

The Utility of PSA Density in Patients with PI-RADs 3 Lesions Across a Large Multi-Institutional Collaborative

Johnathan Drevik, Zafardjan Dalimov, Thomas Guzzo, Lawrence Belkoff, Bret Marlowe, Jay Raman, Marc Smaldone, Jeffrey Tomaszewski, Edouard Trabulsi, Robert Uzzo, Serge Ginzburg

Introduction and Objective: Multiparametric MRI (mpMRI) of the prostate detecting PI-RADs = 3 lesions has a low diagnostic utility. Use of PSA density has been suggested to further risk-stratify these men, to potentially avoid biopsies in favor of monitoring. We evaluate the ability to PSA density to risk-stratify PIRADs 3 lesions across patients who underwent a biopsy in a large multi-institutional collaborative.

Methods: Pennsylvania Urology Regional Collaborative (PURC) is a voluntary quality improvement collaborative of 11 academic and community urology practices in Pennsylvania and New Jersey. A retrospective analysis was performed on all patients in the PURC database that had a mpMRI prostate with PI-RADs 3 lesions only. PSA just prior to the mpMRI and prostate size reported on MRI were used to calculate the PSAd. Clinicopathologic data were evaluated. Univariable analysis using Chi-Square and Kruskal Wallis tests and multivariable logistic regression were used to identify predictors of total and clinically significant prostate cancer (csPCa) defined as \geq Grade Group 2 (GG2.)

Results: Between May 2015 and March 2021, 349 patients with PIRADs 3 lesions only were identified and comprised the cohort of interest. Clinicopathologic characteristics are summarized in Table 1. Significant prostate cancer was detected in 70/349 (20.0%) of men. Smaller prostate volume, abnormal DRE, and higher PSAd were significantly associated with clinically significant prostate cancer. In men with PSAd <0.15 , 31/228 (13.6%) harbored csPCa. Multivariable analysis confirmed that men with PSAd >0.15 were more likely to harbor clinically significant prostate cancer ($p < 0.001$, Table 2).

Conclusions: Across a large regional collaborative, patients with a PIRADs 3 lesions on mpMRI were noted to have clinically significant cancer in 20%. Using PSA density cut-off of 0.15 to further risk stratify these patients would result in missing clinically significant prostate cancer in 13.6%.

Clinical Characteristics	No PCa (n = 217)	Insignificant PCa (n = 62)	Clinically Significant PCa (n = 70)	p value	Total (n = 349)
Age, n (%)				0.4	
49 and below	4 (1.1)	1 (1.6)	0		5 (1.4)
50 to 59	41 (19)	9 (14.5)	7 (10)		57 (16)
60 to 69	95 (44)	29 (47)	34 (49)		158 (45)
70 to 79	74 (34)	21 (34)	26 (37)		121 (35)
80 and above	3 (1.4)	2 (3.2)	3 (4.3)		8 (2.3)
PSA (ng/ml), median (IQR)	5.1 (3.9-7.8)	4.6 (3.8-6.3)	5.3 (3.5-8.0)	0.3	5 (3.8-7.6)
Prostate volume (cc), median (IQR)	68 (48-92)	52 (36-66)	39 (30-60)	<0.001	58 (40-82)
PSA density (ng/ml/cc), median (IQR)	0.11 (0.08-0.16)	0.11 (0.08-0.17)	0.16 (0.10-0.25)	<0.001	0.11 (0.08-0.18)
cT category, n (%)				<0.001	
cTx	200 (92)	0	0		200 (57)
cT1c	16 (7.4)	56 (90)	66 (94)		138 (39)
cT2a	1 (0.5)	5 (8.1)	2 (2.9)		8 (2.3)
cT2b	0	0	1 (1.4)		1 (0.3)
cT2c	0	1 (1.6)	1 (1.4)		2 (0.6)
PSAD group, n (%)				<0.001	
1 (>0.3 ng/ml/cc)	14 (6.5)	4 (6.5)	12 (17.1)		30 (8.6)
2 (0.2-0.3 ng/ml/cc)	16 (7.4)	10 (16)	11 (16)		37 (10.6)
3 (0.15-0.2 ng/ml/cc)	34 (16)	4 (6.5)	16 (23)		54 (15)
4 (<0.15 ng/ml/cc)	153 (70)	44 (71)	31 (44)		228 (65)

Table 1: Clinical characteristics of patients with solely PIRADs 3 lesions on MRI in PURC Database.

	Total Prostate Cancer					Clinically Significant Prostate Cancer			
	N	Univariate Analysis		Multivariate Analysis		Univariate Analysis		Multivariate Analysis	
		HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
Age									
49 and below	5	Reference	-	NA		NA		NA	
50 to 59	57	1.56 (0.16 - 15.05)	0.7						
60 to 69	158	2.65 (0.29 - 24.28)	0.4						
70 to 79	121	2.54 (0.27 - 23.43)	0.4						
80 and above	8	6.67 (0.49 - 91.33)	0.2						
PSA (ng/ml)	349	0.99 (0.95 - 1.02)	0.5	NA		0.99 (0.95 - 1.02)	0.5	NA	
Prostate Volume (cc)	349	0.97 (0.97 - 0.98)	<0.001	NA		0.97 (0.96 - 0.98)	<0.001	NA	
PSAD group (ng/ml/cc)									
<0.15	228	Reference	-	Reference	-	Reference	-	Reference	-
0.15-0.2	54	1.20 (0.65 - 2.22)	0.6	1.20 (0.64 - 2.5)	0.6	2.68 (1.33 - 5.38)	<0.01	2.76 (1.35 - 5.63)	<0.01
0.2-0.3	37	2.68 (1.32 - 5.43)	<0.01	2.35 (1.14 - 4.86)	0.02	2.69 (1.21 - 5.98)	0.01	2.29 (1.01 - 5.22)	0.048
>0.3	30	2.33 (1.08 - 5.03)	0.03	2.05 (0.93 - 4.51)	0.07	4.24 (1.86 - 9.65)	0.001	3.73 (1.60 - 8.72)	<0.01
DRE									
Negative	204	Reference	-	Reference	-	Reference	-	Reference	-
Positive	23	2.75 (1.15 - 6.57)	0.02	2.61 (1.08 - 6.39)	0.03	2.99 (1.12 - 7.97)	0.03	2.95 (1.08 - 8.07)	0.03
Unknown	122	2.60 (1.63 - 4.15)	<0.001	2.41 (1.50 - 3.87)	<0.001	2.98 (1.69 - 5.24)	<0.001	2.76 (1.54 - 4.94)	0.001

Table 2: Univariate and multivariate logistic regression to identify predictors of any prostate cancer and clinically significant prostate cancer