

Application of the prostate health index in the early diagnosis and treatment of prostate cancer

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Prostate cancer (PCa) is one of the common diseases affecting men's health. Early diagnosis and treatment play a crucial role in improving the prognosis of patients. Currently, prostate-specific antigen (PSA) is the most widely used serological indicator in prostate cancer screening, and it plays a very important role in increasing the early diagnosis rate and reducing the mortality rate. However, PSA has a relatively high sensitivity, causing many non-prostate cancer patients to undergo unnecessary biopsy or excessive treatment. Compared with PSA, the new serological indicator, prostate health index (PHI) has higher therapeutic value. PHI can reduce unnecessary biopsy and can also evaluate the prognosis of patients undergoing radical prostatectomy (RP), increase the enthusiasm of patients for active monitoring, and provide important information for clinicians to formulate the next treatment plan. Although PSA and magnetic resonance imaging (MRI) have demonstrated excellent results in improving the diagnostic accuracy of prostate cancer, there are still some unstandardized limitations that require further research. Above all, we aim to explore the limitations of PHI in prostate diagnosis and identify areas for improvement.

Firstly, it is necessary to clearly state the type of grading to obtain the fPSA and tPSA, which is extremely important for the comparison of results. According to Stephan *et al.* [1], there was a difference of 20% between the use of WHO standards and Hybritech standards. However, due to changes adopted by biomedical manufacturers, in recent years a decrease in differences has been described, with values 6.7% higher of tPSA using the Mindray system (WHO standards) compared to beck-man (Hybritech standards). Given these data and the differences they present, it is possible to consider the differences in the calculation methods used when calculating PHI, which may have

an impact on the diagnosis of prostate cancer.

AUA guideline recommends the initiation of prostate cancer screening from the age of 40 to 45 years in patients at higher risk for either family history, identified mutations, among others. In addition to the age range is essential for the evaluation of diagnostic accuracy and whether biomarkers are compared. The little significant difference is observed in the comparison of PSA levels between individuals with and without cancer. This is probably due to the records of the patients themselves; since there is indicative evidence that PSA levels are linked to variables such as infection and even the ingestion of certain drugs. Studies suggest that PHI and fPSA/tPSA ratio perform differently across age groups due to biological changes, influencing biopsy decision-making. In clinical applications, setting different threshold values for these biomarkers based on age can enhance the accuracy of diagnosis, especially in patients over 60 years old, as the risk of having clinically significant prostate cancer increases at this age [2, 3]. Although establishing a unified PHI threshold based on age, race, clinical symptoms and other factors can enhance the diagnostic value of PSA gray zone prostate cancer, the lack of multi-center studies involving different racial populations has hindered the widespread adoption of PHI [4].

Unnecessary biopsy procedures were prevented with the combined use of PHI and multiparametric MRI (mpMRI). Yoshitaka Sekine *et al.* reported that for patients with PI-RADS 3 and $\text{PHI} \geq 43.5$, performing a biopsy can reduce the number of biopsies by 42% [5]. Although the data is considerable, the critical value of PHI, the relatively high PHI of the patients and the small sample size are all limitations. Therefore, further investigations on more cases are needed to determine the critical value of PHI when used in combination with MRI.

Current studies have demonstrated that the combined use of PHI and mpMRI enhances diagnostic accuracy for early-stage prostate cancer. However, given the high cost of MRI examinations, further research is needed to evaluate the effectiveness of combining different diagnostic markers with PHI, thereby improving diagnostic efficiency and clinical benefits. Additionally, the efficacy of integrating various diagnostic markers with PHI requires further investigation to be fully demonstrated.

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