Association of High-Grade Prostatic Intraepithelial Neoplasia, Atypical Small Acinar Proliferation, or Perineural Invasion with the Risk of Upgrading in Active Surveillance Cohort In the MRI-Ultrasound Fusion Biopsy Era

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Introduction
The role of high-grade prostatic intraepithelial neoplasia (HGPIN), atypical small acinar proliferation (ASAP), or perineural invasion (PNI) on the risk of upgrading in subsequent MRI-ultrasound fusion biopsies has not been well studied. We aimed to determine if the presence of those pathological characteristics on prostate biopsy increases the risk of upgrading on subsequent MRI-ultrasound fusion biopsy for active surveillance.

Methods
For grade group (GG) 1 prostate cancer, upgrading in active surveillance cohort was defined as pathological progression from GG1 on initial biopsy to GG≥2 on subsequent biopsy between January 2013 and February 2019. Binary logistic regression was performed to identify clinical, radiological, and biopsy pathological features (HGPIN, ASAP, or PNI) associated with the presence of upgrading on surveillance biopsy.

Results
Our active surveillance cohort included 127 men; 101 (79.5%) and 93 (73.2%) had region(s) of interest on initial and subsequent prostate MRIs, respectively, and therefore underwent MRI-ultrasound fusion biopsy. Among men on active surveillance, 31 (24.4%) showed upgrading on subsequent biopsy. Although HGPIN was associated with upgrading among patients on active surveillance in univariate analysis (p=0.01), there was no independent significance in multivariable analysis (OR 3.84, 95%CI 0.60-24.63, p=0.15). Age (OR 1.07, 95%CI 1.001-1.15, p=0.04) and PI-RADS (4-5 versus ≤3, OR 2.89, 95%CI 1.14-7.35, p=0.02) remained significantly associated with an increased risk of upgrading on subsequent biopsy (Table 1).

Conclusion
No association was found between any of the studied pathological features (HGPIN, ASAP, or PNI) and upgrading on subsequent biopsy in active surveillance cohort. Therefore, the presence of HGPIN, ASAP, or PNI on biopsy should not influence the management of men undergoing active surveillance in the MRI-ultrasound fusion biopsy era.

Table 1. Univariate and multivariate logistic regression models for the prediction of upgrading on subsequent biopsy in men on active surveillance

	Univariable			Multivariable		
	OR	95%CI	P value	OR	95%CI	P value
ASAP	5.03	0.80-31.65	0.08	3.42	0.26-44.55	0.34
HGPIN	9.03	1.65-49.29	0.01	3.84	0.60-24.63	0.15
PNI	2.69	0.67-10.75	0.16			
≥2 above pathologic features	2.13	0.34-13.42	0.41			
Age	1.07	1.01-1.14	0.02	1.07	1.001-1.15	0.04
PI-RADS 4-5	3.27	1.36-7.86	0.008	2.89	1.14-7.35	0.02
PSA density (per 0.1 unit)	1.85	1.08-3.15	0.02	1.70	0.93-3.09	0.08