analyses, Alpha methylacyl CoA racemase (AMACR) positivity and p63 negativity were prominent as characteristic findings. Lymphovascular invasion was rarely observed, while perineural invasion was detected more frequently.

Conclusions: The importance of histopathological and immunohistochemical features in determining the diagnostic and prognostic factors of prostate acinar adenocarcinoma was investigated in our study. This study may contribute to the literature on prostate cancer diagnostic and treatment strategies and may provide contributions for future research.

Keywords: Prostate acinar adenocarcinoma, Gleason score, Prostate specific antigen, immunohistochemistry

Prostate cancer, the most common cancer type in men worldwide, increases in frequency with age and is therefore a very serious public health problem [1].Incidentally detected prostate cancer (IPC) is an important clinical problem encountered in patients undergoing transurethral resection of the prostate (TUR-P) due to benign prostatic hyperplasia (BPH). Recent studies have shown that IPC rates are approximately 10.1%, with clinically significant cases accounting for 20.2% [2]. Careful pathological examination remains crucial for accurate diagnosis as missed cases can lead to delayed treatment and potentially worse outcomes [2, 5]

The detection rate has increased thanks to advanced diagnostic techniques and pathological examinations [3]. The observation of prostate cancer in 28.5% of patients with PSA below 4 ng/mL in our study emphasizes the importance of comprehensive screening approaches, as recent evidence suggests significant cancer detection rates even at low PSA values [4, 29]. Prostate Specific Antigen (PSA) testing is an important part of the diagnostic process in men at risk of prostate cancer [10]. Recent comprehensive reviews have demonstrated that careful pathological examina-

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tion remains crucial for accurate diagnosis [4]. The incidence of prostate cancer is high worldwide and is especially evident in developing countries [1].

Prostate acinar adenocarcinoma originates from the glandular structures of the prostate and is malignant. It constitutes approximately 95% of prostate cancers and its histopathological molecular features have important effects on diagnosis and prognosis [7]. According to the 2022 WHO Classification, proper pathological evaluation and classification are essential for treatment planning [9]. Current guidelines from major organizations provide comprehensive recommendations for disease management. The European Association of Urology guidelines recommend active surveillance and focal therapy options in certain cases [6], while the Advanced Prostate Cancer Consensus Conference has established standards for managing more advanced disease [8].

The use of multiparametric magnetic resonance imaging (mpMRI) along with PSA testing, rectal examination and histopathological examination methods has significantly increased diagnostic accuracy [14]. Standardized reporting systems, including detailed pathological parameters as described by Grignon [5], have improved communication between clinicians. Moreover, MRI-targeted biopsy has demonstrated superior accuracy over traditional methods, marking a significant step in prostate cancer diagnostics [11]. Many studies have shown that MRI-targeted biopsy has higher sensitivity and specificity than standard systematic biopsy for the detection of clinically significant prostate cancer [11, 14].

The Gleason scoring system remains the gold standard for histopathological evaluation. This system, further refined by the International Society of Urological Pathology (ISUP) consensus studies, has become integral in predicting clinical outcomes and tailoring patient-specific treatment plans [12, 13]. ISUP consensus studies have contributed to the development of the Grade Group system by improving the grading criteria, and this updated classification provides more accurate prognostic stratification and is more helpful in clinical decision making [12, 13].

Our study aims to provide a comprehensive analysis that bridges histopathological findings with prognostic implications, ultimately contributing to the advancement of personalized treatment approaches in prostate cancer management.

The aim of our study is to retrospectively examine the prostate acinar adenocarcinoma cases diagnosed by histopathological examination of tissue samples taken by TUR and open surgery and brought to our laboratory, to evaluate them in the light of current literature information and to help improve the medical processes of prostate acinar adenocarcinoma. Our study aims to provide a comprehensive analysis that bridges histopathological findings with prognostic implications, ultimately contributing to the advancement of personalized treatment approaches in prostate cancer management.

METHODS

Study Design and Ethical Approval

Our study was designed as a retrospective analysis and was approved by the Ethics Committee of Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital (Approval No: 2024/301) and was conducted according to the principles of the Declaration of Helsinki. Data confidentiality was protected according to international research guidelines.

Patient Selection and Data Collection

Study Population

Patient selection followed the current European Association of Urology guidelines [6]. Active surveillance protocols were implemented based on established criteria for low-risk prostate cancer patients, as described in current literature [16]. Patients who underwent TUR or open prostatectomy in our hospital between January 1, 2018 and September 1, 2024 and were histopathologically diagnosed with prostate acinar adenocarcinoma were examined in our study.

Exclusion Criteria

Patients with insufficient clinical data were not included in the study.

Data Collection Process

Patients' demographic information, clinical characteristics, laboratory findings, and pathology reports were obtained from hospital medical records. Data quality was ensured by double-checking, following validated multiparametric data collection protocols [15].

Histopathological Evaluation

Tissue Processing and Staining

Histopathological specimens were processed following standardized protocols [5]. Tissue samples were fixed in 10% neutral buffered formalin for 24 hours, embedded in paraffin, sectioned at 4 µm thickness, and stained with hematoxylin and eosin (H&E). All diagnoses were made according to the 2022 WHO Classification [9].

Microscopic Evaluation

Histopathological diagnosis and grading procedures were performed according to the World Health Organization classification [9]. The evaluation process followed established guidelines for prostate cancer pathology [5].

Gleason Scoring and Grade Group Determination

Gleason scoring and grade group determination were performed according to the current recommendations of the ISUP [12, 13]. This standardized approach ensures consistent reporting across all cases.

Tumor Percentage and Other Pathological Features

Tumor percentage was calculated and recorded for all samples individually. Pathological features such as perineural invasion and lymphovascular invasion were analyzed following current protocols [5].

Immunohistochemical Analysis

Immunohistochemical staining was performed using Ventana BenchMark ULTRA (Roche Diagnostics). AMACR, p63, and HMWCK expressions were evaluated following standardized pathological protocols [17]. Results were assessed using current semi-quantitative scoring systems that included staining intensity and percentage of positive cells.

Statistical Analysis

R statistical software (version 4.2.0, R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis. Descriptive statistics were presented as mean ± standard deviation for continuous variables and frequencies (percentages) for categorical variables. Correlations between continuous variables were assessed using Pearson's correlation coefficient. Chi-square test was used for categorical variables. $P<0.05$ was considered statistically significant in all tests.

RESULTS

Demographic and Clinical Features

A total of 1027 patients were included in the study. The mean age was found to be 65.7 ±8.3 years (45-89 years). In the age distribution, 18.2% of the patients were under 55 years of age, 52.6% were between 55-70 years of age, and 29.2% were over 70 years of age. The mean PSA value of the patients was found to be 12.4±15.7 ng/mL (0.3-189 ng/mL). We categorized the values according to the current EAU guidelines. In this context, 28.5% of the patients were found to have PSA values <4 ng/mL, 4-10 ng/mL (41.3%), 10-20 ng/mL (18.7%), and >20 ng/mL (11.5%).

Histopathological Findings

Biopsy and Prostatectomy Specimens

Of the 1027 patients in our study, 900 (87.6%) underwent TUR and 127 (12.4%) underwent open prostatectomy. Prostatic acinar adenocarcinoma was detected in 43 (4.8%) of the TUR specimens and 9 (7.1%) of the open prostatectomy specimens.

Gleason Scores and Grade Groups

Gleason scores: The most common score was found to be 3+3=6 (35.2%). This was followed by 3+4=7 (28.7%), 4+3=7 (18.1%), 4+4=8 (9.6%), 4+5=9 (5.8%) and 5+5=10 (2.6%), respectively (Fig. 1).

Grade Group distribution: Grade Group 1 (35.2%), Grade Group 2 (28.7%), Grade Group 3 (18.1%), Grade Group 4 (9.6%) and Grade Group 5 (8.4%) were determined (see Fig. 1).

Tumor Percentage and Other Pathological Features

The mean tumor percentage was measured as 18.3±22.5% (1-95%). A positive correlation was observed between tumor percentage and Gleason score ($r=0.62$, $P<0.001$). Perineural invasion was detected in 42.7% of patients, while lymphovascular invasion was detected in 15.3%.

Immunohistochemical Findings

The immunohistochemical markers used in our study were AMACR, p63 and HMWCK, which are widely used in the diagnosis of prostate cancer. AMACR positivity was detected in 94.2% of patients in immunohistochemical analyses. p63 and HMWCK

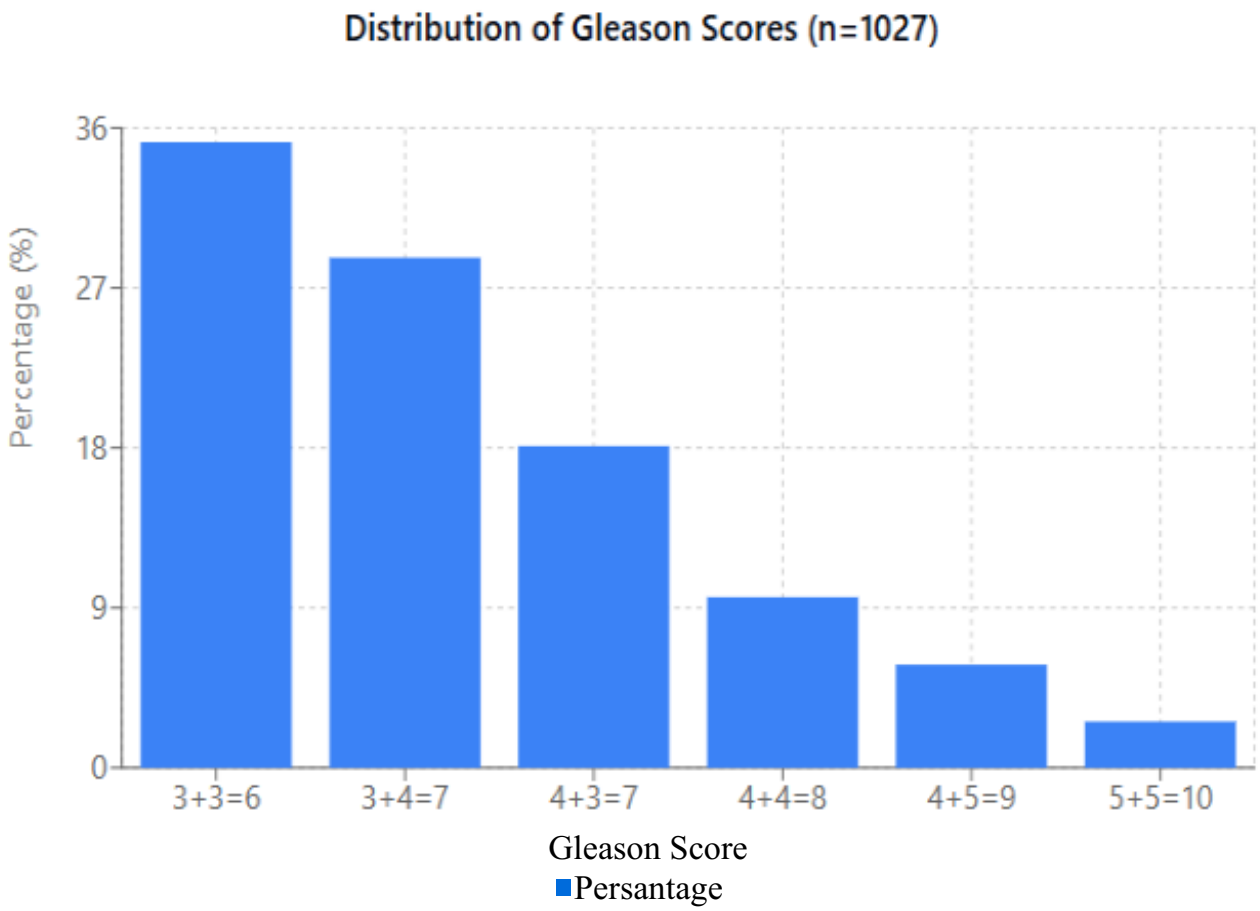

Fig. 1. Distribution of Gleason scores among study population (n=1027). The graph shows that Gleason score 3+3=6 was the most common (35.2%), followed by 3+4=7 (28.7%).

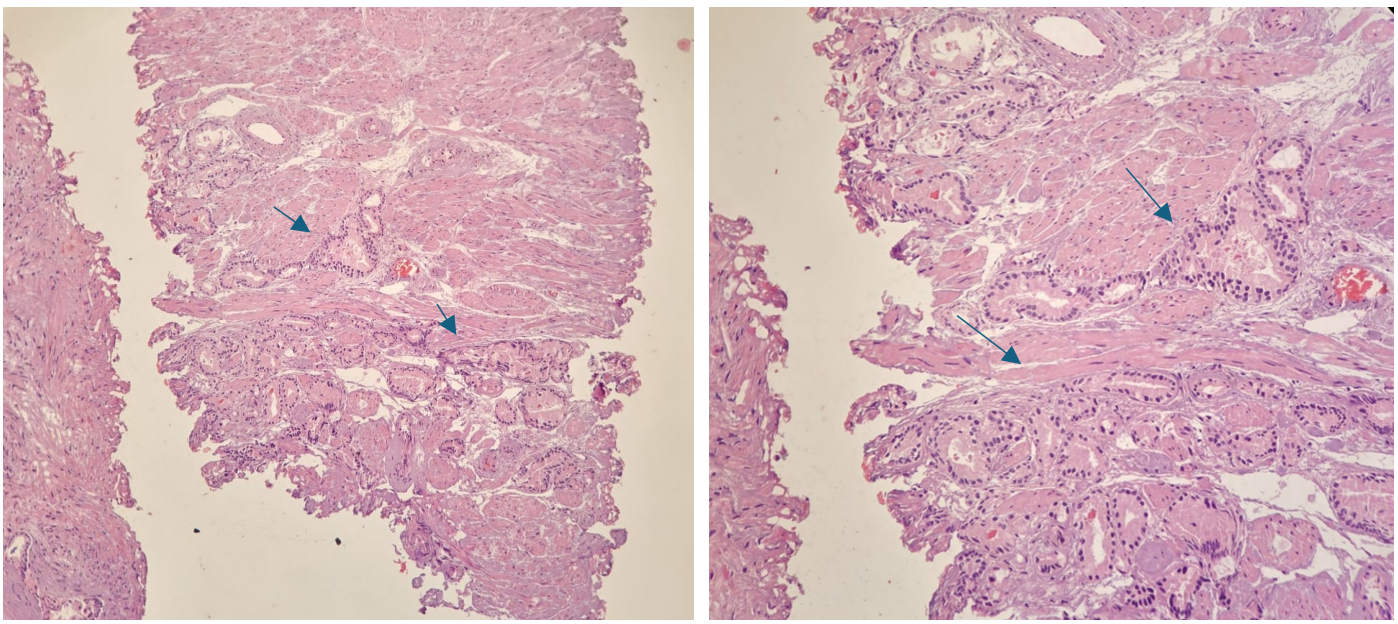

Fig. 2. Left: Acinar structures showing infiltrative growth pattern in prostate tissue are seen in TUR material H&E, ×100. Right: Small-medium sized, atypical glandular structures with uniform nuclear features are observed at higher magnification H&E, ×200.

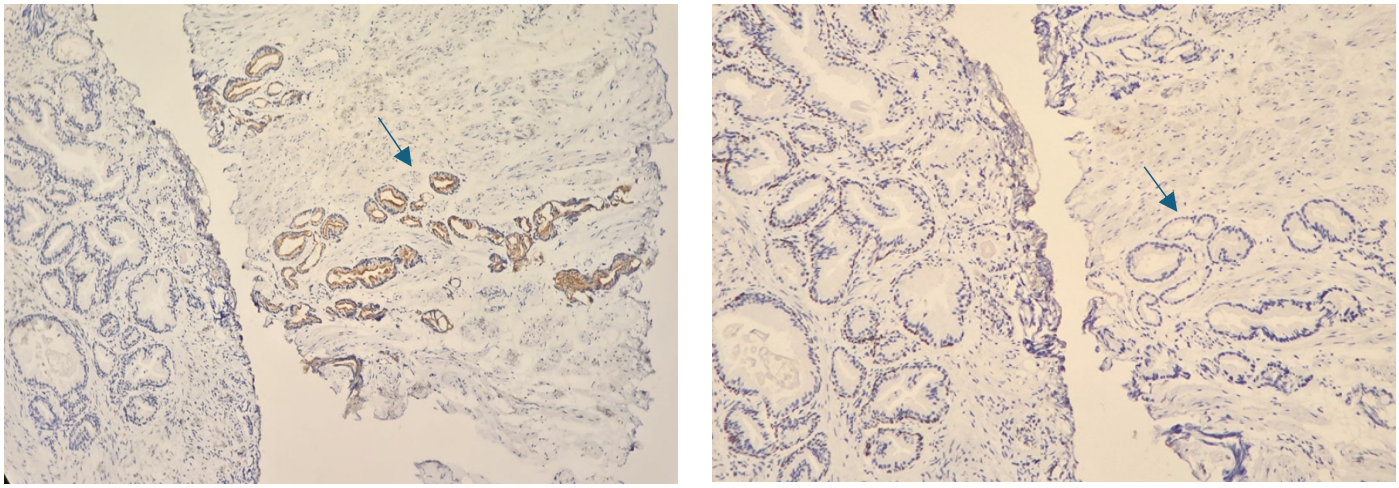

Fig. 3. Left: Brown staining is present in acinar adenocarcinoma foci with AMACR, while no staining is seen in adjacent normal glands (Immunohistochemistry, ×100). Right: While no staining is seen in tumoral glands with P63, brown staining is observed in the basal layer of normal glands (Immunohistochemistry, ×200).%).

negativity were observed in 97.8% and 96.5%, respectively (Figs. 2 and 3)

Clinicopathological Correlations

A significant positive correlation was found between PSA values and Gleason score (r=0.54, P<0.001). In addition, the probability of high-grade (Grade Group 4-5) tumors was measured as 3.2 times higher in patients with PSA values >20 ng/mL compared to those with PSA values <10 ng/mL (95% CI: 2.1-4.8, P<0.001) (Fig. 4)

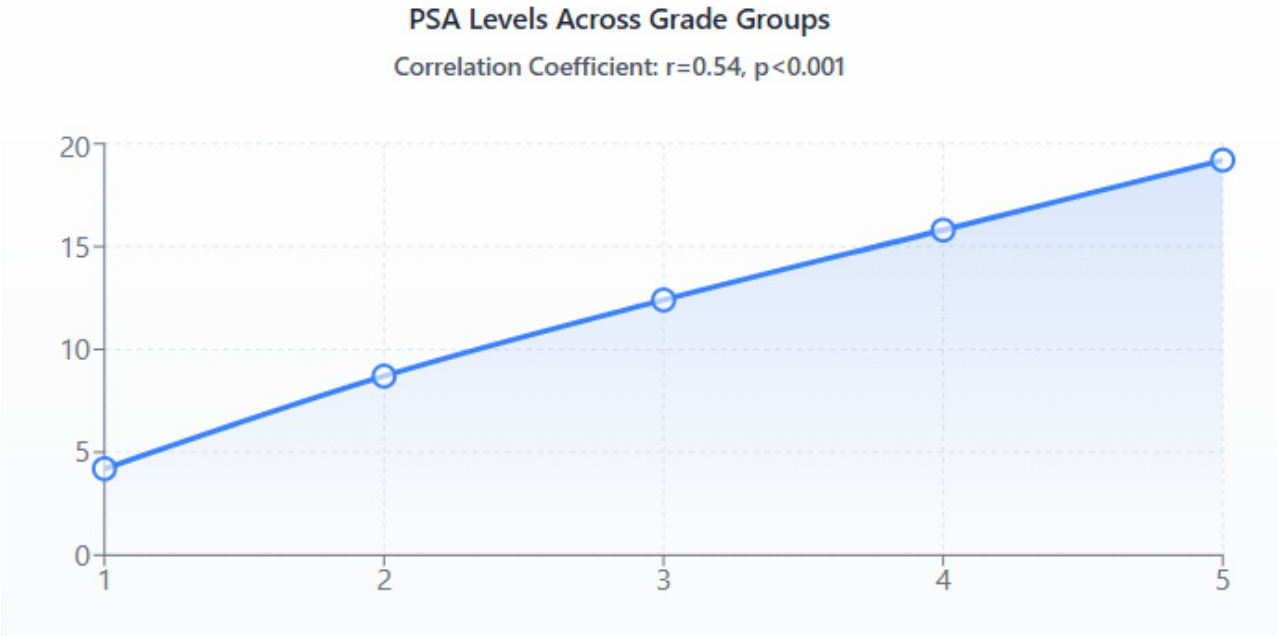

Fig. 4. Correlation between PSA levels and Grade Groups. The graph demonstrates a strong positive correlation between Grade Groups and mean PSA levels (r=0.54, P<0.001). Mean PSA values increased progressively from Grade Group 1 (4.2 ng/mL) to Grade Group 5 (19.2 ng/mL), indicating higher PSA levels are associated with higher Grade Groups.

DISCUSSION

Our study has extensively analyzed the characteristics of prostate acinar adenocarcinoma and evaluated them in the light of current literature. Long-term follow-up results show that the disease is stable in most patients under active surveillance [16, 24]. Our findings support and expand our current knowledge on the diagnosis, prognosis, and treatment approaches of prostate cancer [7].

Demographic and Clinical Features

Our study's age distribution findings (mean age 65.7±8.3 years) align with global cancer statistics [1]. Recent epidemiological studies have shown increasing incidence in developing countries [25, 26]. Our study is consistent with the threshold values recommended by current guidelines in terms of PSA values [6, 27]. The observation of prostate cancer in 28.5% of patients with PSA below 4 ng/mL in our study emphasizes the importance of comprehensive screening approaches, as recent evidence suggests significant cancer detection rates even at low PSA values [4, 29]. Current clinical practice guidelines emphasize this multidisciplinary approach to diagnosis and treatment [10, 23].

Histopathological Findings

Our Gleason scores and grade group distribution follow the current WHO Classification guidelines [9,20]. Recent updates in the WHO Classification system have refined our understanding of prostate cancer pathology [19]. Particularly, Grade Groups 1 and 2 (Gleason score ≤7) being the most common groups align with established reporting standards [5, 13]. The positive correlation we found between tumor percentage and Gleason score demonstrates the importance of tumor burden in prognosis [26,34]. Our perineural invasion and lymphovascular invasion results are consistent with recent pathological assessment guidelines [17, 35].

Advanced Diagnostic Approaches

Recent advances in prostate cancer diagnosis have introduced more precise methods [3, 11]. The use of multiparametric MRI has shown superior accuracy in detecting clinically significant prostate cancer [21, 22]. The integration of MRI-targeted biopsy has demonstrated improved detection rates compared to conventional methods [14, 15]. These findings support the importance of advanced imaging techniques in diagnostic protocols [24].

Immunohistochemical Findings

Our results regarding AMACR, p63 and HMWCK confirm the sensitivity and specificity of these markers in the diagnosis of prostate cancer, as reported in current ISUP guidelines [12]. The high AMACR positivity and p63/HMWCK negativity rates align with established diagnostic criteria [31, 33]. Modern pathological techniques have improved our ability to accurately diagnose and classify prostate cancer [18].

Active Surveillance and Risk Management

Current guidelines support active surveillance for appropriate candidates [28,30]. The European Association of Urology position emphasizes careful patient selection and risk stratification [8, 32]. Recent studies have shown the importance of molecular and genetic factors in risk assessment [7, 19]. Standardized protocols for patient monitoring have been established through international consensus [16].

Main Findings and Clinical Significance

One of the most important results of our study is the validation of the prognostic value of the grade group system [12,13]. Recent advances in artificial intelligence applications in pathological diagnosis show promise for more accurate assessment [18]. The sensitivity and specificity of immunohistochemical markers in our study support current diagnostic protocols [17, 33]. New molecular markers and imaging techniques continue to emerge, potentially improving our diagnostic capabilities [15].

Recommendations for Clinical Applications

Based on our findings and current literature [6, 8], we recommend:

1. Integration of multiparametric MRI and targeted biopsy in diagnostic protocols [21, 22]
2. Standardized reporting following WHO guidelines [9, 20]
3. Risk-adapted follow-up strategies incorporating molecular markers [28, 34]
4. Regular pathological quality assessment and updates to diagnostic criteria [18, 35]

5. Development of precision diagnostic algorithms incorporating both molecular and imaging biomarkers for future research [18, 19]

6. Implementation of artificial intelligence-assisted pathological assessment protocols [18, 35]

7. Investigation of novel immunohistochemical markers for improved risk stratification [17, 33]

Limitations

Since it is a retrospective single-center study, its generalizability is limited. Some small tumors may have been missed in TUR-P samples, which may have underestimated the true prevalence of prostate cancer [2]. Lack of long-term follow-up data prevents us from obtaining clear results about the course of the disease and prognosis [31,32]. The evolving nature of diagnostic criteria and treatment protocols may also affect the interpretation of our results [27].

CONCLUSION

In conclusion, the results obtained in our study regarding prostate acinar adenocarcinoma may benefit the development of prostate cancer diagnostic approaches. While we tried to expand the current knowledge about prostatic acinar adenocarcinoma, which we tried to present in terms of the diagnosis of the disease, we also tried to reveal new questions and potential directions for future research. We believe that future studies examining our findings on a larger number of patient populations may provide significant advances in the diagnostic management of prostate cancer. Our study emphasizes the clinical importance of IPC and reveals the necessity of careful histopathological evaluation of TUR-P and open prostatectomy specimens. In light of our findings, we must state that our study shows that the risk of IPC increases especially in patients over 60 years of age and with PSA levels above 4 ng/mL. In light of the data we obtained, we can say that it would be very useful for future research to focus on long-term clinical outcomes and optimal management strategies in patients. Ultimately, this comprehensive analysis of prostate acinar adenocarcinoma not only enhances our understanding of the disease but also provides valuable insights for improving diagnostic accuracy, optimizing treatment strategies, and establishing more effective clinical protocols, thereby contributing significantly to both the scientific literature and daily clinical practice in urological pathology.

Ethical statement

This research was approved by the Ethics Committee of Sancaktepe Prof. Dr. İlhan Varank Training and Research Hospital (Approval No: 2024/301) and was conducted and concluded in accordance with the ethical standards of the Declaration of Helsinki.

Authors' Contribution

Study Conception: BE, MY, MG, ÇDA, OS; Study Design: BE, MY, MG; Supervision: BE, MY, MG, ÇDA, OS; Funding: BE, ÇDA, OS; Materials: BE, MY, ÇDA, OS; Data Collection and/or Processing: BE, MY, MG, ÇDA, OS; Statistical Analysis and/or Data Interpretation: BE, MY, MG, ÇDA, OS; Literature Review: BE, MY, MG, ÇDA, OS; Manuscript Preparation: BE and Critical Review: BE, MY, MG, ÇDA, OS.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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