Original Article

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Incidental Prostate Cancer After HoLEP: Evaluation of Predictive Factors

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Abstract

Objective: To evaluate the predictive value of demographic, preoperative, and postoperative clinical parameters for detecting incidental prostate cancer (iPCa) in patients undergoing holmium laser enucleation of the prostate (HoLEP).
Materials and Methods: Clinical records of male patients who underwent HoLEP for BPH between 01.01.2023 and 01.01.2024 were retrospectively reviewed. Demographic, preoperative, and postoperative data, including total prostate-specific antigen (PSA), free PSA, and PSA density (PSAd), were analysed. The role of these measurements and data in predicting the likelihood of iPCa in patients whose pathology results revealed iPCa were evaluated.
Results: A total of 112 patients underwent HoLEP, including 96 with BPH (85.7%) (group 1) and 16 with iPCa (Group 2) (14.3%). Median age was 66.5 years. Demographic data and PSA levels were comparable between groups. PSAd was significantly higher in Group 2 (0.06 vs. 0.04 ng/mL/cc, p=0.008), and PSAd ≥0.15 was more frequent in Group 2 (25% vs. 5.2%, p=0.023). Pathology revealed 68.7% Gleason grade group 1, all under active surveillance, and 31.3% grade group 2-5, treated with radiotherapy ± hormonal therapy. Multivariate analysis identified PSAd as the only independent predictor of iPCa (odds ratio: 9.09, 95% confidence interval: 1.12-73.8, p=0.01). Receiver operating characteristic analysis showed moderate diagnostic performance for PSAd (AUC: 0.71), with a 0.08 ng/mL/cc threshold yielding 75% sensitivity and 69.7% specificity.
Conclusion: iPCa after HoLEP is relatively common but mostly low-grade, with favourable oncological outcomes. Preoperative PSAd was identified as a significant predictor of iPCa. These findings may aid in preoperative patient counselling and risk-stratified management. Active surveillance appears safe and effective for low-grade iPCa.
Keywords: Incidental prostate cancer, HoLEP, PSA density, BPH

Introduction

Benign prostatic hyperplasia (BPH) is a common urological condition in aging men and accounts for the majority of urology outpatient visits (1,2). By causing benign enlargement of the prostate, BPH leads to voiding symptoms and storage symptoms (3). If left untreated, it may lead to irreversible alterations in the detrusor muscle, resulting in bladder dysfunction, chronic urinary retention, and eventually upper urinary tract damage and kidney failure (4).

According to the European Association of Urology (EAU) guidelines, the first-line treatment for BPH consists of lifestyle modifications. Pharmacological treatments are recommended as second-line therapies depending on patient symptoms. When these treatments are insufficient, surgical treatment options may be considered (5,6). Among the surgical options for BPH, holmium laser enucleation of the prostate (HoLEP) surgery has become one of the most preferred methods due to advancements in laser technology and its favourable outcomes (7).

During the preoperative evaluation of patients undergoing BPH surgery, in addition to functional assessment, routine screening for prostate cancer is performed via digital rectal examination and measurement of serum prostate-specific antigen (PSA) (6).

However, even when prostate cancer screening is performed in accordance with EAU guidelines and patients without suspicious findings proceed to BPH surgery, incidental prostate cancer (iPCa) may still be detected in postoperative surgical specimens.

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Several studies in the literature have aimed to identify predictive factors for iPCa following BPH surgery (8-10). It is important to make sure patients are aware that this diagnosis could be discovered after undergoing surgery for BPH.

In this study, we aimed to evaluate, based on our institutional experience, the effectiveness of demographic characteristics and preoperative and postoperative clinical parameters in predicting the likelihood of detecting iPCa in patients who underwent HoLEP surgery at our clinic.

Materials and Methods

Clinical records between 01.01.2023 and 01.01.2024 were reviewed for the study. The demographic parameters, preoperative and postoperative data, and pathology results of patients who underwent HoLEP surgery for BPH in our clinic were retrospectively evaluated. Evaluation and treatments for these patients were applied based on the EAU guidelines (6). Ethical approval for the study was obtained from the Local Ethics Committee of Marmara University Faculty of Medicine (protocol no: 09.2025-25.0940, date: 21.11.2025).

Male patients over 40 years of age who underwent surgery for BPH in our hospital during this period were included in the study. Data from patients with at least one year of follow-up were recorded. Patients with incomplete or irregular data, previous BPH surgery, a history of prostate cancer, or abnormal rectal examination findings were excluded from the study. Prostate biopsy or multiparametric magnetic resonance imaging (MRI) was performed selectively in patients with clinical suspicion of malignancy (e.g., elevated PSA, abnormal rectal examination). Patients without a prior diagnosis of prostate cancer underwent HoLEP for benign prostatic enlargement, and iPCa was defined as cancer detected in the surgical specimen.

HoLEP procedures were performed using a 60-watt holmium: YAG laser (Quanta Cyber Ho model) with a 550 µm laser fiber. Laser settings were constant in all patients, being 2 Joules x 30 Hertz in Virtual Basket pulse modulation mode. All surgical procedures were performed by an experienced surgeon who had performed at least 100 HoLEP procedures. All surgeries were carried out using the en bloc technique.

Demographic data, preoperative and postoperative medical histories, physical examination findings, total PSA, free PSA, and PSA density (PSAd) records of male patients over 40 years of age who underwent surgery for BPH were retrospectively analysed statistically. PSAd was calculated as the ratio of serum PSA level (ng/mL) to prostate volume (cc), with prostate volume measured by preoperative imaging. Prostate volume was expressed in cubic centimeters (cc), which is equivalent to milliliters. The role of these measurements and data in predicting the likelihood of iPCa in patients whose pathology results revealed iPCa were evaluated.

Patients without iPCa were considered group 1, while those with iPCa were considered group 2. The demographic, preoperative, and postoperative data of these groups were compared based on the obtained results. Parameters that showed statistically significant differences in the group with iPCa were analysed in more detail, and their effects were discussed. Parameters with significant differences between groups were analysed as continuous variables in regression models to maintain statistical power and prevent potential information loss associated with arbitrary categorization. In addition, pathology data and treatments applied as a result of the diagnosis in patients with iPCa were reported.

The primary outcome of this study was the incidence of iPCa detected in patients undergoing HoLEP for BPH. Secondary outcomes included the assessment of demographic and clinical parameters (age, PSA, PSAd, prostate volume, comorbidities) as potential predictors of iPCa, the distribution of Gleason grade groups among patients with iPCa, and the subsequent management strategies and short-term postoperative outcomes.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS 25.0. Due to non-normal data distribution (Kolmogorov-Smirnov test), non-parametric tests were applied. Numerical data were presented as median interquartile range, and categorical data as counts/percentages. The chi-square test was used to analyse categorical data, while the Mann-Whitney U test was used to compare groups. Receiver operating characteristic (ROC) analysis was performed to evaluate the predictive value of relevant parameters. Multivariate regression analysis was conducted to determine independent predictors. A p-value <0.05 was considered statistically significant.

Results

A total of 112 patients who underwent HoLEP were included in the analysis, of whom 96 (85.7%) had BPH and 16 (14.3%) were incidentally diagnosed with prostate cancer. The median age of the patients included in the study was 66.5 (62-72) years. The median prostate volume was 80 cc (62.75-120), the total PSA was 3.58 ng/mL (1.94-6.71), and the PSAd was 0.048 (0.024-0.091). The demographic and clinical characteristics of the groups are presented in Table 1. There were no significant differences between groups in terms of age, body mass index (BMI), hypertension, dyslipidaemia, or diabetes mellitus. Median prostate volume tended to be lower in Group 2, but the difference did not reach statistical significance. Preoperative total PSA, free PSA, and f/t PSA ratio were comparable between groups. However, PSAd was significantly higher in group 2 (0.06 vs. 0.04 ng/mL/cc, p=0.008). When categorized, PSAd $\geq$0.15 ng/mL/cc was more frequent in Group 2 (25% vs. 5.2%), demonstrating statistical significance (p=0.023). Postoperative PSA and the pre/postoperative PSA ratio showed no significant differences between the groups.

Pathological evaluation of the incidental cancer cohort revealed that 11 patients (68.7%) had Gleason grade group 1 disease, all managed with active surveillance. Five patients (31.3%) had Gleason grade group 2-5 disease; 60% of these were stage T1a and 40% T1b. Four patients received radiotherapy combined with hormonal therapy and one underwent radiotherapy alone (Table 2).

In multivariate logistic regression analysis (Table 3), PSAd emerged as the only significant independent predictor of iPCa [odds ratio: 9.09, 95% confidence interval (CI): 1.12-73.8, p=0.01]. The odds ratio for PSAd reflects the change in the risk of iPCa per 0.01 unit increase in PSAd.

ROC curve analysis demonstrated that PSAd had a moderate diagnostic performance for detecting iPCa, with an AUC of 0.71 (95% CI: 0.583-0.837). As illustrated in Figure 1, PSAd showed a reasonable discrimination ability, with an optimal cut-off value of 0.08 ng/mL/cc providing a sensitivity of 75% and a specificity of 69.7%.

Discussion

In this study of 112 patients undergoing HoLEP, 14.3% were incidentally diagnosed with prostate cancer, while the majority had BPH. The groups were comparable in terms of age, BMI, and comorbidities, and there were no significant differences in preoperative total PSA, free PSA, or f/t PSA ratio. Notably, PSAd was significantly higher in patients with iPCa, with a greater proportion exhibiting PSAd ≥0.15 ng/mL/cc. Most incidental cancers were Gleason grade group 1 and managed with active surveillance, whereas a minority had higher-grade disease requiring radiotherapy, with or without hormonal therapy. Multivariate analysis identified PSAd as the only independent predictor of iPCa. ROC analysis further supported its diagnostic value, showing a moderate performance (AUC: 0.71) with a threshold of 0.08 ng/mL/cc yielding 75% sensitivity and 69.7% specificity. As this study focused on iPCa, only patients without a known diagnosis of prostate cancer prior to surgery were included. However, the lack of a standardized preoperative biopsy or imaging protocol may have resulted in undiagnosed prostate cancer in some patients, which should be considered when interpreting the results.

A review of the literature shows that there are publications investigating predictive factors for iPCa in patients undergoing HoLEP, similar to our study. In a retrospective study by Sid Ahmed and Nkwam (11), iPCa was detected in 259 HoLEP patients at a rate of 14.3%. This rate is very similar to the iPCa incidence observed in our study. In Sid Ahmed and Nkwam's (11) study, most cancers were low-grade (Gleason 6), and only a very small proportion (1.5%) were high-grade (Gleason ≥8). Unlike our study, when evaluating patients with iPCa, only age was significantly higher, while PSA, PSAd, and prostate volume did not differ significantly from patients with benign histology. Most incidental cancers were suitable for conservative management.

In a large cohort of 913 patients undergoing HoLEP, Sakai et al. (12) found that 20% had iPCa. Higher PSAd, preoperative biopsy status, and ongoing 5-alpha reductase inhibitor therapy were associated with iPCa detection, but the authors noted that these factors alone are not sufficient to reliably identify high-risk patients in advance. Their results highlight the importance of a standardized, risk-adapted preoperative approach, including imaging and selective biopsy, to improve detection of clinically significant prostate cancer before non-oncologic surgery.

In a study by Elkoushy et al. (13) including 1,242 HoLEP patients, the rate of iPCa was reported as 5.6%. Considering that reported iPCa rates in the literature range from 5% to 20%, the 14.3% rate observed in our study appears generally consistent with previous findings. Elkoushy et al. (13) identified patient age and PSAd as preoperative factors associated with iPCa, while prostate volume was similar between groups; these findings are in line with our results. In their study, a PSAd cut-off of 0.092 yielded a sensitivity of 0.83 and specificity of 0.67. In our ROC analysis, a PSAd cut-off of 0.08 showed a sensitivity of 0.75 and specificity of 0.69. This comparison supports the value

Table 1. Comparison of parameters

	Group 1 (n=96)	Group 2 (n=16)	p-value
Age (years) median (IQR)	66.5 (62-72)	68.5 (62.25-74.75)	0.407
BMI (kg/m^2) median (IQR)	27.5 (25.18-30.8)	28.08 (26.68-29.91)	0.886
Hypertension, n (%)	35 (36.5)	4 (25)	0.373
Dyslipidaemia, n (%)	23 (24)	4 (25)	0.573
Diabetes mellitus, n (%)	28 (29.2)	4 (25)	0.496
Prostate volume (cc) median (IQR)	85 (65-122)	67 (57-90)	0.107
Total PSA (ng/mL) median (IQR)	3.53 (1.97-6.71)	4.28 (1.67-9.69)	0.812
Total PSA Group (ng/mL), n (%)			
0-4	56 (58.9)	8 (50)	0.506
4-10	26 (27.4)	4 (25)	
10-20	13 (13.7)	4 (25)	
Free PSA (ng/mL) median (IQR)	0.56 (0.33-0.72)	0.96 (0.39-1.72)	0.429
f/t PSA ratio median (IQR)	0.19 (0.14-0.33)	0.22 (0.16-0.3)	0.843
PSAd (ng/mL/cc)	0.04 (0.02-0.09)	0.06 (0.04-0.14)	**0.008**
PSAd group, n (%)			
<0.15	91 (94.8)	12 (75)	**0.023**
≥0.15	5 (5.2)	4 (25)	
Post-operative PSA (ng/mL) median (IQR)	0.37 (0.23-0.52)	1.31 (0.7-2.44)	0.178
Pre/post operative PSA ratio median (IQR)	6.53 (3.01-13.39)	3.03 (2.04-27.48)	0.744

BMI: Body mass index, PSA: Prostate-specific antigen, PSAd: PSA density, f/t PSA: Free-to-total PSA ratio, IQR: Interquartile range

of PSAd as a predictive parameter for iPCa and indicates that, despite slight variations between cohorts, it remains a clinically meaningful indicator. The authors also emphasize that PSAd can be particularly useful in predicting iPCa risk in older patients and that active surveillance after HoLEP is a safe and effective management strategy for low-grade cancers.

In their retrospective study of 777 HoLEP patients, Shvero et al. (14) reported an iPCa rate of 7.1%. Among these patients, 61.8% had low-grade (GG1) iPCa, and clinically significant cancer was rare. This rate is similar to the pathology results in our study, where the proportion of GG1 patients was 68.7%. Unlike our study, smaller preoperative prostate volume was identified as a predictive factor for iPCa, with a 13% reduction in risk for every 10 mL increase in prostate volume. In addition, older age and smaller prostate volume were found to be risk factors for higher-grade (GG2 and above) iPCa. The observed differences in these findings may be attributable to cohort size and patient demographic characteristics.

A review of the literature shows that there are also systematic reviews on this topic. In the review by Cheng et al. (15), the incidence, predictive factors, and oncological outcomes of iPCa in men undergoing endoscopic prostate enucleation were investigated. Sixty-one studies were included in the qualitative synthesis, and 55 studies were included in the meta-analysis. The pooled incidence of iPCa was 8% (95% CI: 7.3-8.8). The results showed that increasing age, higher preoperative PSA and PSAd, smaller prostate volume, higher postoperative PSA velocity, and lower enucleated prostate weight were significantly associated with iPCa. In BPH patients, the mean preoperative and postoperative PSA levels were 5.58±1.48 ng/dL and 1.06±0.27 ng/mL, respectively, while in iPCa patients these values were 7.72±2.90 ng/mL and 2.77±1.66 ng/mL. The mean PSA reduction was 82±1.8% for BPH patients and 68.2±12.1% for iPCa patients. According to pathology results, the majority of iPCa cases (68.7%) were managed with active surveillance.

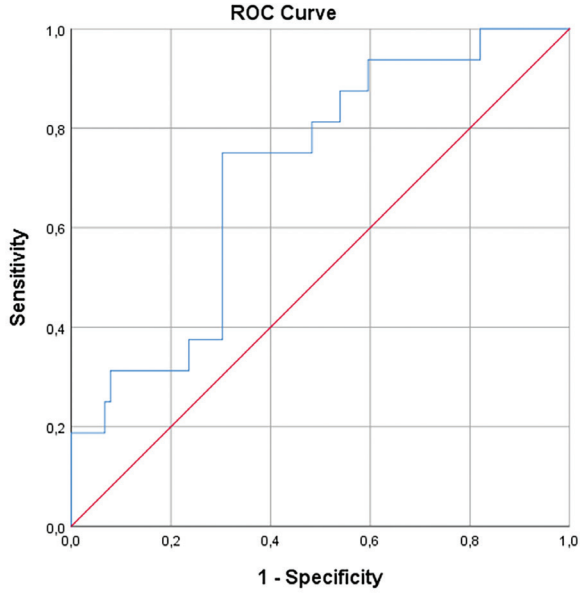
Table 2. Pathological results

	Gleason grade 1 (n=11)	Gleason grade 2-5 (n=5)
Stage n (%)		
T1a	11 (100)	3 (60)
T1b	0	2 (40)
Treatment n (%)		
Active surveillance	11 (100)	0
Radiotherapy	0	1 (20)
Radiotherapy + hormonal therapy	0	4 (80)
Hormonal therapy	0	0
Surgery	0	0

Table 3. Multivariate logistic regression analyses

	OR	95% CI	p-value
PSAd (0.01 ng/mL increase)	9.09	1.12-73.8	0.01
Age (per 1 year increase)	0.97	0.96-1.10	0.33
Prostate volume (per 1 cc increase)	0.99	0.95-1.05	0.12
Total PSA (per 1 ng/mL increase)	0.97	0.95-1.12	0.42

OR: Odds ratio, CI: Confidence interval, PSA: Prostate specific antigen, PSAd: PSA density



Risk factor	AUC (CI %)	Threshold value	p-value	Sensitivity (%)	Specificity (%)
Incidental prostate cancer	0.71 (0.583-0.837)	0.08	0.04	75	69.7

PSA: Prostate specific antigen, CI: Confidence interval, ROC: Receiver operating characteristic

Figure 1. ROC analysis for PSA-density

The study suggests that the incidence of iPCa after enucleation of the prostate is approximately 8%, and in BPH patients a postoperative PSA <2.0 ng/mL and a PSA reduction >70% can be expected.

In the review by Yilmaz et al. (16), which included only studies of patients with iPCa after HoLEP (19 studies in total), the rate of iPCa after HoLEP was found to range from 5.64% to 23.3%. In this review, functional and oncological outcomes were generally reported as favourable, and a wide range of treatment options was suggested to be available.

The results of our study indicate that iPCa after HoLEP is not uncommon, although it is mostly low-grade, and oncological outcomes are generally favourable. Preoperative PSAd was found to be important in predicting the risk of iPCa. The identification of a PSAd cut-off value of 0.08 ng/mL/cc provides clinically relevant information for the preoperative assessment of patients undergoing HoLEP. Given that these patients often present with significantly enlarged prostate volumes, total PSA alone may be insufficient to accurately reflect cancer risk. In this setting, PSAd offers a more refined risk stratification by accounting for prostate volume. Patients with PSAd values above this threshold may warrant further diagnostic evaluation, including multiparametric MRI or targeted biopsy, to exclude clinically significant prostate cancer prior to surgery. On the other hand, patients with low PSAd may be managed more conservatively, potentially avoiding unnecessary invasive procedures. In light of these findings, incorporating PSAd into routine clinical practice may enhance patient counselling, optimize preoperative decision-making, and contribute to a more individualized approach in the management of benign prostatic obstruction.

Study Limitations

This study has several limitations, including its retrospective single-center design and relatively small sample size. These factors may have influenced the detection rate of iPCa and limit the generalizability of the findings. Second, preoperative prostate biopsy and multiparametric MRI were not routinely performed in all patients, as these modalities are generally reserved for individuals with clinical suspicion of prostate cancer. Therefore, some patients may have had undiagnosed malignancy prior to surgery, which was subsequently detected incidentally. Although this approach reflects real-world clinical practice, it may have influenced the incidence and detection of iPCa in our cohort. Additionally, long-term oncological follow-up was available for only a limited number of patients during the study period; therefore, more extensive data are needed regarding the long-term prognosis of iPCa and the management of rare high-grade cases. Future studies with larger, multicentre cohorts are needed to provide more robust evidence regarding the long-term prognosis of iPCa and the management of rare high-grade cases.

Conclusion

In summary, iPCa after HoLEP is not uncommon, although it is mostly low-grade, and oncological outcomes are generally favourable. Our study demonstrates that preoperative PSAd is an important parameters in predicting the risk of iPCa. These findings may help surgeons and clinicians to inform patients preoperatively and to develop risk-stratified approaches. In particular, since the likelihood of iPCa may be higher in patients with elevated PSAd values, appropriate preoperative evaluation and patient counselling are crucial. In low-grade iPCa cases, active surveillance after HoLEP can be considered a safe and effective management strategy.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the Local Ethics Committee of Marmara University Faculty of Medicine (protocol no: 09.2025-25.0940, date: 21.11.2025).

Informed Consent: Retrospective study.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: E.G., G.Ö., M.K., T.E.Ş., Concept: E.G., T.E.Ş., Design: E.G., T.E.Ş., Data Collection or Processing: E.G., T.A., B.K.K., H.T.M., Analysis or Interpretation: E.G., T.A., B.K.K., H.T.M., Literature Search: E.G., T.A., B.K.K., G.Ö., M.K., Writing: E.G., T.A., B.K.K., G.Ö., M.K., T.E.Ş.

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