Original Article - Urological Oncology

Investig Clin Urol 2020;61:582-587.
https://doi.org/10.4111/icu.20200084
pISSN 2466-0493 • eISSN 2466-054X

INVESTIGATIVE AND CLINICAL UROLOGY
ICUROLOGY

Correlation between Gleason score distribution and Prostate Health Index in patients with prostate-specific antigen values of 2.5–10 ng/mL

Joongwon Choi[1], Minyong Kang[2], Hyun Hwan Sung[2], Hwang Gyun Jeon[2], Byong Chang Jeong[2], Seong Il Seo[2], Seong Soo Jeon[2], Hyun Moo Lee[2]

[1]Department of Urology, VHS Medical Center, Seoul, [2]Department of Urology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

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.

Keywords: Biomarkers; Diagnosis; Prostate neoplasms; Prostate-specific antigen

INTRODUCTION

Prostate cancer is the most common cancer in the United States, and there were an estimated 174,650 new cases (20% of total male cancer) in 2019 [1]. Prostate cancer is the second most common cause of cancer-related death (31,620/year, 10% of total) in the United States. In Korea, prostate cancer has the fourth-highest incidence rate and is the third most prevalent cancer in males [2].

Some research has indicated concerns for overdiagnosis [3], which could be related to diagnosis and treatment based on the measurement of prostate-specific antigen (PSA) [4]. Furthermore, as of 2012 the U.S. Preventive Services Task Force does not recommend prostate biopsies based on PSA screening, and they recommended in 2018 that PSA be measured only periodically in men aged 55 to 69 years [5,6].

Received: 12 March, 2020 • **Revised:** 18 June, 2020 • **Accepted:** 23 June, 2020 • **Published online:** 20 October, 2020
Corresponding Author: Hyun Moo Lee https://orcid.org/0000-0003-3969-4540
Department of Urology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Korea
TEL: +82-2-3410-6543, FAX: +82-2-3410-6992, E-mail: hyunmoo.lee@samsung.com

The Prostate Health Index (PHI) is a biomarker approved by the U.S. Food and Drug Administration since 2012, and the PHI, [-2]proPSA, and %free PSA have been reported as being more accurate tools than PSA [7,8]. There have been various reports on the PHI [9,10], since a large observational cohort study revealed the usefulness of the PHI for prostate cancer diagnosis [11]. Although the clinical benefits of the PHI have been reported in relation to detecting clinically significant prostate cancer (CSPC), and reducing unnecessary biopsies, only a limited number of papers have addressed the correlation between diagnosis and the Gleason score (G/S). Moreover, in our literature search, none of the articles analyzed the PHI by group in comparison with G/S distribution.

Regarding the cutoff value of PSA, various values such as 2.5, 3.0, and 4.0 ng/mL are used, depending on the hospital. Samsung Medical Center set 2.5 ng/mL as the cutoff value because our prior study demonstrated that PSA values of 2.5–4.0 and 4.0–10.0 ng/mL were not significantly different for prostate cancer detection or pathological findings [12]. In addition, there were no pathologic differences in G/S or rates of CSPC in the radical prostatectomy specimens with PSA of 2.5 to 4.0 and 4.0 to 10.0 ng/mL [13]. We conducted the present study to determine the clinical significance and correlation between G/S and PHI in patients with PSA values of 2.5 to 10.0 ng/mL.

MATERIALS AND METHODS

1. Study population

The Institutional Review Board of Samsung Medical Center approved this study (approval number: 2019-08-019). After receiving institutional review board approval, we reviewed 403 patients who underwent PSA and PHI tests from November 2018 to July 2019 in our hospital to investigate the usefulness of PHI for diagnosing prostate cancer (Fig. 1).

Patients with a PSA value between 2.5 and 10.0 ng/mL were included. Thirty-five patients who had PSA values below 2.5 ng/mL and 54 patients who had values above 10.0 ng/mL were excluded from the analysis. Of 134 patients who underwent prostate biopsy, 20 patients in whom the PHI was calculated after biopsy were excluded through a chart review because the effect of prostate biopsies on the PHI is unknown.

Finally, 114 patients in whom the PHI and PSA were measured in the outpatient clinic and who were clinically determined to require a prostate biopsy were included in the analysis. Namely, all specimens were collected before an initial prostate biopsy. None of the patients in whom the PHI was calculated took 5-alpha reductase inhibitors and none had associated bacterial prostatitis.

2. Study design

Various parameters were collected for each patient, including PSA, PHI, PSA density (PSAD), free PSA, p2PSA, and %free PSA. Correlations between these parameters and biopsy results were investigated, which included the G/S, cancer detection rate, and CSPC detection rate. We divided the PHI into four groups (0–26.9, 27.0–35.9, 36.0–54.9, and ≥55.0) on the basis of criteria outlined by White et al. [14]. The PHI was calculated using the method (p2PSA/free PSA)×√total PSA in accordance with the Beckman-Coulter Prostate Health Index formula. In addition, the sensitivity, specificity, false-positive rate, and false-negative rate for the diagnosis of prostate cancer and CSPC were compared in each group using parameters such as PSA, PHI, PSAD, and %free PSA. The diagnostic value and cutoff level for PSA, PHI, and PSAD were determined by using multivariable receiver operating characteristic (ROC) curve analysis.

3. Statistical analysis

All results are presented as a number with percent, mean with standard deviation, or median with interquartile range. We used the Kolmogorov-Smirnov test to analyze continuous variables for normality. The independent t-test and Mann-Whitney U-test were used to analyze descriptive variables. To determine if there was a correlation between the PHI and the detection rate of cancer and CSPC (Gleason score≥7), a linear polynomial trend model was used. Statistical analysis was executed using R ver. 3.5.1 (R Core Team, Vienna, Austria).

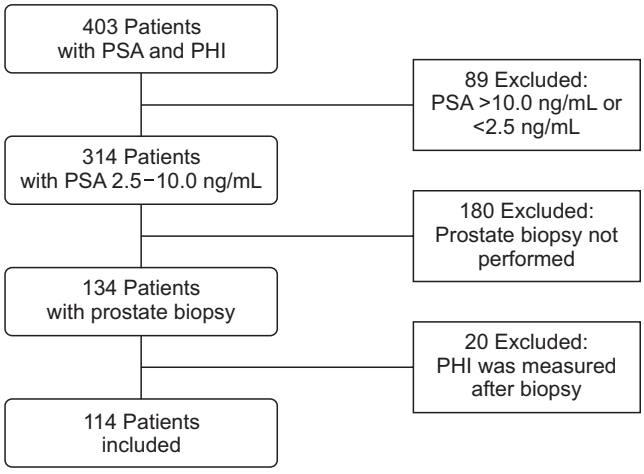

Fig. 1. Patient inclusion flow chart. PSA, prostate-specific antigen; PHI, Prostate Health Index.

Table 1. Baseline demographics

Variable	PHI				
	0–26.9 (n=11)	27.0–35.9 (n=17)	36.0–54.9 (n=50)	≥55.0 (n=36)	p-value
Age (y)	66.0 (62.5–68.0)	63.0 (54.0–67.0)	62.5 (59.0–69.0)	62.0 (55.5–67.0)	0.451
BMI (kg/m^2)	26.7±2.7	25.9±2.1	24.5±1.9	25.5±2.9	0.453
PSA (ng/mL)	4.9 (3.8–5.5)	5.3 (4.2–6.3)	4.8 (3.7–6.8)	6.7 (5.1–8.3)	0.014
PHI	22.7 (20.2–24.1)	32.2 (29.6–34.1)	42.7 (38.9–47.0)	70.2 (61.4–80.5)	<0.001
Prostate size (mL)	40.3 (34.7–75.2)	46.9 (32.7–54.6)	35.3 (27.4–54.5)	29.0 (24.5–50.1)	0.040
Total biopsy core	11.8±0.6	12.1±0.2	15.6±8.4	16.1±7.6	0.022
Target biopsy core	0.4±1.2	0.6±1.6	1.2±1.8	0.6±1.2	0.775
MRI findings (n=46)					
PI-RADS	3.0±1.4	3.6±0.9	3.1±1.0	3.2±1.6	0.957
ECE	0 (0.0)	0 (0.0)	0 (0.0)	3 (8.3)	0.243
Biopsy method					0.052
Transrectal	11 (100.0)	17 (100.0)	41 (82.0)	27 (75.0)	
Transperineal	0 (0.0)	0 (0.0)	9 (18.0)	9 (25.0)	
Free PSA	0.8 (0.5–0.9)	0.9 (0.6–1.3)	0.8 (0.5–1.2)	0.7 (0.5–1.2)	0.830
P2PSA	6.6 (5.3–9.0)	12.8 (6.6–16.9)	14.7 (8.6–19.6)	19.7 (13.1–27.7)	<0.001
%free PSA	13.0 (10.1–17.5)	18.0 (8.0–21.0)	14.5 (8.0–18.0)	10.5 (6.5–13.0)	0.041
Biopsy times					0.344
Initial	10 (90.9)	14 (82.4)	36 (72.0)	24 (66.7)	
Repeat	1 (9.1)	3 (17.6)	14 (28.0)	12 (33.3)	

Values are presented as median (interquartile range), mean±standard deviation, or number (%).
PHI, Prostate Health Index; BMI, body mass index; PSA, prostate-specific antigen; MRI, magnetic resonance imaging; PI-RADS, Prostate Imaging Reporting and Data System; ECE, extracapsular extension.

RESULTS

Table 1 shows the baseline characteristics and age of the patients. Body mass index was comparable between the 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 98 of 114 patients (86.0%) underwent measurement of PHI and PSA on the same day, with an average difference of 1.6 days. Of the total cases, 96 were transrectal biopsies (84.2%) and 18 were transperineal biopsies (15.8%). On average, 12.0 cores (range, 9-14) were obtained during transrectal biopsy, and 30.3 cores (range, 24-38) during transperineal biopsy. A total of 37 patients (32.5%) were diagnosed with prostate cancer and 28 (24.6%) with CSPC after prostate biopsy.

The cancer detection rate gradually increased with PHI group (18%, 24%, 30%, and 44%, respectively, Fig. 2; p=0.052). The same pattern was observed for the detection of CSPC (0%, 18%, 26%, and 33%, respectively) with statistical significance (p=0.022). There was no CSPC in the group with PHI <27.0.

As the PHI increased, the ratio of high G/S also increased (Fig. 3). G/S 7 began to appear in groups with PHI ≥27.0, particularly for G/S 8 and 9 patients, who were distributed only in the groups with PHI ≥36.0. The ratio of G/S 9 was highest in the group with PHI ≥55.0 (24%).

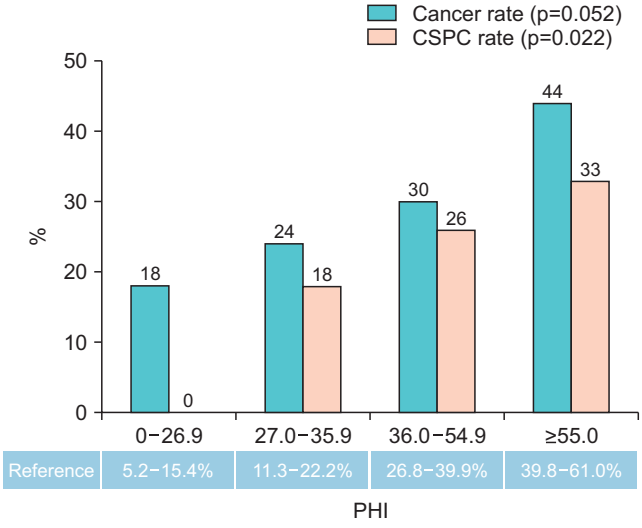

Fig. 2. Prostate cancer detection rate by PHI group. PHI, Prostate Health Index; CSPC, clinically significant prostate cancer.

The sensitivity, specificity, false-positive rate, and false-negative rate for the detection of cancer were calculated for PSA, PHI, PSAD, and %free PSA (Supplementary Table 1). The results indicated acceptable (84%) sensitivity based on a PHI ≥36.0 and PSA ≥2.5.

https://doi.org/10.4111/icu.20200084

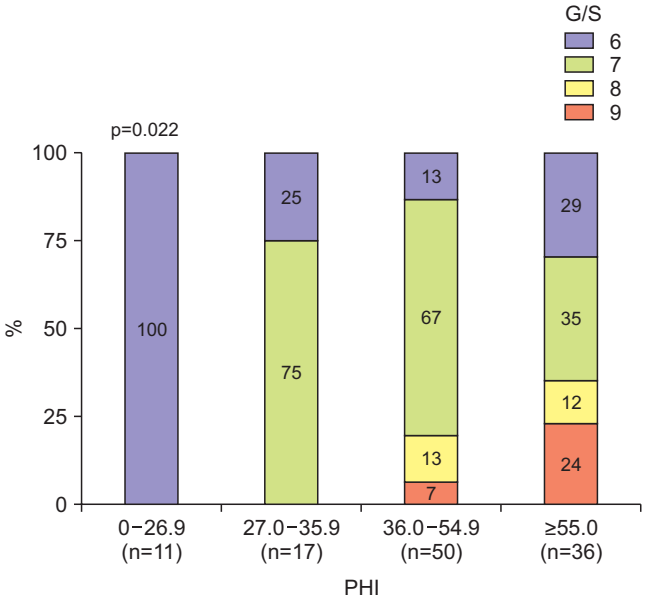

Fig. 3. Gleason score distribution by PHI group. G/S, Gleason score; PHI, Prostate Health Index.

The single PSA, PHI, and PSAD parameters in the univariate ROC analysis had a low detection rate of CSPC (Supplementary Fig. 1), but an optimal cutoff value (PHI=40.7; PSA=2.87; PSAD=0.1) was shown in the multivariable ROC analysis (area under the curve, AUC=0.681). The analysis showed a higher diagnostic value for CSPC when considering various parameters such as PSA, PHI, and PSAD.

If the biopsy criterion was based on a PSA ≥2.5 and PHI ≥27.0, the total number of biopsies could be reduced by 9.6% compared with a single PSA value of 2.5 (103/114), and 24.6% if the criteria were PSA ≥2.5 and PHI ≥36.0 (86/114) in our study. If PHI ≥27.0 is used with PSA ≥2.5 as criteria, the cancer detection decreased 5.4% (2/37) and the detection of CSPC decreased 0% (0/28). If PHI ≥36.0 was used with PSA, cancer detection decreased by 16.2% and CSPC detection by 10.7%.

DISCUSSION

We conducted this study to investigate the usefulness of correlating PHI results with biopsy examinations including G/S. As the PHI increased, the detection rate of prostate cancer and CSPC also showed a gradual increase. A PHI cutoff of 27 served as a boundary with a G/S of 7, and a PHI of 36 was a boundary for G/S 8 and 9 in our study. The study demonstrated that the PHI is an effective tool for assessing patients with PSA levels between 2.5 and 10 ng/mL. Of course, this study was a relatively small-sized study, so there are limitations to generalizing our findings. In a previous study, detection rates of CSPC ranged from 29% to 34% with PHI cutoffs of 20 to 40 [15]. However, with careful recommendation, because no CSPC was detected in patients with a PHI <27.0, biopsy could be omitted in those patients. If the PHI is 36.0 or higher, biopsy should be considered because there is a 20% probability of cancer with G/S 8 or higher. Values of PSA 2.87, PHI 40.7, and PSAD 0.1 were determined to be optimal cutoffs for the detection of CSPC. Similar to our study, Tan et al. [16] suggested considering biopsy with PHI, PSAD, and PI-RADS (Prostate Imaging Reporting and Data System) ≥3 lesions on magnetic resonance imaging (MRI).

Many reports have discussed the usefulness of the PHI, particularly for specific patient groups. First, de la Calle et al. [15] reported that the PHI is effective in biopsy-naïve populations. Second, a prospective study indicated that the PHI is significantly more accurate in obese men, who were previously shown to have a higher risk for aggressive prostate cancer [17]. Third, Abrate et al. [17] suggested that the PHI and %p2PSA are more accurate than a standard PSA test in men under 60. Fourth, correlations between the total tumor volume (>0.5 cc) and the extracapsular extension after radical prostatectomy with PHI have also been evaluated [18]. Finally, in the patient group with PSA of 1.6–8.0 ng/mL, PHI was more useful than total PSA or %freePSA, regardless of an initial or repeat biopsy setting [19]. Additional research focused on the accuracy of PHI is ongoing, and some authors have hypothesized that PHI will gradually replace PSA [20]. Recently, proposals for a better cost-benefit strategy have suggested that the PHI is much more economical than a total PSA-based strategy [21]. In addition, a large-volume, multicenter study reported that the PHI is more effective for cancer detection than PSA in both European and Asian settings [22]. Further, there could be a potential association of the PHI with mpMRI (multiparametric MRI) that could represent a promising combination that would change preoperative therapeutic decisions in selective patients with prostate cancer.

There is currently no clear consensus about a PHI cutoff criterion. In our study, cutoffs of 27, 36, and 55 were used, but other studies have reported cutoffs of 35 and 38 and have even suggested 45.9 [20,23,24]. Some authors have argued that a single cutoff criterion cannot accurately predict the risk for prostate cancer and that multiple factors should be used, taking age, prostate volume, and PHI into account [25].

In addition, although our study covered only patients with PSA values between 2.5 and 10 ng/mL, two other studies have indicated that PHI was more useful than PSA for diagnosing prostate cancer and the studies reported high-

grade conditions even in the patient population with PSA >10 ng/mL [26,27]. We believe that there will be continuous reporting on the value of PHI and that more accurate and sensitive cutoff values will be defined.

Additional studies have focused on other diagnostic parameters. For example, the TK1 protein was reported to be an important factor for diagnosing prostate cancer with consideration of other parameters such as total PSA, free PSA, PSAD, and PHI [28]. It is expected that additional variable parameters will be identified in the future to enhance diagnostic accuracy and prostate cancer treatment.

Consideration of cost-effectiveness is also needed. In Korea, it costs 12.95 dollars for a PSA test and 20.68 dollars for a PHI test. In addition, in most hospitals, PSA can be examined on the same day, but results on the PHI take about 2 to 3 days. In this study, the AUC of the PHI was found to be lower than that of PSAD and, even considering PHI, PSA, and PSAD, the AUC was significantly lower at 0.681 (Supplementary Fig. 1). Therefore, it may be beneficial to consider PSAD more actively when considering cost.

There were some limitations to this study. First, it had a retrospective study design, which limits patient selection, regardless of inclusion and exclusion criteria. Second, transrectal and transperineal biopsy patient data were collected together, and mpMRI was not routinely carried out before biopsies. Third, the PHI is not in use worldwide as a reflex test and is in fact mostly used in the research setting rather than in clinical practice. Fourth, we did not consider several clinical conditions (i.e., chronic renal disease, hemophilia, marked alterations in blood protein levels) that could alter the concentration of fPSA and, consequently, of p2PSA, as p2PSA is the molecular isoform of fPSA. Although many papers have reported that the PHI can help in CSPC detection, or reduce unnecessary biopsies, not many articles have addressed the correlation with G/S. Moreover, only a few papers, including this study, have examined G/S distributions by PHI group. Further, we believe that there is benefit to using a blood test like the PHI that might be cheaper and more practical than other more sophisticated tests (i.e., genomic tests) and that does not require vigorous rectal examination (like PCA3). Therefore, this analysis contributes a unique perspective in this field, and additional studies are needed to further assess these results with a larger patient population.

CONCLUSIONS

In summary, the detection rate of CSPC could be increased when prostate biopsies are performed in patients with PHI ≥36.0. When the PHI cutoff value was set to 27.0 and 36.0, the G/S difference for each respective group was clear. These results suggest that the PHI is an appropriate tool that can be used as a criterion for biopsy, particularly in patients with a PSA value between 2.5 and 10 ng/mL.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

AUTHORS' CONTRIBUTIONS

Research conception and design: Hyun Moo Lee, Seong Soo Jeon, and Seong Il Seo. Data acquisition: Minyong Kang and Hyun Hwan Sung. Data analysis and interpretation: Hwang Gyun Jeon, Byong Chang Jeong, and Joongwon Choi. Drafting of the manuscript: Joongwon Choi. Critical revision of the manuscript: Hyun Moo Lee. Approval of the final manuscript: Seong Soo Jeon and Hyun Moo Lee.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4111/icu.20200084.

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin 2019;69:7-34.
2. Jung KW, Won YJ, Kong HJ, Lee ES. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2016. Cancer Res Treat 2019;51:417-30.
3. To screen or not to screen for prostate cancer? Lancet 2012;379:2024.
4. Kim EH, Andriole GL. Prostate-specific antigen-based screening: controversy and guidelines. BMC Med 2015;13:61.
5. Moyer VA; U.S. Preventive Services Task Force. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2012;157:120-34.
6. US Preventive Services Task Force, Grossman DC, Curry SJ, Owens DK, Bibbins-Domingo K, Caughey AB, et al. Screening for prostate cancer: US Preventive Services Task Force recommendation statement. JAMA 2018;319:1901-13.
7. Lazzeri M, Haese A, Abrate A, de la Taille A, Redorta JP, McNicholas T, et al. Clinical performance of serum prostate-specific antigen isoform [-2]proPSA (p2PSA) and its derivatives, %p2PSA and the prostate health index (PHI), in men with a family history of prostate cancer: results from a multicentre European study, the PROMEtheuS project. BJU Int

2013;112:313-21.
8. Stephan C, Vincendeau S, Houlgatte A, Cammann H, Jung K, Semjonow A. Multicenter evaluation of [-2]proprostate-specific antigen and the prostate health index for detecting prostate cancer. Clin Chem 2013;59:306-14.
9. Lughezzani G, Lazzeri M, Haese A, McNicholas T, de la Taille A, Buffi NM, et al. Multicenter European external validation of a prostate health index-based nomogram for predicting prostate cancer at extended biopsy. Eur Urol 2014;66:906-12.
10. Loeb S, Catalona WJ. The Prostate Health Index: a new test for the detection of prostate cancer. Ther Adv Urol 2014;6:74-7.
11. Lazzeri M, Haese A, de la Taille A, Palou Redorta J, McNicholas T, Lughezzani G, et al. Serum isoform [-2]proPSA derivatives significantly improve prediction of prostate cancer at initial biopsy in a total PSA range of 2-10 ng/ml: a multicentric European study. Eur Urol 2013;63:986-94.
12. Kim HS, Jeon SS, Choi JD, Kim W, Han DH, Jeong BC, et al. Detection rates of nonpalpable prostate cancer in Korean men with prostate-specific antigen levels between 2.5 and 4.0 ng/mL. Urology 2010;76:919-22.
13. Lee HW, Jeon HG, Jeong BC, Seo SI, Jeon SS, Choi HY, et al. Comparison of pathological and biochemical outcomes after radical prostatectomy in Korean patients with serum PSA ranges. J Korean Med Sci 2015;30:317-22.
14. White J, Shenoy BV, Tutrone RF, Karsh LI, Saltzstein DR, Harmon WJ, et al. Clinical utility of the Prostate Health Index (phi) for biopsy decision management in a large group urology practice setting. Prostate Cancer Prostatic Dis 2018;21:78-84.
15. de la Calle C, Patil D, Wei JT, Scherr DS, Sokoll L, Chan DW, et al. Multicenter evaluation of the prostate health index to detect aggressive prostate cancer in biopsy naïve men. J Urol 2015;194:65-72.
16. Tan TW, Png KS, Lee CH, Yuwono A, Yeow Y, Chong KT, et al. MRI fusion-targeted transrectal prostate biopsy and the role of prostate-specific antigen density and prostate health index for the detection of clinically significant prostate cancer in Southeast Asian men. J Endourol 2017;31:1111-6.
17. Abrate A, Lazzeri M, Lughezzani G, Buffi N, Bini V, Haese A, et al. Clinical performance of the Prostate Health Index (PHI) for the prediction of prostate cancer in obese men: data from the PROMEtheuS project, a multicentre European prospective study. BJU Int 2015;115:537-45.
18. Cantiello F, Russo GI, Ferro M, Cicione A, Cimino S, Favilla V, et al. Prognostic accuracy of Prostate Health Index and urinary Prostate Cancer Antigen 3 in predicting pathologic features after radical prostatectomy. Urol Oncol 2015;33:163.e15-23.
19. Boegemann M, Stephan C, Cammann H, Vincendeau S, Houlgatte A, Jung K, et al. The percentage of prostate-specific antigen (PSA) isoform [-2]proPSA and the Prostate Health Index improve the diagnostic accuracy for clinically relevant prostate cancer at initial and repeat biopsy compared with total PSA and percentage free PSA in men aged ≤65 years. BJU Int 2016;117:72-9.
20. Loeb S. Time to replace prostate-specific antigen (PSA) with the Prostate Health Index (PHI)? Yet more evidence that the PHI consistently outperforms PSA across diverse populations. BJU Int 2015;115:500.
21. Mathieu R, Castelli C, Fardoun T, Peyronnet B, Shariat SF, Bensalah K, et al. Cost analysis of prostate cancer detection including the prostate health index (phi). World J Urol 2019;37:481-7.
22. Chiu PK, Ng CF, Semjonow A, Zhu Y, Vincendeau S, Houlgatte A, et al. A 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. Eur Urol 2019;75:558-61.
23. Nordström T, Vickers A, Assel M, Lilja H, Grönberg H, Eklund M. Comparison between the four-kallikrein panel and Prostate Health Index for predicting prostate cancer. Eur Urol 2015;68:139-46.
24. Lopes Vendrami C, McCarthy RJ, Chatterjee A, Casalino D, Schaeffer EM, Catalona WJ, et al. 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. Urology 2019;129:153-9.
25. Zhu Y, Han CT, Zhang GM, Liu F, Ding Q, Xu JF, et al. Development and external validation of a prostate health index-based nomogram for predicting prostate cancer. Sci Rep 2015;5:15341.
26. Na R, Ye D, Qi J, Liu F, Helfand BT, Brendler CB, et al. Prostate health index significantly reduced unnecessary prostate biopsies in patients with PSA 2-10 ng/mL and PSA >10 ng/mL: results from a multicenter study in China. Prostate 2017;77:1221-9.
27. Lazzeri M, Lughezzani G, Haese A, McNicholas T, de la Taille A, Buffi NM, et al. Clinical performance of prostate health index in men with tPSA>10ng/ml: results from a multicentric European study. Urol Oncol 2016;34:415.e13-9.
28. Jagarlamudi KK, Zupan M, Kumer K, Fabjan T, Hlebič G, Eriksson S, et al. The combination of AroCell TK 210 ELISA with Prostate Health Index or prostate-specific antigen density can improve the ability to differentiate prostate cancer from noncancerous conditions. Prostate 2019;79:856-63.