Incidental prostate cancer after HoLEP: factors associated with clinically significant disease

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Introduction

Higher rates of incidental prostate cancer (iPCa) are expected after holmium laser enucleation of the prostate (HoLEP) compared to transurethral resection, owing to larger volumes of tissue resected.[1, 2] While patients with insignificant disease are often placed on active surveillance, a small portion will have clinically significant residual disease which warrants further staging and treatment. Our objective was to assess predictors of clinically significant iPCa after HoLEP to better inform surgical decision-making for patients with benign prostatic hyperplasia (BPH).

Design/Sample

This is a retrospective cohort study of patients who underwent HoLEP from February 2020 to October 2023 at UC Davis (N=491), with follow-up through February 2024. Patients with Grade Group 1 (GG1) iPCa were compared to those with Grade Group 2+ (GG2+) iPCa. Demographics, pre- and post-operative PSA and PSA density, and surgical pathology were assessed. Pre- and post-HoLEP staging MRI was obtained in patients based on age and pathology.

Results

Of 491 patients undergoing HoLEP, 56 (11.4%) were found to have iPCa. 38 patients (7.7%) were found to have GG1 iPCa and 18 patients (3.7%) were found to have GG2+ iPCa. When adjusted for the effects of finasteride, increased pre-operative PSA density was associated with increased risk of iPCa requiring treatment (OR 3.03, 95% CI 1.25-11.72, $p = 0.014$). On univariable analysis, there was no significant difference in risk of iPCa requiring treatment for those with PIRADS 4-5 lesions on MRI versus those without.

Table 2: Univariable logistic regression models of factors associated with treatment vs. active surveillance

Variable	Odds Ratio (95% CI)	*P*-value
Race: African American or Black vs. White	4.091 (0.33, 37.448)	0.240
Race: Asian vs. White	2.922 (0.25, 22.421)	0.347
Race: Hispanic vs. White	4.87 (0.682, 31.979)	0.108
Hx of Smoking: Yes vs. No	1.89 (0.449, 7.69)	0.374
Diabetes: Yes vs. No	3.802 (0.861, 16.587)	0.0767
log2(Preoperative PSA) (Continuous)	1.153 (0.687, 1.963)	0.587
log2(Corrected Pre-op PSA--Finasteride) (Continuous)	1.398 (0.847, 2.566)	0.332
log2(Preoperative PSAD) (Continuous)	1.696 (0.943, 3.388)	0.0807
log2(Corrected Pre-op PSAD--Finasteride) (Continuous)	2.243 (1.169, 5.02)	**0.0131**
Pathology: Grade Group 2+ vs. Grade Group 1	37.889 (5.889, 439.264)	**<0.001**
% Cancer (Continuous)	1.076 (1.026, 1.162)	**<0.001**
log2(Postoperative PSA 3 Months) (Continuous)	1.665 (1.119, 2.761)	**0.0107**
log2(Postoperative PSAD 3 Months) (Continuous)	1.608 (1.164, 2.448)	**0.00324**
Post-Op MRI: PIRADS 4-5 vs. Negative	4.2 (0.684, 29.902)	0.119
PSA Doubling Time <1 year: Yes vs. No	11 (1.752, 77.121)	**0.0115**

Table 3: Multivariable logistic regression model of factors associated with treatment vs. active surveillance

Variable	Odds Ratio (95% CI)	*P*-value
Pathology: Grade Group 2+ vs. Grade Group 1	7.074 (0.308, 186.258)	0.2058
% Cancer (Continuous)	1.066 (0.946, 1.178)	0.2204
log2(Corrected Pre-op PSAD--Finasteride) (Continuous)	3.026 (1.248, 11.716)	**0.0137**
log2(Postoperative PSA 3 Months) (Continuous)	0.946 (0.477, 1.854)	0.8660
PSA Doubling Time <1 year: Yes vs. No	11.154 (0.876, 324.226)	**0.0634**

Table 1: Characteristics of subjects with incidental prostate cancer after holmium laser enucleation of the prostate

	Active Surveillance (N=47)	Treatment (N=9)	Overall (N=56)
Age (years)			
Mean (SD)	74.1 (6.27)	73.6 (9.58)	74.0 (6.80)
Median [Min, Max]	74.0 [63.0, 88.0]	74.0 [60.0, 90.0]	74.0 [60.0, 90.0]
Race			
African American or Black	2 (4.3%)	1 (11.1%)	3 (5.4%)
Asian	3 (6.4%)	1 (11.1%)	4 (7.1%)
Hispanic	3 (6.4%)	2 (22.2%)	5 (8.9%)
White Non-Hispanic	37 (78.7%)	5 (55.6%)	42 (75.0%)
Other	1 (2.1%)	0 (0%)	1 (1.8%)
Missing	1 (2.1%)	0 (0%)	1 (1.8%)
History of Smoking			
No	33 (70.2%)	5 (55.6%)	38 (67.9%)
Yes	14 (29.8%)	4 (44.4%)	18 (32.1%)
Diabetes			
No	39 (83.0%)	5 (55.6%)	44 (78.6%)
Yes	8 (17.0%)	4 (44.4%)	12 (21.4%)
Pre-op PSA			
Mean (SD)	6.50 (6.82)	10.7 (13.30)	7.16 (8.14)
Median [Min, Max]	4.40 [0.60, 31.0]	5.35 [0.70, 40.6]	4.40 [0.60, 40.6]
Missing	4 (8.5%)	1 (11.1%)	5 (8.9%)
Corrected Pre-op PSA (Finasteride)			
Mean (SD)	8.11 (8.27)	14.4 (13.8)	9.08 (9.44)
Median [Min, Max]	5.30 [0, 39.00]	10.2 [1.40, 40.60]	5.30 [0, 40.60]
Missing	3 (6.4%)	1 (11.1%)	4 (7.1%)
Pre-op PSAD			
Mean (SD)	0.07 (0.06)	0.17 (0.19)	0.09 (0.09)
Median [Min, Max]	0.06 [0, 0.26]	0.09 [0.02, 0.56]	0.06 [0, 0.56]
Missing	3 (6.4%)	1 (11.1%)	4 (7.1%)
Corrected Pre-op PSAD (Finasteride)			
Mean (SD)	0.09 (0.08)	0.24 (0.19)	0.12 (0.11)
Median [Min, Max]	0.06 [0, 0.36]	0.18 [0.05, 0.56]	0.07 [0, 0.56]
Missing	3 (6.4%)	1 (11.1%)	4 (7.1%)
Pathology (Gleason Score)			
3+3	37 (78.7%)	1 (11.1%)	38 (67.9%)
3+4	9 (19.1%)	3 (33.3%)	12 (21.4%)
4+3	1 (2.1%)	3 (33.3%)	4 (7.1%)
4+5	0 (0%)	1 (11.1%)	1 (1.8%)
5+4	0 (0%)	1 (11.1%)	1 (1.8%)
% Cancer			
Mean (SD)	3.30 (8.95)	27.4 (28.3)	7.18 (16.2)
Median [Min, Max]	1.00 [1.00, 60.0]	20.0 [1.00, 90.0]	1.00 [1.00, 90.0]
Post-op PSA (3 months)			
Mean (SD)	1.28 (1.32)	11.4 (20.1)	2.90 (8.60)
Median [Min, Max]	0.90 [0.10, 7.30]	6.10 [0.10, 64.0]	1.05 [0.10, 64.0]
Post-op PSA Density (3 months)			
Mean (SD)	0.05 (0.15)	0.74 (1.48)	0.17 (0.64)
Median [Min, Max]	0.03 [0, 1.00]	0.15 [0, 4.57]	0.03 [0, 4.57]
Post-op MRI			
Negative	22 (46.8%)	2 (22.2%)	24 (42.9%)
PIRADS 4	7 (14.9%)	1 (11.1%)	8 (14.3%)
PIRADS 5	0 (0%)	2 (22.2%)	2 (3.6%)
Missing	18 (38.3%)	4 (44.4%)	22 (39.3%)
PSA Doubling Time <1 year			
No	38 (80.9%)	3 (33.3%)	41 (73.2%)
Yes	3 (6.4%)	3 (33.3%)	6 (10.7%)
N/A	6 (12.8%)	3 (33.3%)	9 (16.1%)

SD, Standard Deviation
PSA, prostate specific antigen
Pre-op PSA Density was calculated by: Pre-op PSA/Calculated Prostate Volume by Imaging
Post-op PSA Density was calculated by: Post-op PSA/((100% - pathologic volume resected)*Prostate Volume by Pre-operative Imaging))

Summary

Pre-operative PSA density can help inform those who warrant additional staging MRI, prostate biopsies, and potentially prostatectomy instead of HoLEP. PSA doubling time after HoLEP shows promise as an indicator of clinically significant residual disease, although it failed to reach statistical significance in this single-institution retrospective study, which was limited by sample size and follow-up time. Longitudinal studies are required to further stratify prostate cancer progression risk within the iPCa population.

Acknowledgements/References

References

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