Application of Canary Histology Classifier in Prostate Biopsies for Risk Stratification

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Abstract

Background

Nguyen et al recently proposed an outcome-based radical prostatectomy (RP) histologic classifier (PMID 38828674), combining all high-risk carcinoma histology patterns into "unfavorable histology," versus absence as "favorable histology." We examine whether this classifier, with additional stratification of favorable histology, is applicable to prostate biopsies for risk stratification.

Design

Archival databases were searched for patients with long term clinical follow-up after RP and available prostate biopsy slides. Most recent biopsies underwent blinded re-review. Canary risk groups were assigned based on highest risk patterns in any core. **Unfavorable histology** encompasses all Gleason pattern 5, large cribriform/intraductal carcinoma (>0.25 mm) (Fig. 1A), anastomosing cords of carcinoma (Fig. 1B), grade 3 stromogenic carcinoma, and complex intraluminal papillary architecture (Fig. 1C). To capture patterns potentially predictive of unsampled unfavorable histology, "**biopsy borderline histology**" combines small cribriform/glomeruloid ($\leq$0.25 mm) (Fig. 1D), simple glomerulations **(**Fig. 1E), predominance of extensive poorly formed glands, equivocal small anastomosing cords (Fig. 1F), grade 2 stromal response, and epithelial complexity associated with mucin (beyond mucinous fibroplasia). "**Biopsy favorable**" is defined as void of any unfavorable or biopsy borderline histology. Biopsy and RP Gleason Grade Group (GG), pT stage, and pN stage were recorded from original reports. Biochemical recurrence (BCR) was defined as consecutive PSA of $\geq$0.2 ng/mL 8 weeks after RP or receipt of salvage treatment. RP stage and GG were analyzed using chi-square. BCR-free survival was analyzed using Kaplan-Meier curve.

Results

360 patients were identified (median follow-up 9 years, IQR 7, 12), with biopsy classified as unfavorable (n=63; 27.8%), biopsy borderline (n=92; 25.6%), and biopsy favorable (n=205; 56.9%) (**Table**). The three-tiered classification is significantly associated with earlier BCR (log-rank p-value <.01)(Fig. 2), RP GG (<.01), pT stage (<.01), and pN stage (<.01) (**Table**).

Conclusion

Unfavorable histology on biopsy was associated with highest risk of BCR after RP, compared to "biopsy borderline" and "biopsy favorable" groups. This proof-of-principle study demonstrates the three-tiered classifier could be applicable in biopsies for risk stratification.

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Conflicts of Interest Disclosure Statement

None.

	Unfavorable (n=63)	**Biopsy Borderline (n=92)**	**Biopsy Favorable (n=205)**	**Total (N=360)**
Histologic Patterns	• Gleason pattern 5 • Expansile/large cribriform morphology (> 0.25 mm in diameter) • Intraductal carcinoma (IDC-P) • Complex anastomosing cord • Complex papillary growth • Grade 3 stromogenic carcinoma	• No unfavorable patterns. • Small cribriform glands (≤ 0.25 mm in diameter) • Predominance of extensive poorly formed glands warranting Gleason primary pattern 4 • Equivocal small anastomosing cords • Glomerulations/glomeruloid patterns • Grade 2 stromal response	No unfavorable or borderline histology patterns	
Age at diagnosis (years), median (IQR)	65 (60, 69)	62 (57.5, 66.5)	60 (54, 64)	61 (56, 66)
PSA at diagnosis (ng/mL), median (IQR)	7.87 (5.52, 11.50)	5.36 (4.54, 7.90)	5.01 (3.80, 6.30)	5.38 (4.2, 7.6)
Grade Group at biopsy, n (%)				
GG1	0 (0%)	11 (12%)	163 (80%)	174 (48%)
GG2	10 (16%)	49 (53%)	37 (18%)	96 (27%)
GG3	28 (44%)	24 (26%)	5 (2%)	57 (16%)
GG4	17 (27%)	5 (5%)	0 (0%)	22 (6%)
GG5	8 (13%)	3 (3%)	0 (0%)	11 (3%)
Grade Group at RP				
GG1	0 (0%)	3 (3%)	60 (29%)	63 (18%)
GG2	17 (27%)	68 (74%)	122 (60%)	207 (58%)
GG3	26(41%)	18 (20%)	18 (9%)	62 (17%)
GG4	5 (8%)	1 (1%)	0 (0%)	6 (2%)
GG5	15 (24%)	2 (2%)	4 (2%)	21 (6%)
missing	0	0	1	1

Pathologic T stage, n (%)				
T2	22 (35%)	55 (60%)	133 (65%)	210 (58%)
T3a	30 (48%)	32 (35%)	69 (34%)	131 (36%)
T3b	11 (17%)	5 (5%)	3 (1%)	19 (5%)
Pathology N stage, n (%)				
Nx	15 (24%)	44 (48%)	135 (67%)	194 (54%)
N0	37 (59%)	46 (51%)	68 (33%)	151 (42%)
N1	11 (17%)	1 (1%)	0 (0%)	12 (3%)
Missing	0	1	2	3
7yr BCR-free survival, n (%)				
	53 (15%)	60 (34%)	110 (46%)	223 (37%)

Figure 1.

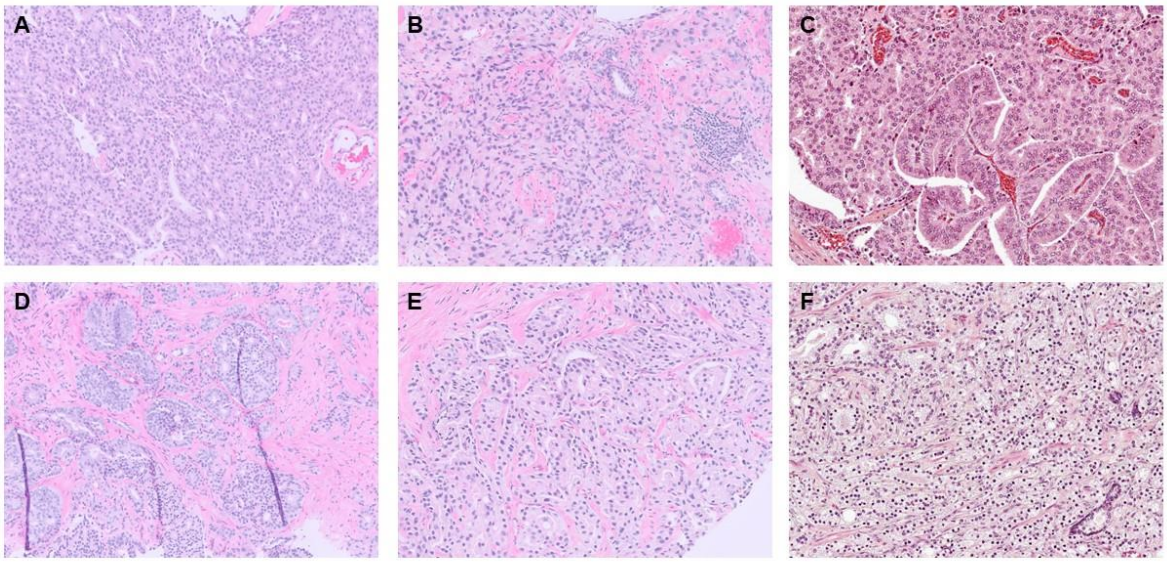
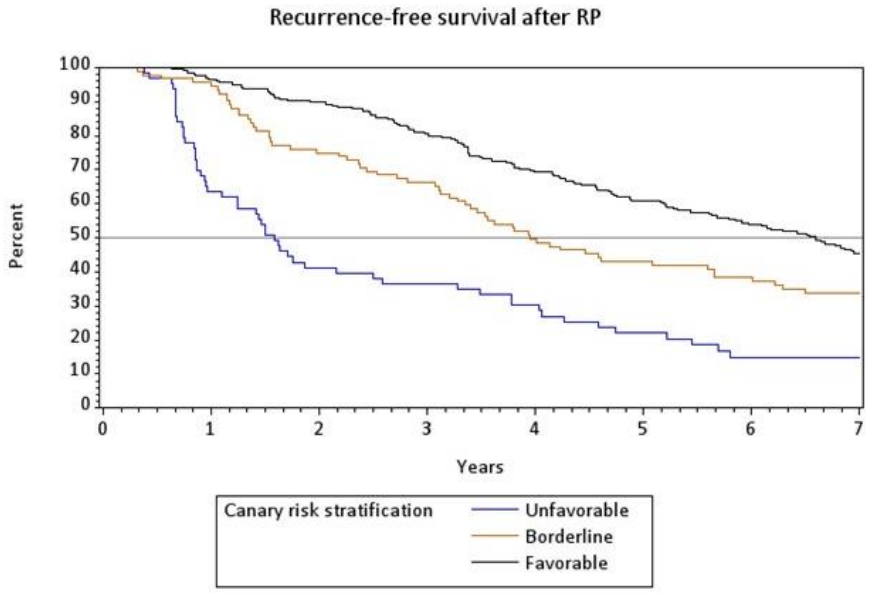


Figure 2.


Recurrence-free survival after RP
Percent
100
90
80
70
60
50
40
30
20
10
0
0
1
2
3
4
5
6
7
Years
Canary risk stratification
Unfavorable
Borderline
Favorable