



New insights on the early prostate cancer diagnosis in a real-world setting

A systemic survey for the global burden of disease (GBD) 2017 study estimation methods described cancer incidence especially prostate cancer (PCa) is 1.3 million cases [1]. The national epidemiological outline of tumor burden in the GBD study manifest large heterogeneities, which are a consideration of various exposures to risk factors, economic status, lifestyles, and opportunity to approach medical care and health screening [1]. As a consequence, number of prostate-specific antigen (PSA) screening resulted number of new cases who diagnosed for PCa is nearly 90% in the United States are clinically localized disease [2]. Recently, a randomized trial done by Johansson et al. [3] and Holmberg et al. [4], described that radical prostatectomy possibly lower the death rate in early PCa by approximately 50%.

Since prostate biopsy as a gold standard technique and considering its pros and cons studies focused on risk prediction models to assess PCa risk thus avoiding negative biopsy. Recent comment on risk-stratified approach for timely diagnostic strategies on imaging and therapy argued and decision on analytical model is based on parameter estimates from available randomized clinical trials and likely reflects how a real-world screening program would occur.

By referring to the Schröder et al. [5] on decision analytical model adhered the protocols and based on the recommendations from the European Randomized Study of Screening for Prostate Cancer (ERSPC) these studies screened strategies that yield the greatest improvements in the harm profile benefit and cost-effectiveness was associated with better outcomes such as fewer PCa-specific deaths, overdiagnoses, and biopsies, it was significantly inferior compared with risk-stratified screening using MRI strategy compared with biopsy-first age-based screening. Moreover, the study highlighted age limits in screening study between ages 55 to 69 years from cohorts receiving PSA testing every 4 years, with all screening stopping at age 69 years. But this model almost half of cancers would not be diagnosed until after the screening period, which naturally raises the question

of whether future screening should be continued beyond age 69 years in a population with a consistently longer life expectancy. One more study on Chinese based population studies using ERSPC risk calculator has been documented via exploration of multivariate model for risk assessments in the PSA gray zone PCa without the need of biopsy. In the view of diagnostic gray zone of PSA, when patients with digital rectal examination (DRE) technique results and elevated PSA levels of 4.0 to 10.0 ng/mL have been considered as a high-risk patients (25% cancer rate) especially total PSA (tPSA) value compared to 4% cancer rate men older than 50 years. Most cases, 75% of biopsy findings are negative and specificity can be improved. Early studies suggest that PSA screening and specificity can be enhanced in the patients' group where the use of free PSA percentage and reduce the number of unnecessary biopsies. An aspect of particular interest that less free PSA or cut-off of 25% showed that the detection rate of cancers nearly 95% those perform a biopsy for patients at or below above said cut-off and spare 20% of patients with benign prostatic disease from biopsy.

Another interesting study from Korean group Jin et al. [6], recently demonstrated PSA with a cut-off value <3 ng/mL is relatively more sensitive and specific than PSA ≥ 3 ng/mL and did not show any significant differences neither sensitivity nor specificity during the diagnosis of PCa. Due to this reason, Jin et al. [6], offers clinicians may select the appropriate PSA cut-off value based on clinical episode regarding patients' attribution related to the risk of PCa.

Collectively, old studies shown the capacity of free PSA % to enhance the specificity of PSA testing in PCa detection, developed guidelines for usage of free PSA % in clinical utility, and resolved the relationships between free PSA % and the histopathologic aspects of the PCa detected. This explains why there is need for predictive model for prostate biopsy. Interestingly, retrospective, multicenter, and real-world approach study on 2,426 Chinese patients undergone first time prostate biopsy demonstrated positive biopsy rate in various

subgroup of patients and assessed the importance of predictive factors for positive biopsy and avoiding unnecessary biopsy by clinicians. In their study, highlighted risk prediction modeling for PSA 4 to 10 ng/mL under gray zone PCa was developed with help of univariate and multivariate logistic regression analyses has been identified the risk factors of PCa among Chinese population for better clinical strategy to overcome negative biopsy.

These authors demonstrated correlation of positive biopsy rate (47.57%, 25.77%, 60.57%) whereas patients with total PSA 4 to 10 ng/mL, patients with PSA >10 ng/mL respectively from the total patients in a clinical setting. Interestingly, in this study focused on the elderly population age 60 to 74 years, ≥ 75 years, pre-operative PSA >10 ng/mL and PSA density (PSAD), multi parametric magnetic resonance imaging (mpMRI) significantly increased the overall positivity rate of population. In their cohort study that targeted PSA 4 to 10 ng/mL population with parameters such as elderly age, mpMRI and positive DRE and free PSA were significant predictors for positive biopsy has been considered. Successfully, patients with positive biopsy rate have been assessed with risk prediction model with PSA in the gray zone were shown and area under curve has been determined in association with low accuracy for all the variables such as tPSA, PSAD, frequency of puncture and mpMRI in prediction of positive rate of biopsy. This model recapitulates with the indicate report recently align to univariate analysis revealed that PSAD, prostate volume, and mpMRI examination show in their report statistically significant predictors of PCa and PCa with Gleason score (clinically significant PCa [csPCa] ≥ 7) whereas the multivariate models PCa and csPCa performed significantly better than mpMRI study for patients with PSA level in the gray zone detected PCa and csPCa. Collectively, supporting data suggest that considering sensitivity and diagnostic accuracy by mpMRI study for PCa, implementing models such as multivariate might decrease the number of biopsies by 5% compared with mpMRI approach. This in concordance with Korean study from Choi et al. [7], correlates the diagnostic accuracy of CSPCa detection could be increased when prostate biopsy is assessed in patients with a Prostate Health Index (PHI) ≥ 36.0 . Interestingly, their study from Samsung Medical Center (Seoul, Korea) revealed that there was a clear Gleason score difference when the PHI cutoff value was set to 27.0 or 36.0 summarizing PHI is an additional tool that can be used as a selection criteria for biopsy, especially in patients with a PSA value ranging from 2.5 and 10 ng/mL [7].

Overall, study revealed that multivariate model can reduce unnecessary biopsies without distinctly affecting

the ability to diagnose PCa and csPCa. In this perspective, the potential usage of univariate and multivariate models support as a risk prediction would pave a new avenue and paradigm for accurate diagnosis and avoiding unnecessary prostate biopsy with gray zone PSA in the real-world settings.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHORS' CONTRIBUTIONS

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