INCORPORATING PROSTATE HEALTH INDEX DENSITY, MRI, AND PRIOR NEGATIVE BIOPSY STATUS TO IMPROVE THE DETECTION OF CLINICALLY SIGNIFICANT PROSTATE CANCER

Sasha C. Druskin, Jeffrey J. Tosoian, Allen Young, Sarah Collica, Arnav Srivastava, Kamyar Ghabili, Katarzyna J. Macura, H. Ballentine Carter, Alan W. Partin, Lori J. Sokoll, Ashley E. Ross, Christian P. Pavlovich

The James Buchanan Brady Urological Institute and Department of Urology at the Johns Hopkins University School of Medicine, Baltimore, MD, USA.

Introduction

•We determined the performance of Prostate Health Index (PHI) density (PHID) combined with MRI and prior negative biopsy (PNB) status for the diagnosis of clinically-significant prostate cancer (CSPCa).

Methods

•Patients without a prior diagnosis of PCa, with elevated PSA and a normal DRE who had PHI testing prospectively prior to prostate biopsy were included.
•PHID was calculated using prostate volume.
•Univariable and multivariable logistic regression modeling, along with receiver operating characteristic analysis, was used to determine the ability of serum biomarkers to predict CSPCa (Grade group (GG) ≥2 or GG1 PCa detected in >2 cores or >50% of any one core) on biopsy.
•Age, PNB status and PIRADS score were incorporated into the regression models.

Conclusions

•In this contemporary cohort of men undergoing prostate biopsy for the diagnosis of PCa, PHID outperformed PHI and other PSA-derivatives for the diagnosis of CSPCa. Incorporating age, PNB status, and PIRADS score led to even further gains in the diagnostic performance of PHID.
•Furthermore, PIRADS score was found to be complementary to PHID. Using 0.44 as a cutoff for PHID, 35.3% of unnecessary biopsies could have been avoided at the cost of missing 7.7% of CSPCa. Despite these encouraging results, prospective validation is needed.

Twitter: @SashaDruskinMD; @brady_urology
Facebook: Brady Urology at Johns Hopkins
Web: urology.jhu.edu | www.hopkinsmedicine.org/brady-urology-institute/

Results

•Of the 241 men who qualified for the study, 91 (37.8%) had CSPCa on biopsy.
•The median PHID was 0.74 (IQR 0.44-1.24); it was 1.18 (IQR 0.77-1.83) and 0.55 (IQR 0.38-0.89) in those with and without CSPCa on biopsy, respectively (p<0.0001).
•On univariable regression, age and PNB status were associated with CSPCa.
•Of the tested biomarkers, PHID demonstrated the highest discriminative ability for CSPCa (AUC 0.78 for the univariable model).
•That continued to be the case in multivariable regression models incorporating age and PNB status (AUC 0.82).
•At a threshold of 0.44, representing the 25th percentile of PHID in the cohort, PHID was 92.3% sensitive and 35.3% specific for CSPCa; the sensitivity/specificity was 93.0/32.4 and 97.4/29.1 for GG≥2 and GG≥3 disease, respectively.
•In the 104 men who had MRI, PIRADS score was complementary to PHID, with PIRADS score ≥3 or, if PIRADS score ≤2, PHID≥0.44 detecting 100% of CSPCa. For that subgroup, of the biomarkers tested, PHID (AUC 0.90) demonstrated the highest discriminative ability for CSPCa on multivariable regression incorporating age, PNB status and PIRADS score.

Table 1. Characteristics of the study cohort.

	Overall (n=241)	Clinically-significant PCa (n=91)	Negative or clinically-insignificant PCa (n=150)	P-value
Age (years), median (IQR)	65.0 (59.3-70.8)	67.0 (61.2-73.1)	63.3 (58.3-70.1)	0.015
African-American race, n (%)	28 (11.6)	14 (15.4)	14 (9.3)	0.2
Prior negative biopsy, n (%)	82 (34.0)	17 (18.7)	65 (43.3)	<0.0001
Time since prior negative biopsy (y), median (IQR)[A]	3.5 (2.0-7.3)	3.1 (1.9-6.5)	3.5 (2.1-7.3)	0.9
PSA (ng/mL), median (IQR)	7.0 (4.9-10.2)	6.9 (4.9-10.1)	7.1 (4.8-10.3)	0.8
%fPSA, median (IQR)	15.8 (12.0-22.6)	13.5 (9.8-17.5)	18.6 (13.7-24.3)	<0.0001
PHI, median (IQR)	38.0 (28.9-50.6)	46.7 (38.4-63.4)	32.5 (25.9-42.0)	<0.0001
Prostate volume (mL), median (IQR)	50.0 (37.32-70.0)	42.0 (29.0-58.0)	55.5 (41.0-80.0)	<0.0001
PSAD, median (IQR)	0.14 (0.096-0.21)	0.17 (0.12-0.26)	0.12 (0.079-0.18)	<0.0001
%fPSA*volume, median (IQR)	8.14 (4.36-14.16)	5.13 (3.26-8.52)	11.31 (6.00-16.52)	<0.0001
PHID, median (IQR)	0.74 (0.44-1.24)	1.18 (0.77-1.83)	0.55 (0.38-0.89)	<0.0001

A. Excludes 3 patients with a negative or insignificant biopsy and 1 patient with a significant biopsy for whom data is missing.

Table 2. Univariable logistic regression models for the prediction of clinically-significant prostate cancer on biopsy (n=241).

	Predictor	OR (95% CI)	P-value
Clinical Predictors	Age	1.04 (1.01-1.07)	0.020
	African-American race	1.77 (0.80-3.90)	0.2
	Prior negative biopsy	0.30 (0.16-0.56)	<0.001
	Time since prior negative biopsy	0.99 (0.85-1.16)	0.9
Biomarkers	PSA	1.03 (0.99-1.08)	0.2
	PSAD[A]	1.69 (1.30-2.20)	<0.001
	%fPSA	0.91 (0.88-0.95)	<0.001
	%fPSA*volume	0.90 (0.86-0.94)	<0.001
	PHI	1.05 (1.03-1.07)	<0.001
	PHID	5.15 (2.98-8.91)	<0.001

A. Odds ratio per unit change of 0.1

Table 3. Diagnostic performance of the 25th percentile cut-off of PHID in the cohort (0.44) for the prediction clinically-significant prostate cancer on prostate biopsy. All values are % (95% CI), unless otherwise specified.

Definition of clinically-significant cancer: primary definition (GG≥2 or GG1 in >2 cores or >50% of any one core)	
Prevalence, n (%)	91 (37.8)
Sensitivity	92.3 (84.8-96.9)
Specificity	35.3 (27.7-43.5)
PPV	46.4 (39.0-54.0)
NPV	88.3 (77.4-95.2)
Definition of clinically-significant cancer: GG≥2	
Prevalence, n (%)	71 (29.5)
Sensitivity	93.0 (84.3-97.7)
Specificity	32.4 (25.4-39.9)
PPV	36.5 (29.5-43.9)
NPV	91.7 (81.6-97.2)
Definition of clinically-significant cancer: GG≥3	
Prevalence, n (%)	38 (15.8)
Sensitivity	97.4 (86.2-99.9)
Specificity	29.1 (22.9-35.8)
PPV	20.4 (14.8-27.1)
NPV	98.3 (91.1-100.0)

GG=Grade group. PPV=Positive predictive value. NPV=Negative predictive value.

Figure 1: ROC analysis curves for the multivariable logistic regression models for the prediction of clinically-significant prostate cancer on biopsy, including the baseline model variables: age and prior negative biopsy status (n=241).

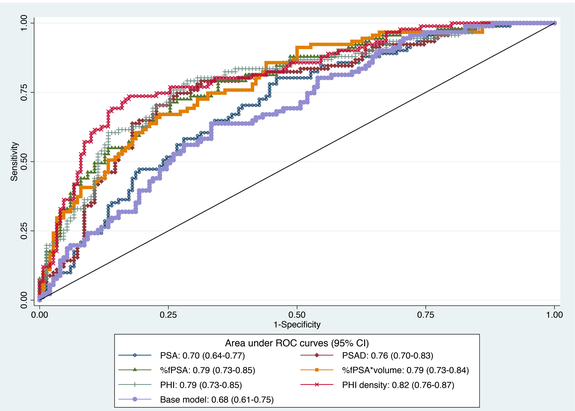


Figure 2. PHID values by PIRADS score (n=104 with MRI; n=137 without MRI). The short-dashed line indicates the PHID value of 0.44 (the 25th percentile of PHID for the cohort). The long-dashed line indicates the PHID value of 1.24 (the 75th percentile of PHID for the cohort). Xs represent a negative biopsy or clinically-insignificant prostate cancer. Red dots represent clinically-significant prostate cancer.

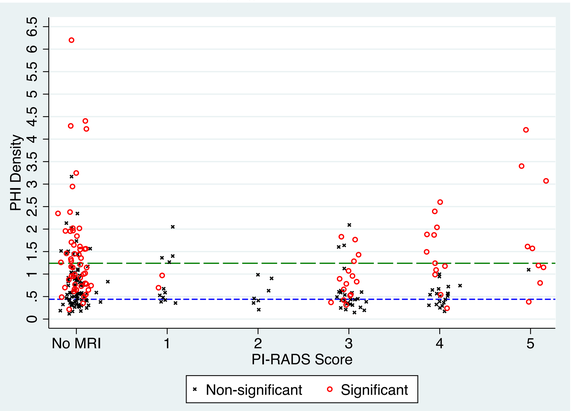
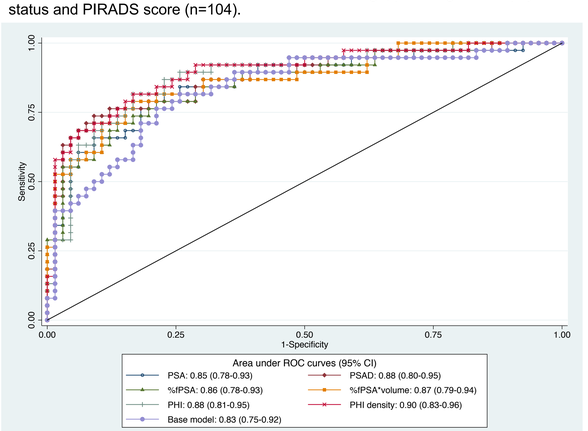


Figure 3: ROC analysis curves for multivariable logistic regression models for the prediction of clinically-significant prostate cancer on biopsy in the subgroup of men with mpMRI, including the baseline model variables: age, prior negative biopsy status and PIRADS score (n=104).



Supplementary Figure. PHID values by biopsy grade group (n=241). The short-dashed line indicates the PHID value of 0.44 (the 25th percentile of PHID for the cohort). The long-dashed line indicates the PHID value of 1.24 (the 75th percentile of PHID for the cohort). Xs represent a negative biopsy or clinically-insignificant prostate cancer. Red dots represent clinically-significant prostate cancer.