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


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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 G1/G2 PCa detected in >2 cores or >90% of any one core) on biopsy.
• Age, PNB status and PI-RADS 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 PI-RADS score led to even further gains in the diagnostic performance of PHID.
• Furthermore, PI-RADS 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.

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 1.16 (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 GG2g and GG2g3 disease, respectively.
• In the 104 men who had MRI, PI-RADS score was complementary to PHID, with PI-RADS score ≥3 or, if PI-RADS 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 PI-RADS score.

Table 1. Characteristics of the study cohort.

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

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

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: PI-RADS values by PI-RADS 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 PI-RADS score (n=104).

Supplementary Figure: PI-RADS 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.