PUBLISHED SCIENTIFIC EVIDENCE ON THE USE OF PROSTATE HEALTH INDEX 2019-2023

PROSTATE HEALTH INDEX (*phi*)

BECKMAN COULTER

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phi IS A RELIABLE MARKER FOR THE DETECTION OF CLINICALLY SIGNIFICANT PROSTATE CANCER

Int. J. Mol. Sci. 2020, 21, 1184

BEYOND PSA:
THE ROLE OF PROSTATE HEALTH INDEX (PHI)

Authors: Ferro M., De Cobelli O., Lucarelli G. et al.

Background

Widespread use of prostate specific antigen (PSA) in screening procedures allowed early identification of an increasing number of prostate cancers (PCas), mainly including indolent cancer. Availability of different therapeutic strategies which have a very different impact on the patient's quality of life suggested a strong need for tools able to identify clinically significant cancer at diagnosis. Multi-parametric magnetic resonance showed very good performance in pre-biopsy diagnosis. However, it is an expensive tool and requires an experienced radiologist. In this context, a simple blood-based test is worth investigating. In this context, researchers focused their attention on the development of a laboratory test able to minimize overdiagnosis without losing the identification of aggressive tumors.

Results

Recent literature data on PCa biomarkers revealed a clear tendency towards the use of panels of biomarkers or a combination of biomarkers and clinical variables. Phi, the 4Kscore, and Stockholm3 as circulating biomarkers and the Mi-prostate score, Exo DX Prostate, and Select MD-X as urinary biomarker-based tests have been developed. In this scenario, phi is worthy of attention as a noninvasive test significantly associated with aggressive PCa.

Conclusions

Literature data showed that phi had good diagnostic performance to identify clinically significant (cs) PCa, suggesting that it could be a useful tool for personalized treatment decision-making. In this review, phi potentialities, limitations, and comparisons with other blood- and urinary-based tests were explored.

Clin Chem Lab Med 2022; 60(8): 1261–1277

PROSTATE HEALTH INDEX (PHI) AS A RELIABLE BIOMARKER FOR PROSTATE CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

Authors: Agnello L., Vidali M., Giglio R.V. et al.

Objectives

Prostate cancer (PCa) represents the second most common solid cancer in men worldwide. In the last decades, the prostate health index (PHI) emerged as a reliable biomarker for detecting PCa and differentiating between non-aggressive and aggressive forms. However, before introducing it in clinical practice, more evidence is required. Thus, we performed a systematic review and meta-analysis for assessing the diagnostic performance of PHI for PCa and for detecting clinically significant PCa (csPCa).

Methods

Relevant publications were identified by a systematic literature search on PubMed and Web of Science from inception to January 11, 2022.

Results

Sixty studies, including 14,255 individuals, met the inclusion criteria for our meta-analysis. The pooled sensitivity and specificity of PHI for PCa detection was 0.791 (95%CI 0.739–0.834) and 0.625 (95%CI 0.560–0.686), respectively. The pooled sensitivity and specificity of PHI for csPCa detection was 0.874 (95%CI 0.803–0.923) and 0.569 (95%CI 0.458–0.674), respectively. Additionally, the diagnostic odds ratio was 6.302 and 9.206, respectively, for PCa and csPCa detection, suggesting moderate to good effectiveness of PHI as a diagnostic test.

Conclusions

PHI has a high accuracy for detecting PCa and discriminating between aggressive and non-aggressive PCa. Thus, it could be useful as a biomarker in predicting patients harbouring more aggressive cancer and guiding biopsy decisions.

Int. J. of Urol. 2021, Vol. 28, Issue 3, 315-325

DIAGNOSTIC PERFORMANCE OF PROSTATE CANCER ANTIGEN 3 AND THE PROSTATE HEALTH INDEX IN DETECTING OVERALL AND CLINICALLY SIGNIFICANT PROSTATE CANCER IN MEN AT FIRST BIOPSY: A META-ANALYSIS

Authors: Jia W., Wu B., Shao Y. et al.

Objective

To evaluate the diagnostic value of prostate cancer antigen 3 and the Prostate Health Index for the detection of overall and clinically significant prostate cancer at initial biopsy.

Methods

A search was conducted in the online databases PubMed, Embase and the Cochrane database, and relevant articles published up to 23 February 2020 were extracted.

Results

Twenty studies including 10 376 patients were included in the meta-analysis. The pooled sensitivity and specificity were 0.55 (95% confidence interval 0.53–0.57) and 0.74 (95% confidence interval 0.72–0.75) for prostate cancer antigen 3 and 0.88 (95% confidence interval 0.86–0.90) and 0.36 (95% confidence interval 0.34–0.38) for the Prostate Health Index. The area under the curve was 0.72 for prostate cancer antigen 3 and 0.76 for the Prostate Health Index. The combination of prostate cancer antigen 3 and the Prostate Health Index had a higher area under the curve (0.79) and diagnostic odds ratio (5.83) than the use of Prostate Health Index (area under the curve 0.75, diagnostic odds ratio 4.69) or prostate cancer antigen 3 (area under the curve 0.77, diagnostic odds ratio 4.84) alone. For clinically significant prostate cancer detection, the pooled sensitivity and specificity were 0.80 (95% confidence interval 0.76–0.84) and 0.53 (95% confidence interval 0.50–0.55), respectively, for prostate cancer antigen 3, and 0.77 (95% confidence interval 0.71–0.82) and 0.64 (95% confidence interval 0.61–0.67), respectively, for the Prostate Health Index. The area under the curve was 0.71 for prostate cancer antigen 3 and 0.77 for the Prostate Health Index.

Conclusion

Both the **Prostate Health Index and prostate cancer antigen 3 showed acceptable and similar results for the detection of overall and clinically significant prostate cancer at first biopsy.** A combination of these two diagnostic tests may be more helpful than the use of either test alone in prostate cancer management.

Investig Clin Urol. 2020, Nov; 61(6): 582–587.

CORRELATION BETWEEN GLEASON SCORE DISTRIBUTION AND PROSTATE HEALTH INDEX IN PATIENTS WITH PROSTATE-SPECIFIC ANTIGEN VALUES OF 2.5–10 NG/ML

Authors: Choi J., Kang M., Sun H.H. et al.

Purpose

To determine the clinical significance and correlation between the Prostate Health Index (PHI) and Gleason score in patients with a prostate-specific antigen (PSA) value of 2.5–10 ng/mL.

Materials and Methods

This retrospective analysis included 114 patients who underwent biopsy after completion of the PHI from November 2018 to July 2019. Various parameters such as PSA, PHI, PSA density, free PSA, p2PSA, and %free PSA were collected, and correlations with biopsy Gleason score and cancer detection rates were investigated.

Results

Baseline characteristics were comparable between PHI groups (0–26.9 [n=11], 27.0–35.9 [n=17], 36.0–54.9 [n=50], and ≥55.0 [n=36]). A total of 37 patients (32.5%) were diagnosed with prostate cancer, and 28 (24.6%) were diagnosed with clinically significant prostate cancer (CSPC, Gleason score ≥7) after prostate biopsy. The cancer detection rate gradually increased with a corresponding increase in the PHI (18%, 24%, 30%, and 44%, respectively). The same pattern was observed with detecting CSPC (0%, 18%, 26%, and 33%, respectively). There was no CSPC in the groups with PHI <27.0, and Gleason score 7 began to appear in groups with PHI ≥27.0. In particular, patients with Gleason score 8 and 9 were distributed only in the groups with PHI ≥36.0.

Conclusions

The diagnostic accuracy of detection of CSPC could be increased when prostate biopsy is performed in patients with a PHI ≥36.0. In this study, there was a clear Gleason score difference when the PHI cutoff value was set to 27.0 or 36.0.

J Korean Med Sci, 2018. 33(11):e94

DIAGNOSTIC PERFORMANCE OF %[-2]PROPSA AND PROSTATE HEALTH INDEX FOR PROSTATE CANCER: PROSPECTIVE, MULTI-INSTITUTIONAL STUDY

Authors: Park H, Lee SW, Song G, Kang TW, et al.

Objectives

To evaluate the clinical performance of [-2]proPSA (p2PSA) and its derivatives in predicting the presence and aggressiveness of prostate cancer (PCa) in Korean men

Methods

A total of 246 men with total prostate-specific antigen (tPSA) ≥ 3.5 ng/mL who underwent their first prostate biopsy were included in this prospective, multicenter, observational study. Diagnostic accuracy of tPSA, free-to-total PSA ratio (%fPSA), p2PSA, %p2PSA, and the Beckman Coulter prostate health index (PHI) was assessed by receiver operating characteristic curve analyses and logistic regression analyses.

Results

Overall, PCa was detected in 125 (50.8%) subjects. In men with tPSA 3.5–10 ng/mL, the detection rate of PCa was 39.4% (61/155). In this group, PHI and %p2PSA were the most accurate predictors of PCa and significantly outperformed tPSA and %fPSA; area under the curve for tPSA, %fPSA, %p2PSA, and PHI was 0.56, 0.69, 0.74, and 0.76, respectively. PHI was also the strongest predictor of PCa with Gleason score ≥ 7.

Conclusion

This study demonstrates the superior clinical performance of %p2PSA and **PHI in predicting the presence and aggressiveness of PCa in Korean men**. The %p2PSA and PHI appear to improve detection of PCa and provide prognostic information.

BMC Urology, 2021;21:131

USEFULNESS OF THE PROSTATE HEALTH INDEX IN PREDICTING THE PRESENCE AND AGGRESSIVENESS OF PROSTATE CANCER AMONG KOREAN MEN: A PROSPECTIVE OBSERVATIONAL STUDY

Authors: Kim JY, Yu JH, Sung LH, Cho DY, Kim HJ and Yoo SJ.

Objectives

To evaluate the usefulness of the Beckman Coulter prostate health index (PHI) and to compare it with total prostate-specific antigen (PSA) levels and related derivatives in predicting the presence and aggressiveness of prostate cancer (PCa) in the Korean population

Methods

A total of 140 men who underwent their first prostate biopsy for suspected PCa were included in this prospective observational study. The diagnostic performance of total PSA, free PSA, %free PSA, [–2] proPSA (p2PSA), %p2PSA, and PHI in detecting and predicting the aggressiveness of PCa was estimated using the receiver operating characteristic curve (ROC) and logistic multivariate regression analyses.

Results

Of 140 patients, PCa was detected in 63 (45%) of participants, and 48 (76.2%) of them had significant cancer with a Gleason score (GS) ≥ 7. In the whole group, the area under the curve (AUC) for ROC analysis of tPSA, free PSA, %fPSA, p2PSA, %p2PSA, and PHI were 0.63, 0.57, 0.69, 0.69, 0.72, and 0.76, respectively, and the AUC was significantly greater in the PHI group than in the tPSA group ($p = 0.005$). For PCa with GS ≥ 7, the AUCs for tPSA, free PSA, %fPSA, p2PSA, %p2PSA, and PHI were 0.62, 0.58, 0.41, 0.79, 0.86, and 0.87, respectively, and the AUC was significantly greater in the PHI group than in the tPSA group ($p < 0.001$). In the subgroup with tPSA 4–10 ng/mL, both %p2PSA and PHI were strong independent predictors for PCa ($p = 0.007$, $p = 0.006$) and significantly improved the predictive accuracy of a base multivariable model, including age, tPSA, fPSA and %fPSA, using multivariate logistic regression analysis ($p = 0.054$, $p = 0.048$). Additionally, at a cutoff PHI value > 33.4, 22.9% (32/140) of biopsies could be avoided without missing any cases of aggressive cancer.

Conclusions

This study shows that **%p2PSA and PHI are superior to total PSA and %fPSA in predicting the presence and aggressiveness (GS ≥ 7) of PCa among Korean men.** Using PHI, a significant proportion of unnecessary biopsies can be avoided.

phi PREDICTS THE INITIAL AND REPEATED BIOPSY OUTCOME

Journal of Chinese Medical Association. (2019) 82: 772–777

PROSTATE HEALTH INDEX OUTPERFORMS OTHER PSA DERIVATIVES IN PREDICTING A POSITIVE BIOPSY IN MEN WITH TPSA <10 NG/ML: LARGEST PROSPECTIVE COHORT IN TAIWAN

Authors: Fan Y-H., Pan P-H., Lin T-P. et al.

Background

Few prospective studies have focused on the performance of the Prostate Health Index (PHI) in Asian populations. Therefore, we aimed to evaluate the performance of the PHI in predicting prostate cancer (PCa) compared with standard prostatespecific antigen (PSA) tests.

Methods

We prospectively enrolled patients with suspected PCa with a total PSA (tPSA) level 4 to 10 ng/mL or tPSA <4 ng/mL and a suspicious digital rectal examination between February 2017 and September 2018. All of the patients underwent a 12-core transrectal ultrasound-guided prostate biopsy. Prebiopsy blood samples were analyzed for tPSA, free PSA (fPSA), percentage of fPSA (%fPSA), [-2]proPSA (p2PSA), and percentage of p2PSA (%p2PSA). The PHI was calculated as (p2PSA/fPSA) × √tPSA. The areas under the receiver operating characteristic curve (AUCs) were estimated for the PSA derivatives in addition to their specificities at a prespecified sensitivity of 90%.

Results

Of the 307 enrolled patients, 95 (30.9%) had PCa on biopsy. Excluding fPSA, all of the PSA derivatives were significantly different between the positive and negative biopsy groups. Of the various derivatives, the PHI (AUC: 0.783) showed the best performance in predicting the results of the initial biopsy compared with tPSA (AUC: 0.611). At a sensitivity of 90%, the PHI had the best specificity of 46.7% compared with 23.2% for tPSA. Using a PHI cutoff value of 35.15 for biopsy, 108 (35.2%) patients could have avoided undergoing a biopsy. To detect Gleason score ≥ 7 disease at 90% sensitivity, the threshold for PHI was 36.96 with a specificity of 52.1%.

Conclusion

PHI was the best biomarker among the PSA derivatives in predicting PCa at biopsy in men with tPSA < 10 ng/mL. The risk of a Gleason score ≥ 7 increased with increasing PHI.

Prostate Cancer Prostatic Dis 25, 684–689 (2022)

INITIAL PROSTATE HEALTH INDEX (PHI) AND PHI DENSITY PREDICTS FUTURE RISK OF CLINICALLY SIGNIFICANT PROSTATE CANCER IN MEN WITH INITIAL NEGATIVE PROSTATE BIOPSY: A 6-YEAR FOLLOW-UP STUDY

Authors: Liu A.Q., Remmers S., Lau SY. et al.

Background

Men with elevated prostate-specific antigen (PSA) and initial negative prostate biopsy may have risk of prostate cancer (PCa) in the future. The role of Prostate Health Index (phi) in determining future PCa risk has not been studied before. This study aims to investigate the role of initial phi and phi density in predicting future PCa risk in men with initial negative biopsy.

Methods

Five hundred sixty nine men with PSA 4–10 ng/mL were recruited between 2008 and 2015 for prostate biopsy with prior phi. Electronic clinical record of men with initial negative biopsy was reviewed. Patients and follow-up doctors were blinded to phi. Kaplan–Meier curves were used to analyze the PCa-free survival in different baseline phi and phi density groups.

Results

Four hundred sixty-one men with complete follow-up data were included. Median follow-up is 77 months. PCa and HGPCa was diagnosed in 8.2% (38/461) and 4.8% (22/461) of cohort respectively. A higher baseline phi value was associated with PCa ($p = 0.003$) and HGPCa ($p < 0.001$). HGPCa was diagnosed in 0.6% (1/163) of phi < 25, 4.6% (9/195) of phi 25–34.9, and 11.7% (12/103) of phi ≥ 35 ($p < 0.001$). HGPCa was diagnosed in 0% (0/109) and 21.0% (13/62) with phi density of <0.4 and ≥1.2, respectively, ($p < 0.001$). Kaplan–Meier curves showed phi and phi density predicted PCa and HGPCa diagnoses (log-rank test, all $p \leq 0.002$).

Conclusions

Initial phi or phi density predicted 6-year risk of PCa in men with initial negative prostate biopsy. Men with higher phi (≥35) or phi density (≥1.2) need closer follow-up and repeated investigation, while men with lower phi (<25) or phi density (<0.4) could have less frequent follow-up.

phi PREDICTS THE INITIAL AND REPEATED BIOPSY OUTCOME

Ferro, M., et al., Beyond PSA: The Role of Prostate Health Index (phi).
Int J Mol Sci, 2020. 21(4):

"On this basis, since 2015, phi was recommended by the European Association of Urology to reduce the number of unnecessary prostate biopsies in PSA-tested men, to improve prediction of csPCa, in men with a PSA between 4–10 ng /mL and between 2–10 ng /mL, and phi also has a role in monitoring men under active surveillance"

phi and mpMRI: A COMBINATORIAL USAGE IN THE IDENTIFICATION OF CLINICALLY SIGNIFICANT PROSTATE CANCER

Cancers 2022, 14(17), 4174

CLINICAL UTILITY OF PROSTATE HEALTH INDEX FOR DIAGNOSIS OF PROSTATE CANCER IN PATIENTS WITH PI-RADS 3 LESIONS

Authors: Lee C-U., Lee S-M., Chung J-H. et al.

Simple Summary

Multi-parametric magnetic resonance imaging (mpMRI) is regarded as an essential tool for identifying prostate cancer (PCa) in suspected cases. However, unnecessary biopsies continue to be performed in real clinics, especially for prostate imaging reporting and data system version 2 (PI-RADS v2) score-3 lesions, corresponding to the "gray zone". To aid the diagnosis of PCa, as well as of clinically significant PCa (csPCa), in patients with PI-RADSv2 score-3 lesions, we evaluated the clinical utility of the prostate health index (PHI). When a biopsy was restricted to those patients with PI-RADSv2 score-3 lesions and a PHI of ≥30, 34.4% of unnecessary biopsies could be avoided at the cost of missing 8.3% of overall PCa cases. However, there were no cases of missed csPCa diagnosis. The combination of PHI and PI-RADSv2 score-3 lesions offered higher accuracy in the diagnosis of PCa as well as of csPCa.

The risk of prostate cancer (PCa) in prostate imaging reporting and data system version 2 (PI-RADSv2) score-3 lesions is equivocal; it is regarded as an intermediate status of presented PCa. In this study, we evaluated the clinical utility of the prostate health index (PHI) for the diagnosis of PCa and clinically significant PCa (csPCa) in patients with PI-RADSv2 score-3 lesions. The study cohort included patients who underwent a transrectal ultrasound (TRUS)-guided, cognitive-targeted biopsy for PI-RADSv2 score-3 lesions between November 2018 and April 2021. Before prostate biopsy, the prostate-specific antigen (PSA) derivatives, such as total PSA (tPSA), [-2] proPSA (p2PSA) and free PSA (fPSA) were determined. The calculation equation of PHI is as follows: [(p2PSA/fPSA) × tPSA ½]. Using a receiver operating characteristic (ROC) curve analysis, the values of PSA derivatives measured by the area under the ROC curve (AUC) were compared. For this study, csPCa was defined as Gleason grade 2 or higher. Of the 392 patients with PI-RADSv2 score-3 lesions, PCa was confirmed in 121 (30.9%) patients, including 59 (15.1%) confirmed to have csPCa. Of all the PSA derivatives, PHI and PSA density (PSAD) showed better performance in predicting overall PCa and csPCa, compared with PSA (all $p < 0.05$). The AUC of the PHI for predicting overall PCa and csPCa were 0.807 (95% confidence interval (CI): 0.710–0.906, $p = 0.001$) and 0.819 (95% CI: 0.723–0.922, $p < 0.001$), respectively.

By the threshold of 30, PHI was 91.7% sensitive and 46.1% specific for overall PCa, and was 100% sensitive for csPCa. Using 30 as a threshold for PHI, 34.4% of unnecessary biopsies could have been avoided, at the cost of 8.3% of overall PCa, but would include all csPCa.

Cancers 2021, 13, 4723

PROSTATE HEALTH INDEX AND MULTIPARAMETRIC MRI: PARTNERS IN CRIME FIGHTING OVERDIAGNOSIS AND OVERTREATMENT IN PROSTATE CANCER

Authors: Ferro M., Crocetto F.,Bruzzese D. et al.

Simple Summary

In the last decades, the widespread use of PSA as the standard tool for prostate cancer diagnosis led to a high rate of overdiagnosis and overtreatment. More recently, ultiparametric magnetic resonance imaging (mpMRI) became part of the diagnostic pathway, and several next-generation PSA-based tests (PHI, PHI density, 4Kscore, STHLM3) have been proposed. The multivariable approach promises to help with a better stratification of PCa patients at initial diagnosis. In this study, we evaluated the performance of the prostate health index (PHI) and mpMRI for the prediction of positive biopsy and of high-grade PCa at radical prostatectomy (RP). Our findings suggested that PHI had a better ability than mpMRI to predict positive biopsy, whereas a comparable performance in the identification of pathological aggressive PCa was pointed out. Notably, PHI and PHI density might represent useful biomarkers to recognize high-grade PCa in patients with low or uncertain PI-RADS scores on mpMRI.

Widespread use of PSA as the standard tool for prostate cancer (PCa) diagnosis led to a high rate of overdiagnosis and overtreatment. In this study, we evaluated the performance of the prostate health index (PHI) and multiparametric magnetic resonance imaging (mpMRI) for the prediction of positive biopsy and of high-grade PCa at radical prostatectomy (RP). To this end, we prospectively enrolled 196 biopsy-naïve patients who underwent mpMRI. A subgroup of 116 subjects with biopsy proven PCa underwent surgery. We found that PHI significantly outperformed both PI-RADS score (difference in AUC: 0.14; $p < 0.001$) and PHI density (difference in AUC: 0.08; $p = 0.002$) in the ability to predict positive biopsy with a cut-off value of 42.7 as the best threshold. Conversely, comparing the performance in the identification of clinically significant prostate cancer (csPCa) at RP, we found that PHI > 61.68 and PI-RADS score > 4 were able to identify csPCa (Gleason score > 7 (3 + 4)) both alone and added to a base model including age, PSA, fPSA-to-tPSA ratio and prostate volume.

In conclusion, PHI had a better ability than PI-RADS score to predict positive biopsy, whereas it had a comparable performance in the identification of pathological csPCa.

Investig Clin Urol, 2022;63:631-638

THE PROSTATE HEALTH INDEX AND MULTI-PARAMETRIC MRI IMPROVE DIAGNOSTIC ACCURACY OF DETECTING PROSTATE CANCER IN ASIAN POPULATIONS

Authors: Ye C., Ho J.N., Kim D.H., Song S.H., et al.

Objectives

To evaluate the effectiveness of the Prostate Health Index (PHI) and prostate multi-parametric magnetic resonance imaging (mpMRI) in predicting prostate cancer (PCa) and clinically significant prostate cancer (csPCa) during initial prostate biopsy.

Methods

In total, 343 patients underwent initial prostate biopsy and were screened by use of PHI and prostate specific antigen (PSA) levels between April 2019 and July 2021. A subgroup of 232 patients also underwent prostate mpMRI. Logistic regression analysis was performed to evaluate the accuracies of PSA, PHI, and mpMRI as predictors of PCa or csPCa. These predictive accuracies were quantified by using the area under the receiver operating characteristic curve. The different predictive models were compared using the DeLong test.

Results

Logistic regression showed that age, PSA, PHI, and prostate volume were significant predictors of both PCa and csPCa. In the mpMRI subgroup, age, PSA level, PHI, prostate volume, and mpMRI were predictors of both PCa and csPCa. The PHI (area under the curve [AUC]=0.693) was superior to the PSA level (AUC=0.615) as a predictor of PCa (p=0.038). Combining PHI and mpMRI showed the most accurate prediction of both PCa and csPCa (AUC=0.833, 0.881, respectively).

Conclusions

The most accurate prediction of both PCa and csPCa can be performed by combining PHI and mpMRI. In the absence of mpMRI, PHI is superior to PSA alone as a predictor of PCa, and adding PHI to PSA can increase the detection rate of both PCa and csPCa.

Scientific Reports, 2021, 11:1286

THE PROSTATE HEALTH INDEX AIDS MULTI-PARAMETRIC MRI IN DIAGNOSING SIGNIFICANT PROSTATE CANCER

Authors: Fan Y-H., Pan P-H., Cheng W-M. et al.

To evaluate the performance of the Prostate Health Index (PHI) in magnetic resonance imaging-transrectal ultrasound (MRI-TRUS) fusion prostate biopsy for the detection of clinically significant prostate cancer (csPCa). We prospectively enrolled 164 patients with at least one Prostate Imaging Reporting and Data System version 2 (PI-RADS v2) ≥ 3 lesions who underwent MRI-TRUS fusion prostate biopsy. Of the PSA-derived biomarkers, the PHI had the best performance in predicting csPCa (AUC 0.792, CI 0.707–0.877) in patients with PI-RADS 4/5 lesions. Furthermore, the predictive power of PHI was even higher in the patients with PI-RADS 3 lesions (AUC 0.884, CI 0.792–0.976). To minimize missing csPCa, we used a PHI cutoff of 27 and 7.4% of patients with PI-RADS 4/5 lesions could have avoided a biopsy. At this level, 2.0% of cases with csPCa would have been missed, with sensitivity and NPV rates of 98.0% and 87.5%, respectively. However, the subgroup of PI-RADS 3 was too small to define the optimal PHI cutoff.

PHI was the best PSA-derived biomarker to predict csPCa in MRI-TRUS fusion prostate biopsies in men with PI-RADS ≥ 3 lesions, especially for the patients with PI-RADS 3 lesions who gained the most value.

Clinical Genitourinary cancer, 2022, Vol 20, Issue 5

A COMBINATORIAL NEURAL NETWORK ANALYSIS REVEALS A SYNERGISTIC BEHAVIOUR OF MULTIPARAMETRIC MAGNETIC RESONANCE AND PROSTATE HEALTH INDEX IN THE IDENTIFICATION OF CLINICALLY SIGNIFICANT PROSTATE CANCER

Authors: Gentile F., La Civita E., Della Ventura B. et al.

Background

The widespread use of prostate specific antigen (PSA) caused high rate of overdiagnosis. Overdiagnosis leads to unnecessary definitive treatments of prostate cancer (PCa) with detrimental side effects, such as erectile dysfunction and incontinence. The aim of this study was to evaluate the feasibility of an artificial neural network-based approach to develop a combinatorial model including prostate health index (PHI) and multiparametric magnetic resonance (mpMRI) to recognize clinically significant PCa at initial diagnosis.

Methods

To this aim we prospectively enrolled 177 PCa patients who underwent radical prostatectomy and had received PHI tests and mpMRI before surgery. We used artificial neural network to develop models that can identify aggressive PCa efficiently. The model receives as an input PHI plus PI-RADS score.

Results

The output of the model is an estimate of the presence of a low or high Gleason score. After training on a dataset of 135 samples and optimization of the variables, the model achieved values of sensitivity as high as 80% and 68% specificity.

Conclusions

Our preliminary study suggests that combining mpMRI and PHI may help to better estimate the risk category of PCa at initial diagnosis, allowing a personalized treatment approach. The efficiency of the method can be improved even further by training the model on larger datasets.

Life 2021, 11, 324.

PROSTATE CANCER DIAGNOSTIC ALGORITHM AS A "ROAD MAP" FROM THE FIRST STRATIFICATION OF THE PATIENT TO THE FINAL TREATMENT DECISION

Authors: Sedláčková H., Dolejšová O., Hora M. et al.

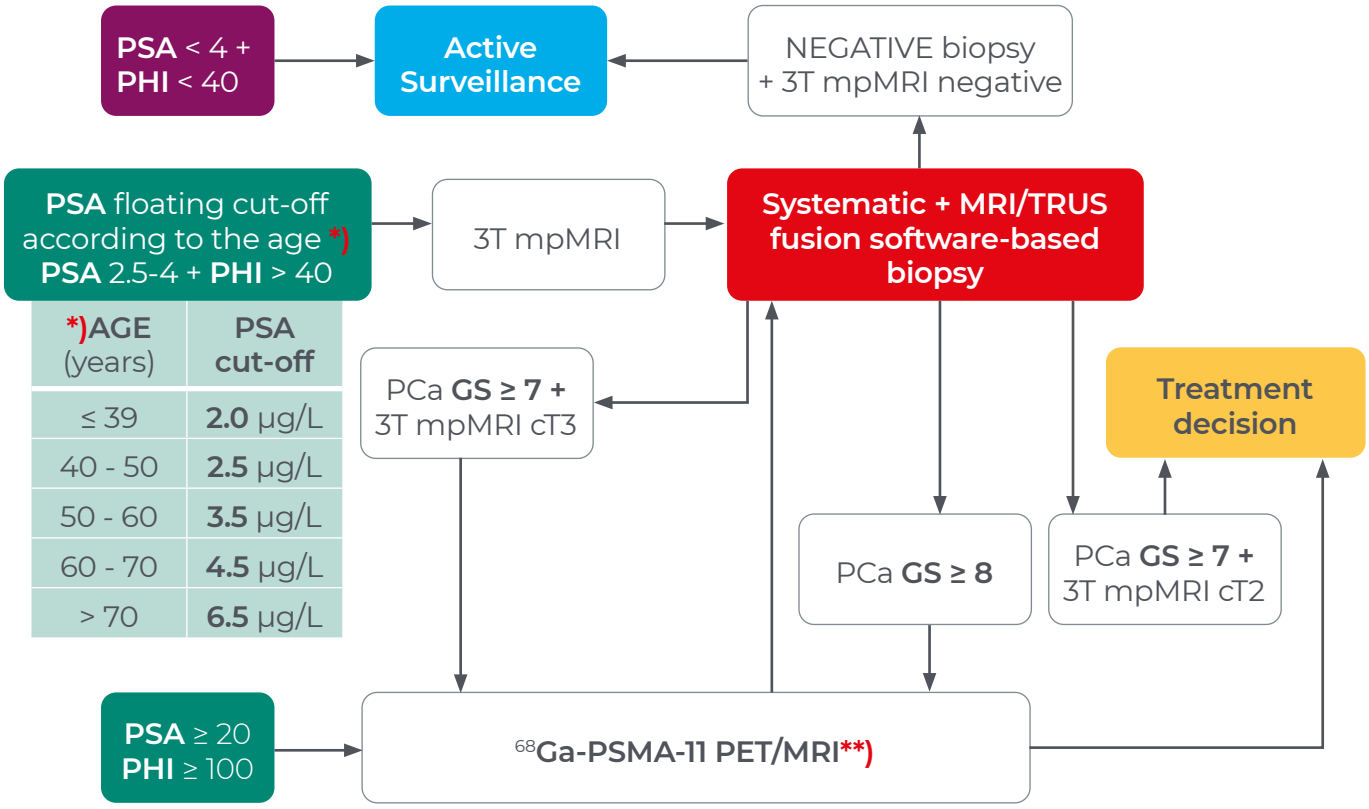
The diagnostics of prostate cancer are currently based on three pillars: prostate biomarker panel, imaging techniques, and histological verification. This paper presents a diagnostic algorithm that can serve as a "road map": from initial patient stratification to the final decision regarding treatment. The algorithm is based on a review of the current literature combined with our own experience. Diagnostic algorithms are a feature of an advanced healthcare system in which all steps are consciously coordinated and optimized to ensure the proper individualization of the treatment process. The prostate cancer diagnostic algorithm was created using the prostate specific antigen and in particular the Prostate Health Index in the first line of patient stratification. It then continued on the diagnostic pathway via imaging techniques, biopsy, or active surveillance, and then on to the treatment decision itself.

In conclusion, the prostate cancer diagnostic algorithm presented here is a functional tool for initial patient stratification, comprehensive staging, and aggressiveness assessment. Above all, emphasis is placed on the use of the Prostate Health Index (PHI) in the first stratification of the patients as a predictor of aggressiveness and clinical stage of prostrate cancer (PCa). The inclusion of PHI in the algorithm significantly increases the accuracy and speed of the diagnostic procedure and allows to choose the optimal pathway just from the beginning. The use of advanced diagnostic techniques allows us to move towards to a more advanced level of cancer care. This diagnostics algorithm has become a standard of care in our hospital. The algorithm is continuously validated and modified based on our results.

Sedláčková H. et al. Prostate Cancer Diagnostic Algorithm as a "Road Map" from the First Stratification of the Patient to the Final Treatment Decision. Life 2021, 11, 324:

Prostate cancer diagnostic algorithm:

The diagnostic algorithm for suspected prostrate cancer at University Hospital in Pilsen



**)^{68}Ga-PSMA-11 PET/MRI is currently prefered in the Hospital, when PSMA PET is not available ^{18}F-choline PET/MRI is recommended

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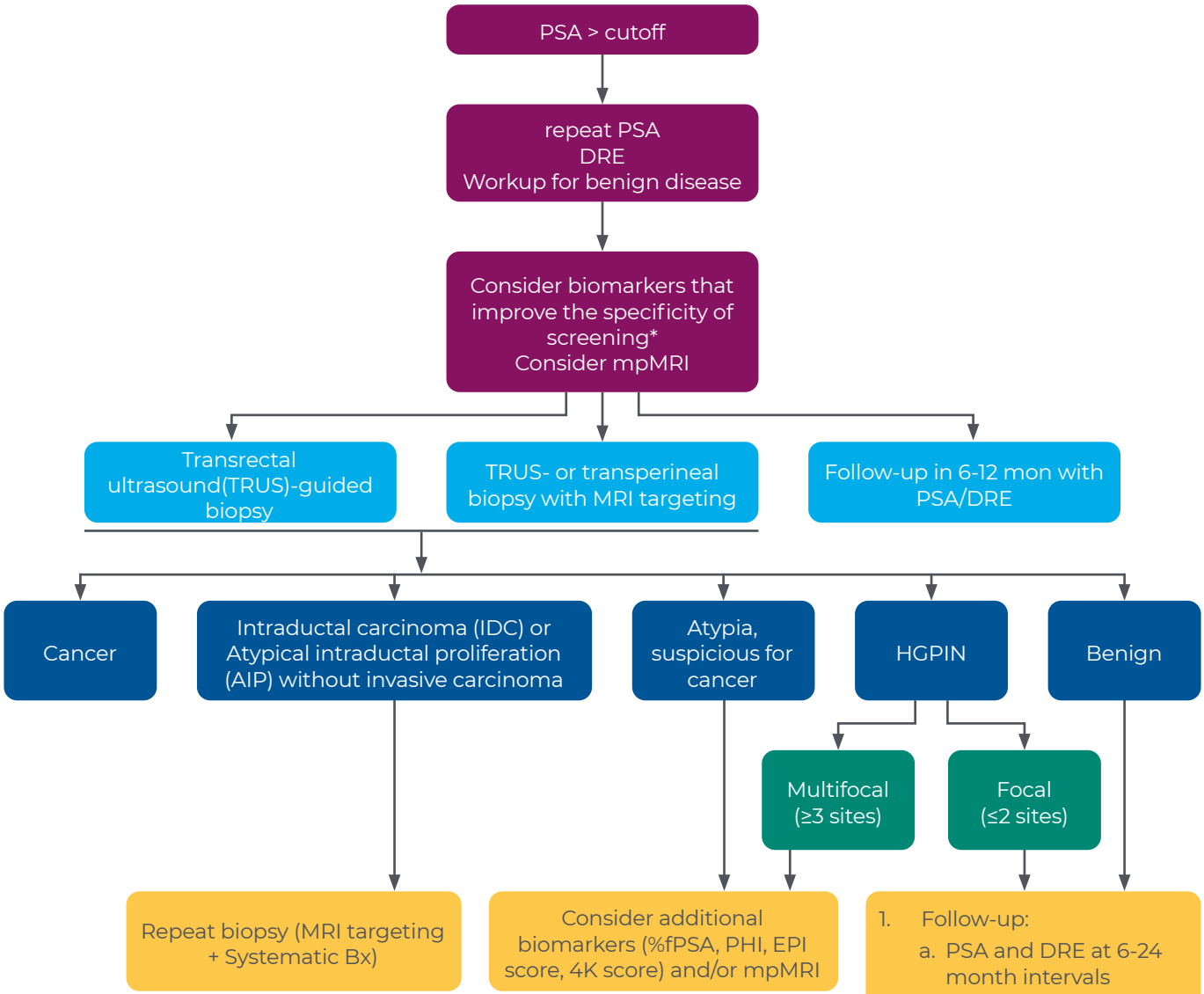
GS: Glisson score
mpMRI: multiparametric magnetic resonance imaging
PSMA: prostate-specific membrane antigen
Ga-PSMA: gallium-68 prostate-specific membrane antigen
PET: positron emission tomography

Prostate cancer practice guidelines published by the Korean Urological Oncological Society (2020)



*Biomarkers that can improve the specificity of prostate cancer diagnosis are being used clinically, but their clinical application in Korea is still limited. Even in the NCCN guidelines, it is currently not recommended to use commercially available new biomarkers as first-line screening tests. However, it can be used for the purpose of additional evaluation of the risk in some of the patients who need to consider prostate biopsy based on the PSA level. Free PSA may improve cancer detection. PHI, SelectMDx, 4Kscore, and ExoDx provide additional information about the likelihood of high-risk prostate cancer (Gleason score ≥3, Grade group 2 or greater). The PCA score provides potential information in the case of a negative previous biopsy. Since the predictive power of biochemical markers and MRI has not been compared, the effectiveness of the combination of these two methods has not yet been elucidated.

(Prostate cancer practice guidelines published by The Korean Urological Oncology Society, 2020)

BMC Urol . 2021 Nov 20;21(1):161

COMBINING PROSTATE HEALTH INDEX AND MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING IN ESTIMATING THE HISTOLOGICAL DIAMETER OF PROSTATE CANCER

Authors: Hsieh P-H., Li T., Lin W-C. et al.

Background

Although multiparametric magnetic resonance imaging (mpMRI) is widely used to assess the volume of prostate cancer, it often underestimates the histological tumor boundary. The aim of this study was to evaluate the feasibility of combining prostate health index (PHI) and mpMRI to estimate the histological tumor diameter and determine the safety margin during treatment of prostate cancer.

Methods

We retrospectively enrolled 72 prostate cancer patients who underwent radical prostatectomy and had received PHI tests and mpMRI before surgery. We compared the discrepancy between histological and radiological tumor diameter stratified by Prostate Imaging-Reporting and Data System (PI-RADS) score, and then assessed the influence of PHI on the discrepancy between low PI-RADS (2 or 3) and high PI-RADS (4 or 5) groups.

Results

The mean radiological and histological tumor diameters were 1.60 cm and 2.13 cm, respectively. The median discrepancy between radiological and histological tumor diameter of PI-RADS 4 or 5 lesions was significantly greater than that of PI-RADS 2 or 3 lesions (0.50 cm, IQR (0.00-0.90) vs. 0.00 cm, IQR (-0.10-0.20), p = 0.02). In the low PI-RADS group, the upper limit of the discrepancy was 0.2 cm; so the safety margin could be set at 0.1 cm. In the high PI-RADS group, the upper limits of the discrepancy were 1.2, 1.6, and 2.2 cm in men with PHI < 30, 30-60, and > 60; so the safety margin could be set at 0.6, 0.8, and 1.1 cm, respectively.

Conclusions

Radiological tumor diameter on mpMRI often underestimated the histological tumor diameter, especially for PI-RADS 4 or 5 lesions. **Combining mpMRI and PHI may help to better estimate the histological tumor diameter.**

World J Urol 39, 1889–1895 (2021)

THE PREDICTIVE VALUE OF THE PROSTATE HEALTH INDEX VS. MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING FOR PROSTATE CANCER DIAGNOSIS IN PROSTATE BIOPSY

Authors: Stejskal J., Adamcová V., Zálesk M. et al.

Purpose

To compare the ability of Prostate Health Index (PHI) to diagnose csPCa, with that of total PSA, PSA density (PSAD) and the multiparametric magnetic resonance (mpMRI) of the prostate.

Methods

We analysed a group of 395 men planned for a prostate biopsy who underwent a mpMRI of the prostate evaluated using the PIRADS v1 criteria. All patients had their PHI measured before prostate biopsy. In patients with an mpMRI suspicious lesions, an mpMRI/ultrasound software fusion-guided biopsy was performed first, with 12 core systematic biopsy performed in all patients. A ROC analysis was performed for PCa detection for total PSA, PSAD, PIRADS score and PHI; with an AUC curve calculated for all criteria and a combination of PIRADS score and PHI. Subsequent sub-analyses included patients undergoing first and repeat biopsy.

Results

The AUC for predicting the presence of csPCa in all patients was 59.5 for total PSA, 69.7 for PHI, 64.9 for PSAD and 62.5 for PIRADS. In biopsy naive patients it was 61.6 for total PSA, 68.9 for PHI, 64.6 for PSAD and 63.1 for PIRADS. In patients with previous negative biopsy the AUC for total PSA, PHI, PSAD and PIRADS was 55.4, 71.2, 64.4 and 69.3, respectively. Adding of PHI to PIRADS increased significantly ($p = 0.007$) the accuracy for prediction of csPCa.

Conclusions

Prostate Health Index could serve as a tool in predicting csPCa. When compared to the mpMRI, it shows comparable results. The **PHI** cannot, however, help us guide prostate biopsies in any way, and its **main use may**, therefore, **be in pre-MRI or pre-biopsy triage.**

World J Urol. 2020 May;38(5):1207-1214

COMBINING PROSTATE HEALTH INDEX AND MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING IN THE DIAGNOSIS OF CLINICALLY SIGNIFICANT PROSTATE CANCER IN AN ASIAN POPULATION

Authors: Hsieh P-F., Li W-J., Lin W-C. et al.

Objective

To evaluate the practicability of combining prostate health index (PHI) and multiparametric magnetic resonance imaging (mpMRI) for the detection of clinically significant prostate cancer (csPC) in an Asian population.

Patients and methods

We prospectively enrolled patients who underwent prostate biopsy due to elevated serum prostate-specific antigen (PSA > 4 ng/mL) and/or abnormal digital rectal examination in a tertiary referral center. Before prostate biopsy, the serum samples were tested for PSA, free PSA, and p2PSA to calculate PHI. Besides, mpMRI was performed using a 3-T scanner and reported in the Prostate Imaging Reporting and Data System version 2 (PI-RADS v2). The diagnostic performance of PHI, mpMRI, and combination of both was assessed.

Result

Among 102 subjects, 39 (38.2%) were diagnosed with PC, including 24 (23.5%) with csPC (Gleason ≥ 7). By the threshold of PI-RADS ≥ 3, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) to predict csPC were 100%, 44.9%, 35.8%, and 100%, respectively. By the threshold of PHI ≥ 30, the sensitivity, specificity, PPV, and NPV to predict csPC were 91.7%, 43.6%, 33.3%, and 94.4%, respectively. The area under the receiver operator characteristic curve of combining PHI and mpMRI was greater than that of PHI alone (0.873 vs. 0.735, p = 0.002) and mpMRI alone (0.873 vs. 0.830, p = 0.035). If biopsy was restricted to patients with PI-RADS 5 as well as PI-RADS 3 or 4 and PHI ≥ 30, 50% of biopsy could be avoided with one csPC patient being missed.

Conclusion

The combination of PHI and mpMRI had higher accuracy for detection of csPC compared with PHI or mpMRI alone in an Asian population.

phi PREDICTS PROSTATE CANCER DETECTION AFTER RADICAL PROSTATECTOMY

BMC Urology (2020) 20:144

PREOPERATIVE PROSTATE HEALTH INDEX PREDICTS ADVERSE PATHOLOGY AND GLEASON SCORE UPGRADING AFTER RADICAL PROSTATECTOMY FOR PROSTATE CANCER

Authors: Novak V., Vesely S., Luksanová H. et al.

Background

We aimed to explore the utility of prostate specific antigen (PSA) isoform [− 2] proPSA and its derivatives for prediction of pathological outcome after radical prostatectomy (RP).

Methods

Preoperative blood samples were prospectively and consecutivelyanalyzed from 472 patients treated with RP for clinically localized prostate cancerat four medical centers. Measured parameters were PSA, free PSA (fPSA), fPSA/PSA ratio, [− 2] proPSA (p2PSA), p2PSA/fPSA ratio and Prostate Health Index (PHI)(p2PSA/fPSA)*√PSA]. Logistic regression models were fitted to determine the accuracy of markers for prediction of pathological Gleason score (GS) ≥7, Gleason score upgrading, extracapsular extension of the tumor (pT3) and the presence of positive surgical margin (PSM). The accuracy of predictive models was compared using area under the receiver operating curve (AUC).

Results

Of 472 patients undergoing RP, 339 (72%) were found to have pathologic GS ≥ 7, out of them 178 (53%) experienced an upgrade from their preoperative GS = 6. The findings of pT3 and PSM were present in 132 (28%) and 133 (28%) cases, respectively. At univariable analysis of all the preoperative parameters, PHI was the most accurate predictor of pathological GS ≥7 (OR 1.02, 95% CI 1.01–1.03, p<0.001), GS upgrading (OR 1.02, 95% CI 1.01–1.03, p<0.003), pT3 disease (OR 1.01, 95% CI 1.00–1.02, p<0.007) and the presence of PSM (OR 1.01, 95% CI 1.00–1.02, p<0.002). Adding of PHI into the base multivariable model increased significantly the accuracy for predictionof pathological GS by 4.4% to AUC = 66.6 (p = 0.015) and GS upgrading by 5.0% to AUC = 65.9 (p = 0.025), respectively.

Conclusions

Preoperative PHI levels may contribute significantly to prediction of prostate cancer aggressiveness and expansion of the tumor detected at final pathology.

Scientific Reports (2021) 11:17447

ROLE OF PROSTATE HEALTH INDEX TO PREDICT GLEASON SCORE UPGRADING AND HIGH-RISK PROSTATE CANCER IN RADICAL PROSTATECTOMY SPECIMENS

Authors: Kim H., Jung G., Kim J.H. et al.

We evaluated the role of prostate health index (PHI) in predicting Gleason score (GS) upgrading in International Society of Urological Pathology Grade Group (ISUP GG) 1 & 2 prostate cancer (PCa) or adverse pathologic outcomes at radical prostatectomy (RP). A total of 300 patients with prostate specific antigen ≥ 3 ng/mL, PHI and prostate biopsy (71 patients with RP included) were retrospectively included in the study. The primary study outcomes are PCa and clinically significant PCa (csPCa, defined as ISUP GG ≥ 2) diagnostic rate of PHI, and GS upgrading rate at RP specimen. The secondary outcomes are the comparison between GS upgrading and non-upgrading group, GS upgrading and high-risk PCa (ISUP GG ≥ 3 or ≥ pT3a) predictability of preoperative clinical factors. Overall, 139 (46.3%) and 92 (30.7%) were diagnosed with PCa and csPCa, respectively. GS upgrading rate was 34.3% in all patients with RP. Significant differences were shown in the total prostate volume (p = 0.047), the distribution of ISUP GG at biopsy (p = 0.001) and RP (p = 0.032), respectively. PHI values ≥ 55 [Odds ratio (OR): 3.64 (95% confidence interval (CI) = 1.05–12.68, p = 0.042] and presence of PI-RADS lesion ≥ 4 (OR: 7.03, 95% CI = 1.68–29.51, p = 0.018) were the significant predictors of GS upgrading in RP specimens (AUC = 0.737). PHI values ≥ 55 (OR: 9.05, 5% CI = 1.04–78.52, p = 0.046) is a significant factor for predicting adverse pathologic features in RP specimens (AUC = 0.781).

PHI could predict GS upgrading in combination with PIRADS lesions ≥ 4 in ISUP GG 1 & 2. PHI alone could evaluate the possibility of high-risk PCa after surgery as well.

Investig Clin Urol, 2020;61:42-50

PREOPERATIVE PROSTATE HEALTH INDEX AND %P2PSA AS THE SIGNIFICANT BIOMARKERS OF POSTOPERATIVE PATHOLOGICAL OUTCOMES OF PROSTATE CANCER IN KOREAN MALES: A PROSPECTIVE MULTI-INSTITUTIONAL STUDY

Authors: Park H, Lee SW, Song G, Kang TW, et al.

Objective

To evaluate the clinical utility of percentage of serum prostate-specific antigen (proPSA) to free PSA (%p2PSA) and the prostate health index (PHI) for predicting aggressive pathological outcomes of radical prostatectomy (RP) in Korean males.

Methods

This prospective observational multicenter study included 160 Korean males who consecutively underwent RP. The predictive utility of preoperative %p2PSA and PHI for predicting the following pathological outcomes of RP including pT3 disease, pathologic Gleason sum ≥7, and Gleason sum upgrading was investigated using multivariate and decision-curve analyses.

Results

The PHI and %p2PSA levels were significantly higher in patients with pT3 disease, pathologic Gleason sum ≥7, and Gleason sum upgrading. On univariate analysis, PHI was an accurate predictor of pT3 disease, pathologic Gleason sum ≥7, and Gleason sum upgrading. Multivariate and decision curve analyses revealed that inclusion of PHI to a base multivariate model including total PSA, percentage free PSA, PSA density, percentage of positive biopsy core, biopsy Gleason sum, and clinical stage factors significantly increased its predictive accuracy; %p2PSA showed a similar result. However, PHI was a more valuable predictor of pathological outcomes of RP.

Conclusion

This study revealed **PHI and %p2PSA as preoperative biomarkers of pathological outcomes in Korean males who underwent RP for prostate cancer.**

Asian Journal of Andrology (2022) 24, 406–410

PROSTATE HEALTH INDEX (PHI) AND ITS DERIVATIVES PREDICT GLEASON SCORE UPGRADING AFTER RADICAL PROSTATECTOMY AMONG PATIENTS WITH LOW-RISK PROSTATE CANCER

Authors: Yan J-Q., Huang D., Huang J.-Y. et al.

To analyze the performance of the Prostate Health Index (phi) and its derivatives for predicting Gleason score (GS) upgrading between prostate biopsy and radical prostatectomy (RP) in the Chinese population, an observational, prospective RP cohort consisting of 351 patients from two medical centers was established from January 2017 to September 2020. Pathological reclassification was determined by the Gleason Grade Group (GG). The area under the receiver operating characteristic curve (AUC) and logistic regression (LR) models were used to evaluate the predictive performance of predictors. In clinically low-risk patients with biopsy GG ≤2, phi (odds ratio [OR] = 1.80, 95% confidence interval [95% CI]: 1.14–2.82, P = 0.01) **and its derivative phi density (PHID; OR = 2.34, 95% CI: 1.30–4.20, P = 0.005) were significantly associated with upgrading to GG ≥3 after RP, and the results were confirmed by multivariable analysis.** Similar results were observed in patients with biopsy GG of 1 for the prediction of upgrading to RP GG ≥2. Compared to the base model (AUC = 0.59), addition of the phi or PHID could provide additional predictive value for GS upgrading in low-risk patients (AUC = 0.69 and 0.71, respectively, both P < 0.05).

In conclusion, phi and PHID could predict GS upgrading after RP in clinically low-risk patients.

Scientific Reports (2020) 10:776

PREOPERATIVE %P2PSA AND PROSTATE HEALTH INDEX PREDICT PATHOLOGICAL OUTCOMES IN PATIENTS WITH PROSTATE CANCER UNDERGOING RADICAL PROSTATECTOMY

Authors: Cheng Y.-T., Huang C.-Y., Chen C.-H. et al.

To evaluate the predictive accuracy of the %p2PSA and prostate health index (PHI) in predicting aggressive pathological outcomes in patients with prostate cancer (PCa) undergoing radical prostatectomy (RP), we enrolled 91 patients with organ-confined PCa who were treated with robotassisted RP. p2PSA levels and the PHI were investigated for their ability to predict pathological results. The %p2PSA and PHI were both significantly higher in patients with ≥pT3 disease, high-risk disease, positive surgical margin, or seminal vesical invasion (SVI). In univariable analysis, p2PSA derivatives were significant predictors of the presence of ≥pT3 disease, high-risk disease, positive surgical margin, and SVI. To predict adverse pathological outcomes at a sensitivity of 90%, p2PSA derivatives had higher specificity than standard PSA derivatives. In multivariable analysis, additional increases in the area under the receiver operating characteristic curve (AUC) were observed with the %p2PSA and PHI for ≥pT3 disease, high-risk disease, and positive surgical margin (8.2% and 2.7%, 6.2% and 4.1%, and 8.6% and 5.4%, respectively).

A PHI ≥61.26 enhanced the predictive accuracy of the model for SVI by increasing the AUC from 0.624 to 0.819 (p = 0.009). **The preoperative %p2PSA and PHI accurately predict adverse pathological results and are useful for decision-making.**

Journal of Chinese Medical Association. (2019) 82: 835-839.

PROSTATE HEALTH INDEX DENSITY PREDICTS AGGRESSIVE PATHOLOGICAL OUTCOMES AFTER RADICAL PROSTATECTOMY IN TAIWANESE PATIENTS

Authors: Huang Y.-P., Lin T-P., Cheng W-M et al.

Background

There are models to predict pathological outcomes based on established clinical and prostate-specific antigen (PSA)-derived parameters; however, they are not satisfactory. p2PSA and its derived biomarkers have shown promise for the diagnosis and prognosis of prostate cancer (PCa). The aim of this study was to investigate whether p2PSA-derived biomarkers can assist in the prediction of aggressive pathological outcomes after radical prostatectomy (RP).

Methods

We prospectively enrolled patients who were diagnosed with PCa and treated with RP between February 2017 and December 2018. Preoperative blood samples were analyzed for tPSA, free PSA (fPSA), percentage of fPSA (%fPSA), [-2]proPSA (p2PSA), and percentage of p2PSA (%p2PSA). Prostate health index (PHI) was calculated as (p2PSA/fPSA) × √tPSA. Prostate volume was determined by transrectal ultrasound using the ellipsoid formula, and PHI density was calculated as PHI/prostate volume. The areas under the receiver operating characteristic curve were estimated for various PSA/p2PSA derivatives. Aggressive pathological outcomes measured after RP were defined as pathological T3 or a Gleason score (GS) >6 as determined in RP specimens.

Results

One hundred and forty-four patients were included for analysis. Postoperative GS was >6 in 86.1% of the patients, and pT stage was T3a or more in 54.2%. Among all PSA- and p2PSA-derived biomarkers, PHI density was the best biomarker to predict aggressive pathological outcomes after RP. The odds ratio of having an aggressive pathological outcome of RP was 8.796 ($p = 0.001$). In multivariate analysis, adding %fPSA to base model did not improve the accuracy (area under curve), but adding PHI and PHI density to base model improved the accuracy by 2% and 16%, respectively, in predicting pT3 stage or GS ≥ 7. The risk of pT3 stage or GS ≥ 7 was 20.8% for PHI density <1.125, and 64.6% for PHI density >1.125 (sensitivity: 74.6% and specificity: 88.9%).

Conclusion

PHI density may further aid in predicting aggressive pathological outcomes after RP. This biomarker may be useful in preoperative counseling and may have potential in decision making when choosing between definitive treatment and active surveillance of newly diagnosed PCa.

BJU Int. 2020 Sep;126(3):373-378

PROSTATE HEALTH INDEX AND MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING TO PREDICT PROSTATE CANCER GRADE RECLASSIFICATION IN ACTIVE SURVEILLANCE

Authors: Schwen Z.R., Mamawala M., Tosoian J.J. et al.

Objective

To identify the value of combining the Prostate Health Index (PHI) and multiparametric magnetic resonance imaging (mpMRI), tools which have previously been shown to be independently predictive of prostate cancer (PCa) grade reclassification (GR; Gleason score >6), for the purpose of predicting GR at the next surveillance biopsy to reduce unnecessary prostate biopsies for men in PCa active surveillance (AS).

Patients and methods

Between 2014 and 2019, we retrospectively identified 253 consecutive men in the Johns Hopkins AS programme who had mpMRI and PHI followed by a systematic ± targeted biopsy. PHI and PHI density (PHID) were evaluated across Prostate Imaging-Reporting and Data System version 2.0 (PI-RADSv2) scores and compared to those with and without GR. Next, the negative predictive value (NPV) and area under the receiver operating curve (AUC) were calculated to compare the diagnostic value of PI-RADSv2 score combined with PHI, PHID, or prostate-specific antigen density (PSAD) for GR using their respective first quartile as a cut-off.

Results

Of the 253 men, 38 men (15%) had GR. Men with GR had higher PHI values (40.7 vs 32.0, P = 0.001), PHID (0.83 vs 0.57, P = 0.007), and PSAD (0.12 vs 0.10, P = 0.037). A PI-RADSv2 ≤3 alone had a NPV of 91.6% for GR (AUC 0.67). Using a PHI cut-off of 25.6 in addition to PI-RADSv2 ≤3, the NPV and AUC were both increased to 98% and 0.70, respectively. Using a PSAD cut-off of 0.07 ng/mL/mL with PI-RADSv2 had an AUC of 0.69 and NPV of 95.4%. PHI and PI-RADSv2 together could have avoided 20% of biopsies at the cost of missing 2.6% of GRs.

Conclusions

The combination of PHI and mpMRI can aid in the prediction of GR in men on AS and may be useful for decreasing the burden of surveillance prostate biopsies.

European Urology, vol. 75, Issue 4, April 2019, pages 558-561

MULTICENTRE EVALUATION OF THE ROLE OF THE PROSTATE HEALTH INDEX (PHI) IN REGIONS WITH DIFFERING PREVALENCE OF PROSTATE CANCER: ADJUSTMENT OF PHI REFERENCE RANGES IS NEEDED FOR EUROPEAN AND ASIAN SETTINGS

Authors: Chiu P., Chi-Fai Ng C.-F., Semjonow A. et al.

Abstract

Asians have a lower incidence of prostate cancer (PC). We compared the performance of the Prostate Health Index (PHI) for 2488 men in different ethnic groups (1688 Asian and 800 European men from 9 sites) with PSA 2–20 ng/ml and PHI test and transrectal ultrasound-guided biopsy results available. Of these, 1652 men had PSA 2–10 ng/ml and a normal digital rectal examination and underwent initial biopsy. The proportions of PC (Gleason ≥6) and higher-grade PC (HGPC, Gleason ≥7) across different PHI ranges were compared. The performance of PSA and PHI was compared using the area under the receiver operating characteristic curve (AUC) and decision curve analyses (DCA). Among Asian men, HGPC would be diagnosed in 1.0%, 1.9%, 13%, and 30% of men using PHI thresholds of <25, 25–35, 35–55, and >55, respectively. At 90% sensitivity for HGPC (PHI >30), 56% of biopsies and 33% of Gleason 6 PC diagnoses could have been avoided. Among European men, HGPC would be diagnosed in 4.1%, 4.3%, 30%, and 34% of men using PHI thresholds of <25, 25–35, 35–55, and >55, respectively. At 90% sensitivity for HGPC (PHI >40), 40% of biopsies and 31% of Gleason 6 PC diagnoses could have been avoided. AUC and DCA confirmed the benefit of PHI over PSA. The benefit of PHI was also seen at repeat biopsy (n = 397) and for PSA 10–20 ng/ml (n = 439). PHI is effective in cancer risk stratification for both European and Asian men. However, population specific PHI reference ranges should be used.

Patient summary:

The Prostate Health Index (PHI) blood test helps to identify individuals at higher risk of prostate cancer among Asian and European men, and could significantly reduce unnecessary biopsies and overdiagnosis of prostate cancer. Different PHI reference ranges should be used for different ethnic groups.

phi: THRESHOLDS IN DIFFERENT POPULATIONS

P. K.-F. Chiu, C.-F. Ng, A. Semjonow, Y. Zhu, S. Vincendeau, A. Houlgatte, M. Lazzeri, G. Guazzoni, C. Stephan, A. Haese, I. Bruijne, J. Y.-C. Teoh, C. H. Leung, P.Casale, C. H. Chiang, L. G.-L. Tan, E. Chiong, C. Y. Huang, H. C. Wu, D. Nieboer, D.-W. Ye, C.H. Bangma, M. J. Roobol.

Multicentre Evaluation of the Role of the Prostate Health Index (PHI) in Regions with Differing Prevalence of Prostate Cancer: Adjustment of PHI Reference Ranges is Needed for European and Asian Settings.
European Urology, vol. 75, Issue 4, April 2019, 558-561

PCs for different PHI cutoffs for men with prostate-specific antigen 2–10 ng/ml, normal digital rectal examination, and initial biopsies

	PHI cutoff				Total	p value [a]
	<25	25–35	35–55	>55		
European cohort (*n* =503)						
PC	17/49 (35%)	30/116 (26%)	100/178 (56%)	115/160 (72%)	262/503 (52%)	<0.001
Gleason ≥ 3 + 4 PC	2/49 (4.1%)	5/116 (4.3%)	53/178 (30%)	55/160 (34%)	115/503 (23%)	<0.001
Gleason ≥ 4 + 3 PC	0/49 (0%)	0/49 (0%)	12/178 (6.7%)	16/160 (10%)	30/503 (6.0%)	<0.001
Asian cohort (*n* = 1149)						
PC	20/397 (5.0%)	31/412 (7.5%)	72/276 (26%)	28/64 (44%)	151/1149 (13%)	<0.001
Gleason ≥ 3 + 4 PC	4/397 (1.0%)	8/412 (1.9%)	35/276 (13%)	19/64 (30%)	66/1149 (5.7%)	<0.001
Gleason ≥ 4 + 3 PC	2/397 (0.5%)	6/412 (1.5%)	11/276 (4.0%)	8/64 (13%)	27/1149 (2.3%)	<0.001

PC = prostate cancer; PHI = Prostate Health Index.

[a] x^2 test for PC versus the different PHI cutoffs.

P. K.-F. Chiu, C.-F. Ng, A. Semjonow, Y. Zhu, S. Vincendeau, A. Houlgatte, M. Lazzeri, G. Guazzoni, C. Stephan, A. Haese, I. Bruijne, J. Y.-C. Teoh, C. H. Leung, P.Casale, C. H. Chiang, L. G.-L. Tan, E. Chiong, C. Y. Huang, H. C. Wu, D. Nieboer, D.-W. Ye, C.H. Bangma, M. J. Roobol.

Multicentre Evaluation of the Role of the Prostate Health Index (PHI) in Regions with Differing Prevalence of Prostate Cancer: Adjustment of PHI Reference Ranges is Needed for European and Asian Settings.
European Urology, vol. 75, Issue 4, April 2019, 558-561

Biopsies and Gleason 6 PC diagnoses that could be avoided at different PHI cutoffs (for Gleason ≥7 PC) in European and Asian cohorts

PHI cutoff	HGPC SV	HGPC SP	Bx saved (%) [a]	*n*	Gleason ≥ 7 PC missed *n* (%) [b]	Gleason 6 Dx reduced *n* (%) [c]
European (*n* = 503)						
25	99%	10%	49 (9.7)		2 (1.7)	15 (10)
32	95%	28%	116 (23)		6 (5.2)	29 (20)
35	94%	37%	165 (33)		7 (6.1)	40 (27)
40	90%	48%	199 (40)		12 (10)	45 (31)
45	78%	59%	258 (51)		26 (23)	62 (42)
55	53%	72%	343 (68)		60 (52)	87 (59)
Asian (*n* = 1149)						
25	96%	36%	392 (34)		3 (4.5)	15 (18)
30	89%	59%	646 (56)		7 (11)	28 (33)
35	82%	74%	810 (71)		12 (18)	39 (46)
45	55%	92%	1021 (89)		29 (44)	69 (81)
55	27%	96%	1086 (95)		47 (71)	76 (89)

PC = prostate cancer; HGPC = higher-grade PC; PHI = Prostate Health Index;
SV = sensitivity; SP = specificity; Bx = biopsy; Dx = diagnosis.

[a] Biopsies saved if all men with a PHI score below cutoff are not biopsied (% of all biopsies, *n* = 503 for the European and *n* = 1149 for the Asian cohort).

[b] Expressed as a percentage of all Gleason ≥ 7 cancers (*n* = 115 for the Asian cohort).

[c] Expressed as a percentage of all Gleason 6 cancers (*n* = 147 for the European and *n* = 85 for the Asian cohort).

"Men in the European cohort had a fourfold higher risk of PC and HGPC compared to Asian men. The European cohorts had a higher percentage of repeat biopsies, higher median PHI, lower PSA, and similar median prostate size in comparison to the Asian cohorts."

International Urology and Nephrology volume 52, pages893–901 (2020)

OPTIMAL THRESHOLD OF THE PROSTATE HEALTH INDEX IN PREDICTING AGGRESSIVE PROSTATE CANCER USING PREDEFINED COST–BENEFIT RATIOS AND PREVALENCE

Authors: Stojadinovic M., Vukovic I., Ivanovic M. et al.

Purposes

The aim of the study was to determine optimal threshold of the Prostate Health Index (Phi) for predicting aggressive prostate cancer (PCa), taking into account misclassification costs, prevalence, and plausible risk factors.

Methods

This prospective cohort study analyzed patients undergoing prostate biopsy and Phi testing. The primary endpoint was aggressive PCa, defined as biopsy Gleason score ≥ 7. The data about age, total prostate-specific antigen (PSA), percentage of free PSA (%fPSA), and digital rectal examination (DRE) were extracted from the patient files. We divided the patients to the low- and high-risk group. The clinical usefulness of the Phi was assessed by the decision curve analysis. The predictive performance was assessed using the area under the receiver operating characteristic curve (AUC), per-class metrics, and the potential reduction in unnecessary biopsies. The uncertain interval of Phi values was also determined.

Results

There were 200 men included in the study, 35 (17.5%) of them having aggressive PCa. Important predictors of aggressive PCa were %fPSA, DRE, Phi, and belonging to the high-risk group. With optimal threshold of 30.7, about 32% unnecessary biopsies would be avoided. The optimal threshold of Phi was lower in the high-risk group than in the low-risk group. The AUC for detection of aggressive PCa was 0.791. Per-class metrics showed that the Phi has insufficient diagnostic accuracy. The lower and upper limits of the uncertain interval were 41.8 and 51.4, respectively.

Conclusion

Different thresholds of the Phi could be optimal, depending on prevalence, patient characteristics, and misclassification costs. Further studies with a larger patient sample are necessary to confirm our conclusions.

Asian J Androl, 2020 Sep-Oct;22(5):539-543

PROSTATE VOLUME DOES NOT PROVIDE ADDITIONAL PREDICTIVE VALUE TO PROSTATE HEALTH INDEX FOR PROSTATE CANCER OR CLINICALLY SIGNIFICANT PROSTATE CANCER: RESULTS FROM A MULTICENTER STUDY IN CHINA

Authors: Huang D., Yi-Shuo Wu Y-S., Ye D-W et al.

To evaluate whether prostate volume (PV) would provide additional predictive utility to the prostate health index (phi) for predicting prostate cancer (PCa) or clinically significant prostate cancer, we designed a prospective, observational multicenter study in two prostate biopsy cohorts. Cohort 1 included 595 patients from three medical centers from 2012 to 2013, and Cohort 2 included 1025 patients from four medical centers from 2013 to 2014. Area under the receiver operating characteristic curves (AUC) and logistic regression models were used to evaluate the predictive performance of PV-based derivatives and models. Linear regression analysis showed that both total prostate-specific antigen (tPSA) and free PSA (fPSA) were significantly correlated with PV (all $P < 0.05$). [-2]proPSA (p2PSA) was significantly correlated with PV in Cohort 2 ($P< 0.001$) but not in Cohort 1 ($P= 0.309$), while no significant association was observed between phi and PV. When combining phi with PV, phi density (PHID) and another phi derivative (PHIV, calculated as phi/PV0.5) did not outperform phi for predicting PCa or clinically significant PCa in either Cohort 1 or Cohort 2. Logistic regression analysis also showed that phi and PV were independent predictors for both PCa and clinically significant PCa (all $P < 0.05$); however, PV did not provide additional predictive value to phi when combining these derivatives in a regression model (all models vs phi were not statistically significant, all $P > 0.05$).

In conclusion, PV-based derivatives (both PHIV and PHID) and models incorporating PV did not improve the predictive abilities of phi for either PCa or clinically significant PCa.

Urol Int 2022;106:878–883

COMPARISON OF PHI AND PHI DENSITY FOR PROSTATE CANCER DETECTION IN A LARGE RETROSPECTIVE CAUCASIAN COHORT

Authors: Peters R., C. Stephan C., Jung K. et l.

Background

Beyond prostate-specific antigen (PSA), other biomarkers for prostate cancer (PCa) detection are available and need to be evaluated for clinical routine.

Objective

The aim of the study was to evaluate the Prostate Health Index (PHI) density (PHID) in comparison with PHI in a large Caucasian group >1,000 men. Methods: PHID values were used from available patient data with PSA, free PSA, and [−2]proPSA and prostate volume from 3 former surveys from 2002 to 2014. Those 1,446 patients from a single-center cohort included 701 men with PCa and 745 with no PCa. All patients received initial or repeat biopsies. The diagnostic accuracy was evaluated by receiver operating characteristic (ROC) curves comparing area under the ROC curves (AUCs), precision- recall approach, and decision curve analysis (DCA).

Results

PHID medians differed almost 2-fold between PCa (1.12) and no PCa (0.62) in comparison to PHI (48.6 vs. 33; p always <0.0001). However, PHID and PHI were equal regarding the AUC (0.737 vs. 0.749; p = 0.226), and the curves of the precision-recall analysis also overlapped in the sensitivity range between 70 and 100%. DCA had a maximum net benefit of only ~5% for PHID versus PHI between 45 and 55% threshold probability. Contrary, in the 689 men with a prostate volume ≤40 cm3, PHI (AUC 0.732) showed a significant larger AUC than PHID (AUC 0.69, p = 0.014).

Conclusions

Based on DCA, PHID had only a small advantage in comparison with PHI alone, while ROC analysis and precision-recall analysis showed similar results. In smaller prostates, PHI even outperformed PHID. The increment for PHID in this large Caucasian cohort is too small to justify a routine clinical use.

Biomed Res Int, . 2020 Jul 21; 2020:9872146

PROSTATE HEALTH INDEX AND PROSTATE HEALTH INDEX DENSITY AS DIAGNOSTIC TOOLS FOR IMPROVED PROSTATE CANCER DETECTION

Authors: Barisiene M., Bakavicius A., Stanciute D. et al.

Background

To evaluate the diagnostic potential of [-2] proPSA (p2PSA), %p2PSA, Prostate Health Index (phi), and phi density (PHID) as independent biomarkers and in composition of multivariable models in predicting high-grade prostatic intraepithelial neoplasia (HGPIN) and overall and clinically significant prostate cancer (PCa).

Methods

210 males scheduled for prostate biopsy with total PSA (tPSA) range 2-10 ng/mL and normal digital rectal examination were enrolled in the prospective study. Blood samples to measure tPSA, free PSA (fPSA), and p2PSA were collected immediately before 12-core prostate biopsy. Clinically significant PCa definition was based on Epstein's criteria or ISUP grade ≥ 2 at biopsy.

Results

PCa has been diagnosed in 112 (53.3%) patients. Epstein significant and ISUP grade ≥ 2 PCa have been identified in 81 (72.3%) and 40 (35.7%) patients, respectively. Isolated HGPIN at biopsy have been identified in 24 (11.4%) patients. Higher p2PSA and its derivative mean values were associated with PCa. At 90% sensitivity, PHID with cut-off value of 0.54 have demonstrated the highest sensitivity of 35.7% for overall PCa detection, so PHID and phi with cut-off values of 33.2 and 0.63 have demonstrated the specificity of 34.7% and 34.1% for ISUP grade ≥ 2 PCa detection at biopsy, respectively. In univariate ROC analysis, PHID with AUC of 0.77 and 0.80 was the most accurate predictor of overall and Epstein significant PCa, respectively, so phi with AUC of 0.77 was the most accurate predictor of ISUP grade ≥ 2 PCa at biopsy. In multivariate logistic regression analysis, phi improved diagnostic accuracy of multivariable models by 5% in predicting ISUP grade ≥ 2 PCa.

Conclusions

PHID and phi have shown the greatest specificity at 90% sensitivity in predicting overall and clinically significant PCa and would lead to significantly avoid unnecessary biopsies. PHID is the most accurate predictor of overall and Epstein significant PCa, so phi is the most accurate predictor of ISUP grade ≥ 2 PCa. phi significantly improves the diagnostic accuracy of multivariable models in predicting ISUP grade ≥ 2 PCa.

Urology, 2019 Jul;129:153-159

THE UTILITY OF PROSTATE SPECIFIC ANTIGEN DENSITY, PROSTATE HEALTH INDEX, AND PROSTATE HEALTH INDEX DENSITY IN PREDICTING POSITIVE PROSTATE BIOPSY OUTCOME IS DEPENDENT ON THE PROSTATE BIOPSY METHODS

Authors: Vendrami C.L., McCarthy R.J., Chatterjee A. et al.

Objective

To evaluate prognostic markers, prostate-specific antigen, prostate health index (PHI), and prostate volume indexed measures (prostate-specific antigen density and prostate health index density) for predicting positive prostate cancer biopsies in magnetic resonance (MR) transrectal ultrasound fused versus nonfused transrectal ultrasonography biopsy.

Methods

A retrospective cohort of 211 patients that had at least 1 suspected MR lesion, Prostate Imaging-Reporting and Data System ≥3, and subsequent biopsy (2015-2017). Clinical characteristics and prognostic biomarkers were evaluated as predictors of prostate cancer detection by type of biopsy guidance (fused vs nonfused).

Results

One-hundred twenty-one patients had nonfused and 90 had fused biopsies. **PHI and PHID had greater area under the receiver operating characteristics curve (AUC) in predicting positive biopsies than prostate-specific antigen or PSAD for both nonfused and fused biopsy. PHI 0.78 (95% CI 0.67-0.88) and PHID 0.82 (95% CI 0.73-0.91) had the greatest AUC for predicting biopsy results for nonfused and fused biopsies, respectively. Multiple-variable models did not improve model fit compared to single variables.** Based on Youden's index, a cut-off value of 45.9 for PHI in nonfused and 0.64 for PHID in fused biopsies would reduce the number of negative biopsies by 77.3% and 63.4%, respectively, but the percentage of missed clinically significant cancer biopsies would be 19% and 12%, respectively.

Conclusion

Our findings demonstrate that the choice of prognostic biomarkers for predicting positive biopsies is a function of the biopsy guidance method. Volume indexed derivatives appear to have greater value when a MRI-US fused method is used.

BJUI Compass. 2021 Nov; 2(6): 370–376

PERFORMANCE OF PROSTATE HEALTH INDEX AND PSA DENSITY IN A DIVERSE BIOPSY-NAÏVE COHORT WITH mpMRI FOR DETECTING SIGNIFICANT PROSTATE CANCER

Authors: Carbunaru S., Stinson J., Babajide R. et al.

Objective

To compare Prostate Health Index (PHI) and prostate-specific antigen (PSA) density as secondary tests after multiparametric magnetic resonance imaging (mpMRI) in improving the detection accuracy of Gleason grade group (GG) 2-5 prostate cancer (PCa) and in decreasing unnecessary biopsies in a multiethnic biopsy-naïve population.

Methods

From February 2017 to February 2020, we recruited consecutive biopsy-naïve men in participating urology clinics for elevated PSA levels. They all had a PHI score, mpMRI, and prostate biopsy. Experienced genitourinary radiologists read all mpMRI studies based on PIRADS version 2.0. Logistic regression models were used to generate receiver operating characteristic curves. Models were tested for effect modification between Race (Black vs White) and both PHI and PSA density, and Race and PIRADS to determine if race impacted their prediction accuracy. Sensitivity, specificity, and predictive values of PHI and PSA density thresholds were calculated by PIRADS scores. The primary outcome was GG2-5 PCa, that is, Gleason score ≥3 + 4.

Results

The study included 143 men, of which 65 (45.5%) were self-reported Black. Median age was 62.0 years and 55 men (38.4%) had GG2-5 PCa. Overall, 18.1% had PIRADS 1-2, 32.9% had PIRADS 3, and 49.0% had PIRADS 4-5. For the binary logistic regressions, the interactions between PIRADS and Race (P = .08), Log (PHI) and Race (P = .17), and Log (PSA density) and Race (P = .42) were not statistically significant. Within PIRADS 3 lesions, a PHI ≥49 prevented unnecessary biopsies in 55% of men and missed no GG2-5 PCa, yielding a negative predictive value of 100%. There was no reliable PHI or PSA density threshold to avoid PCa biopsies in PIRADS 1-2 or 4-5.

Conclusions

PHI and PSA density can be used after mpMRI to improve the detection of GG2-5 PCa in a biopsy-naïve cohort. PHI may be superior to PSA density in PIRADS 3 lesions by avoiding 55% of unnecessary biopsies. Using both PHI and PSA density in series may further increase specificity and lead to fewer unnecessary biopsies, but further larger studies are warranted to determine the optimal threshold of each biomarker.

Urol Int., 2020;104(3-4):181-186

USE OF THE PROSTATE HEALTH INDEX AND DENSITY IN 3 OUTPATIENT CENTERS TO AVOID UNNECESSARY PROSTATE BIOPSIES

Authors: Schulze A., Christoph F., Sachs M. et al.

Objectives

We investigated the diagnostic efficacy of the prostate health index (PHI) and PHI density (PHID) to avoid unnecessary prostate biopsies in 3 urological practices.

Methods

In 122 patients, total prostate-specific antigen (PSA), free PSA (f-PSA), the quotient from total PSA and f-PSA (f-PSA%), and [-2]pro-PSA were measured in the serum; PHI, PHID, and PSA density (PSAD) were calculated prior to prostate biopsy. Tissue sampling via transrectal biopsy was indicated in case of suspicious PSA (progression and/or elevation of PSA) and/or suspicious digital rectal examination. PSAD, PHI, and PHID were not used for biopsy indication. The diagnostic efficacy was determined with receiver-operating characteristic (ROC)and decision curve analyses.

Results

Based on prostate biopsies, 38% (n = 46) of the cases had no prostate carcinoma (PCa), 21% (n = 26) no clinically significant (insignificant) PCa, and 41% (n = 50) had clinically significant PCa. ROC analyses of the PSA parameters showed higher diagnostic efficacy for PHI and PHID (AUC 0.722 and 0.739) than for f-PSA%, PSA, and PSAD (AUC 0.612, 0.595, and 0.698, respectively) regarding carcinoma diagnosis. With a combined use of PHI and PHID (cutoff >40 and >0.9, respectively), only 1 clinically significant PCa would have been missed (sensitivity 98%); in 24 (20%) patients, biopsy could have been avoided.

Conclusion

The integration of PHI and PHID could improve the diagnostic efficacy of risk calculators to avoid unnecessary prostate biopsies. However, as a prerequisite, validation of cutoff values in prospective studies is urgently required.

World Journal of Urology volume 39, pages3273–3279 (2021)

PHI DENSITY PROSPECTIVELY IMPROVES PROSTATE CANCER DETECTION

Authors: Stephan C., Jung K., Lein M. et al.

Purpose

To evaluate the Prostate Health Index (PHI) density (PHID) in direct comparison with PHI in a prospective large cohort.

Methods

PHID values were calculated from prostate-specific antigen (PSA), free PSA and [−2]proPSA and prostate volume. The 1057 patients included 552 men with prostate cancer (PCa) and 505 with no evidence of malignancy (NEM). In detail, 562 patients were biopsied at the Charité Hospital Berlin and 495 patients at the Sana Hospital Offenbach. All patients received systematic or magnetic resonance imaging (MRI)/ultrasound fusion-guided biopsies. The diagnostic accuracy was evaluated by receiver operating characteristic (ROC) curves comparing areas under the ROC-curves (AUC). The decision curve analysis (DCA) was performed with the MATLAB Neural Network Toolbox.

Results

PHID provided a significant larger AUC than PHI (0.835 vs. 0.801; p = 0.0013) in our prospective cohort of 1057 men from 2 centers. The DCA had a maximum net benefit of ~ 5% for PHID vs. PHI between 35 and 65% threshold probability. In those 698 men within the WHO-calibrated PSA grey-zone up to 8 ng/ml, PHID was also significantly better than PHI (AUC 0.819 vs. 0.789; p = 0.0219). But PHID was not different from PHI in the detection of significant PCa.

Conclusions

Based on ROC analysis and DCA, PHID had an advantage in comparison with PHI alone to detect any PCa **but PHI and PHID performed equal in detecting significant PCa.**

PLoS ONE, 2019, 14(4): e0215279

ECONOMIC EVALUATION OF THE INTRODUCTION OF THE PROSTATE HEALTH INDEX AS A RULE-OUT TEST TO AVOID UNNECESSARY BIOPSIES IN MEN WITH PROSTATE SPECIFIC ANTIGEN LEVELS OF 4-10 IN HONG KONG

Authors: Bouttell J., Teoh J., Chiu P.K. et al.

A recent study showed that the Prostate Health Index may avoid unnecessary biopsies in men with prostate specific antigen 4-10ng/ml and normal digital rectal examination in the diagnosis of prostate cancer in Hong Kong. This study aimed to conduct an economic evaluation of the impact of adopting this commercially-available test in the Hong Kong public health service to determine whether further research is justified. A cost-consequence analysis was undertaken comparing the current diagnostic pathway with a proposed diagnostic pathway using the Prostate Health Index. Data for the model was taken from a prospective cohort study recruited at a single-institution and micro-costing studies. Using a cut off PHI score of 35 to avoid biopsy would cost HK$3,000 and **save HK$7,988 per patient in biopsy costs and HK$511 from a reduction in biopsy-related adverse events. The net cost impact of the change was estimated to be HK$5,500 under base case assumptions**. At the base case sensitivity and specificity for all grades of cancer (61.3% and 77.5% respectively) all grade cancer could be missed in 4.22% of the population and high grade cancer in 0.53%.

The introduction of the prostate health index into the diagnostic pathway for prostate cancer in Hong Kong has the potential to reduce biopsies, biopsy costs and biopsy-related adverse events. Policy makers should consider the clinical and economic impact of this proposal.

Kim et al. BMC Medicine (2020) 18:95

CLINICAL UTILITY AND COST MODELLING OF THE PHI TEST TO TRIAGE REFERRALS INTO IMAGE-BASED DIAGNOSTIC SERVICES FOR SUSPECTED PROSTATE CANCER: THE PRIM (PHI TO REFINE MRI) STUDY

Authors: Kim L., Boxall N., George A. et al.

Background

The clinical pathway to detect and diagnose prostate cancer has been revolutionised by the use of multiparametric MRI (mpMRI pre-biopsy). mpMRI however remains a resource-intensive test and is highly operator dependent with variable effectiveness with regard to its negative predictive value. Here we tested the use of the phi assay in standard clinical practice to pre-select men at the highest risk of harbouring significant cancer and hence refine the use of mpMRI and biopsies.

Methods

A prospective five-centre study recruited men being investigated through an mpMRI-based prostate cancer diagnostic pathway. Test statistics for PSA, PSA density (PSAd) and phi were assessed for detecting significant cancers using 2 definitions: ≥ Grade Group (GG2) and ≥ Cambridge Prognostic Groups (CPG) 3. Cost modelling and decision curve analysis (DCA) was simultaneously performed.

Results

A total of 545 men were recruited and studied with a median age, PSA and phi of 66 years, 8.0 ng/ml and 44 respectively. Overall, ≥ GG2 and ≥ CPG3 cancer detection rates were 64% (349/545), 47% (256/545) and 32% (174/545) respectively. There was no difference across centres for patient demographics or cancer detection rates. The overall area under the curve (AUC) for predicting ≥GG2 cancers was 0.70 for PSA and 0.82 for phi. AUCs for ≥ CPG3 cancers were 0.81 and 0.87 for PSA and phi respectively. AUC values for phi did not differ between centres suggesting reliability of the test in different diagnostic settings. Pre-referral phi cut-offs between 20 and 30 had NPVs of 0.85–0.90 for ≥ GG2 cancers and 0.94–1.0 for ≥ CPG3 cancers. A strategy of mpMRI in all and biopsy only positive lesions reduced unnecessary biopsies by 35% but missed 9% of ≥ GG2 and 5% of ≥ CPG3 cancers. Using PH ≥ 30 to rule out referrals missed 8% and 5% of ≥ GG2 and ≥ CPG3 cancers (and reduced unnecessary biopsies by 40%). This was achieved however with 25% fewer mpMRI. Pathways incorporating PSAd missed fewer cancers but necessitated more unnecessary biopsies. The phi strategy had the lowest mean costs with DCA demonstrating net clinical benefit over a range of thresholds.

Conclusion

phi as a triaging test may be an effective way to reduce mpMRI and biopsies without compromising detection of significant prostate cancers.

Prostate Cancer Prostatic Dis 23, 615–621 (2020)

THE COST-EFFECTIVENESS OF PROSTATE HEALTH INDEX FOR PROSTATE CANCER DETECTION IN CHINESE MEN

Authors: Teoh J. Y.-C., Leung C.-H., Wang M.H., et al.

Background

Prostate-specific antigen (PSA) and prostate health index (PHI) have been used as biomarkers for prostate cancer detection. In this study, we aimed to evaluate the cost-effectiveness of PHI for prostate cancer detection in Chinese men.

Methods

We developed a Markov model for Chinese male patient aged 50–75 years old. The PSA strategy was to offer TRUS-PB for all patients with elevated PSA of 4–10 ng/mL. The PHI strategy was to offer PHI for patients with elevated PSA of 4–10 ng/mL. TRUS-PB would only be offered for patients with PHI >35.0. Model inputs were extracted from local data when available. The cost per quality-adjusted life years gained for both strategies were calculated. The incremental cost-effectiveness ratios in relation to the willingness-to-pay (WTP) threshold were compared. One-way sensitivity analysis and probabilistic sensitivity analysis were performed. Cost-effectiveness acceptability curves were also constructed.

Results

With a Markov model of 25 screening cycles from age 50 to 75 years, the mean total costs per man were estimated to be USD 27,439 in the PSA strategy and USD 22,877 in the PHI strategy. The estimated effects were estimated to be 15.70 in the PSA strategy and 16.05 in the PHI strategy. The PHI strategy was associated with an expected decrease in cost of USD 4562 and an expected gain of 0.35 quality-adjusted life year (QALY), resulting in an Incremental Cost-Effectiveness Ratio (ICER) of USD −13056.56. The results were shown to be robust upon one-way sensitivity analysis. Upon Monte Carlo simulation, the PHI strategy was more cost-effective for 100% of the iterations. The PHI strategy demonstrated dominance over the PSA strategy regardless of what WTP threshold we use.

Conclusions

A PHI-based screening strategy may be more cost-effective than a PSA-based strategy for prostate cancer detection in Chinese men. These results support consideration of a PHI-based approach for prostate cancer in Hong Kong.

Front. Oncol., 24 November 2020
Sec. Genitourinary Oncology Volume 10 - 2020

COST-EFFECTIVENESS ANALYSIS OF PROSTATE HEALTH INDEX IN DECISION MAKING FOR INITIAL PROSTATE BIOPSY

Authors: Huang D., Yang X., Wu Y. et al.

Background

Clinical studies have suggested that prostate health index (phi) outperforms prostate-specific antigen (PSA) tests in prostate cancer detection. The cost-effectiveness of phi with different cutoffs is poorly understood in the context of decision making for prostate biopsy.

Methods

In a multicenter cohort, 3,348 men with elevated total PSA (tPSA) underwent initial prostate biopsy from August 2013 to May 2019. We constructed a decision model to evaluate the incremental cost-effectiveness ratios of different phi cutoffs. Total costs and reimbursement payments were based on the fee schedule of Shanghai Basic Medical Insurance and converted into United States dollars ($). Two willingness-to-pay thresholds were estimated as one or three times the average gross domestic product per capita of China ($7,760 or $23,279, respectively).

Results

The total costs of prostate biopsy and PSA tests were estimated at $315 and $19, respectively. The cost of phi test varied between $72 to $130 in different medical centers. Under different phi cutoffs (from 23 to 35), phi test predicted reductions of 420 (21.7%) to 972 (50.2%) in unnecessary biopsies, with a total gain of 23.77–57.58 quality adjusted life-years compared to PSA tests. All the cutoffs would be cost-effective for patients with tPSA levels of 2–10 ng/ml. Applying 27 as the cutoff was cost-effective for each tPSA range, with missing positive cases ranging from 11 (3.4%) to 33 (11.5%).

Conclusions

Using phi test was cost-effective in the decision-making process for initial prostate biopsy, especially for patients with tPSA values between 2–10 ng/ml. **The phi cutoff of 27 was cost-effective regardless of tPSA ranges and should be recommended from a health-economic perspective.**

Clin Chem Lab Med, 2019, Mar 26;57(4):521-531

PREANALYTICAL STABILITY OF [-2]proPSA IN WHOLE BLOOD STORED AT ROOM TEMPERATURE BEFORE SEPARATION OF SERUM AND PLASMA: IMPLICATIONS TO PHI DETERMINATION

Authors: Dittadi R., Fabricio A., Rainato G. et al.

Background

[-2]proPSA seems to outperform free/total prostate-specific antigen (PSA) ratio in prostate cancer diagnosis. However, [-2]proPSA stability remains an underestimated issue. We examined [-2]proPSA stability over time in whole blood before separation of serum and plasma and its implications for prostate health index (Phi) determination. Total PSA (tPSA) and free PSA (fPSA) stabilities were also assessed.

Methods

Blood was drawn from 26 patients and separated in two tubes for plasma (K2EDTA and K2EDTA plus protease inhibitors - P100) and one for serum (clot activator plus gel separator). Tubes were stored at room temperature before centrifugation 1, 3 and 5 h for serum and EDTA plasma or 1 and 5 h for P100 plasma. To investigate the influence of gel separator on markers' stability, blood was collected from 10 patients in three types of tubes to obtain serum: tubes with clot activator plus gel separator, with silica particles or glass tubes. Biomarkers were assayed with chemiluminescent immunoassays.

Results

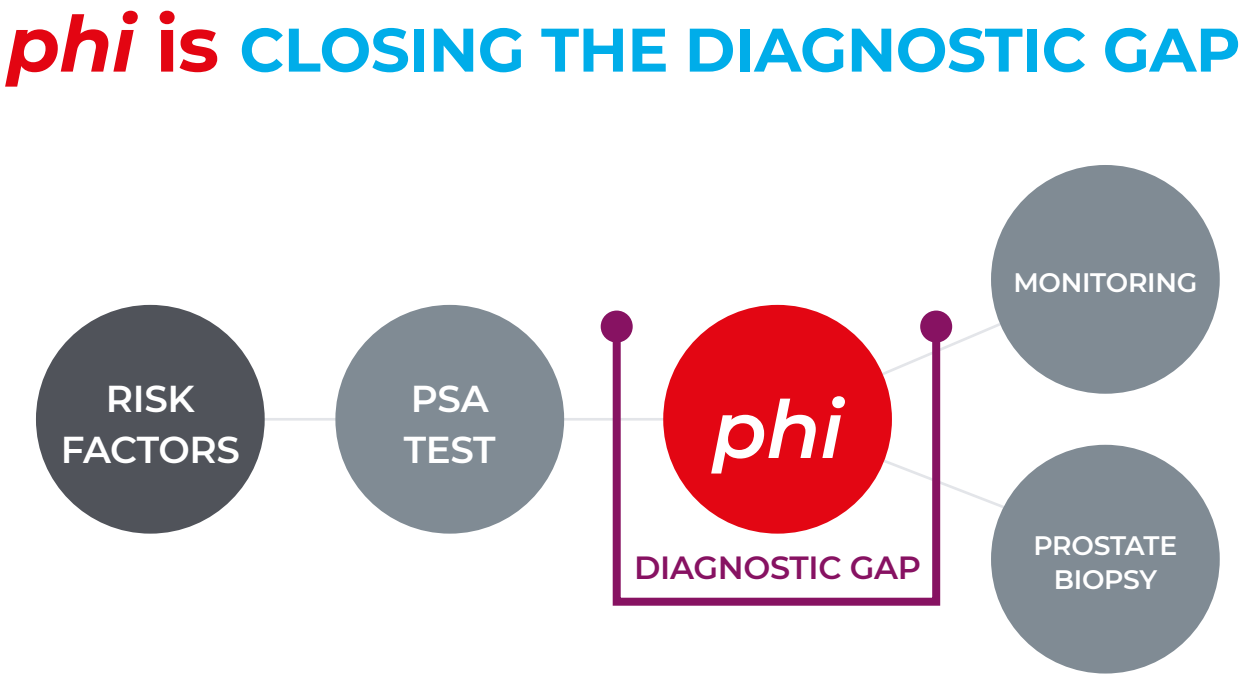
[-2]proPSA and Phi levels significantly and progressively increased over time in serum (+4.81% and +8.2% at 3 h; +12.03% and +14.91% at 5 h, respectively, vs. 1 h; $p<0.001$). Conversely, [-2]proPSA levels did not change in plasma (EDTA or P100). tPSA levels did not change over time in serum or plasma, whereas fPSA decreased in serum. All markers were higher in plasma than in serum at any time point. This difference did not seem to be attributable to the use of gel for serum preparation.

Conclusions

EDTA prevented spurious in vitro modifications in PSA-related isoforms, confirming that a stabilized blood sample is a prerequisite for [-2]proPSA measurement and Phi determination.

Agnello L. et al. “Prostate health index (PHI) as a reliable biomarker for prostate cancer: a systematic review and meta-analysis”, Clin Chem Lab Med 2022; 60(8): 1261–1277:

“PHI has a high accuracy for detecting PCa and discriminating between aggressive and non-aggressive PCa. Thus, it could be useful as a biomarker in predicting patients harbouring more aggressive cancer and guiding biopsy decisions.”



1 BLOOD COLLECTION

FOR *phi* TESTING

= 3 TESTS:

- **PSA**
- **%fPSA**
- ***phi***

BECKMAN COULTER