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AUA2022: BEST POSTERS SelectMDx and Multiparametric Magnetic Resonance Imaging Improve the Diagnostic Workup for the Detection of Prostate Cancer in Biopsy-naive Men

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The current paradigm of early detection of prostate cancer (PCa) based on the sole prostate specific antigen (PSA) testing has poor specificity, and it is associated with a substantial risk of over-diagnosis and over-treatment in many healthy men.[1] In order to tailor risk stratification and optimize PCa detection workup (ie, to reduce unnecessary prostate biopsies and diagnosis of indolent PCa cases), several tools have been introduced to overcome PSA limits.[2-5] In this scenario, improvements have been reached with the increased use of multiparametric magnetic resonance imaging (mpMRI) as one of the main diagnostics for PCa and as a tool for target biopsy.[1] Indeed, mpMRI has recently transformed the way PCa is diagnosed and risk stratified, it having proved to minimize the number of unnecessary biopsies in men with a clinical suspicious of PCa and to improve the detection of clinically significant prostate cancer (csPCa), so that it is currently recommended before performing prostate biopsy.[1] With the same intent, during the last decade, several urine and blood biomarkers have been developed.[6,7] SelectMDx is a novel biomarker-based risk score for assessing urinary HOXC6 and DLX1 mRNA expression combined with traditional clinical risk factors.[8]

The aim of our prospective multi-institutional study was to evaluate the diagnostic accuracy of SelectMDx and its interplay with mpMRI for the prediction of PCa and csPCa in prostate biopsies.[9] In our cohort, 310 consecutive biopsy-naïve men scheduled for prostate biopsy based on PSA values and/or digital rectal examination (DRE) results, underwent SelectMDx and mpMRI prior to prostate biopsy.

According to our analysis, SelectMDx demonstrated to be a valid diagnostic tool for the detection of PCa, yet, with regards to csPCa diagnosis, it showed a reliable diagnostic performance, comparable to that of mpMRI. Specifically, SelectMDx score was positive in 86.5% of PCa, in 87.1% of csPCa, and in 26.2% of cases with no PCa at biopsy. Compared to mpMRI, SelectMDx had the best performance in predicting PCa and csPCa after biopsy. We reported that in patients before initial biopsy it could achieve high levels of sensitivity and specificity for the diagnosis of all PCa (AUC 0.80), while it seems slightly less effective in detecting csPCa (AUC 0.75). On the contrary, mpMRI demonstrated a better diagnostic performance with respect to csPCa outcome (AUC 0.73), than to PCa outcome (AUC 0.70; parts A and B of Figure).

Figure. SelectMDx score and multiparametric magnetic resonance imaging (mpMRI) Prostate Imaging-Reporting and Data System score performance evaluated as area under the curve (AUC) of the receiver operating characteristics in predicting prostate cancer (A) and clinically significant prostate cancer (B) histological diagnosis at biopsy. CI indicates confidence interval; SE, standard error.

In the era of mpMRI pathway, to aid clinicians in decision making (ie, to decide whether a prostate biopsy can be omitted as an effort to avoid/delay unnecessary biopsy), and to optimize PCa diagnosis (ie, to improve the detection of csPCa while minimizing the detection of indolent cases), combining mpMRI with serum biomarkers would be of clinical value. According to our data, SelectMDx showed a significant association with mpMRI results in terms of Prostate Imaging-Reporting and Data System (PI-RADS®) score, as test positivity significantly increased according to PI-RADS score ($P < .001$). Moreover, the association of mpMRI and SelectMDx compared to the association of mpMRI and other clinical tools (ie, PSA and PSA density) had the best performance.

To further explore the potential interplay of SelectMDx and mpMRI for an improved workup for the detection of PCa, we simulated several strategies of combining and sequencing these 2 tools, evaluating their impact in terms of number of avoided biopsies, missed PCa and csPCa (see Table). According to our results, limiting biopsy to men with a mpMRI PI-RADS score 4-5 would have resulted in avoiding 74.8% of biopsies, yet missing 38.7% of csPCa. Interestingly, implementing SelectMDx evaluation after a mpMRI PI-RADS score 1-3 to prompt biopsy appeared to be a reliable strategy to avoid unnecessary biopsies, with a reasonable csPCa detection rate. Indeed, up-front mpMRI followed by biopsy for positive mpMRI cases (PI-RADS 4-5) and negative mpMRI cases (PI-RADS 1-3) only if SelectMDx was positive, would have resulted in avoiding 45.8% of biopsies, while only missing 7.7% of PCa and 6.5% of csPCa. SelectMDx could also have a potential role in lowering the number of mpMRI scans and biopsies performed, without increasing the risk of missing csPCa. However, according to our data, up-front SelectMDx, although associated with 82.6% of avoided biopsies, has led to a high rate of missed csPCa (45.2%).

Table. Prostate Cancer and Clinically Significant Prostate Cancer Detection Rate, Avoided Biopsies and Missed Prostate Cancer and Clinically Significant Prostate Cancer Among the Study Population According to Different Strategies

Strategy	Avoided biopsies (n=310) No. (%)	PCa (n=104) No. (%)		csPCa (n=62) No. (%)	
		Detected	Missed	Detected	Missed
1	166 (53.5)	90 (86.5)	14 (13.5)	54 (87.1)	8 (12.9)
2	178 (57.4)	86 (82.7)	18 (17.3)	52 (83.9)	10 (16.1)
3	232 (74.8)	54 (51.9)	50 (48.1)	38 (61.3)	24 (38.7)
4	220 (71.0)	74 (71.1)	30 (28.9)	46 (74.2)	16 (25.8)
5	256 (82.6)	48 (46.1)	116 (53.9)	34 (54.8)	28 (45.2)
6	124 (40.0)	102 (98.1)	2 (1.9)	60 (96.8)	2 (3.2)
7	142 (45.8)	96 (92.3)	8 (7.7)	58 (93.5)	6 (6.5)

Abbreviations: csPCa, clinically significant prostate cancer; PCa, prostate cancer.
Strategy 1: get a SelectMDX test alone and biopsy any positive test; strategy 2: get a multiparametric magnetic resonance imaging (mpMRI) alone and biopsy any positive mpMRI, considered as Prostate Imaging-Reporting and Data System (PI-RADS) score 3-5; strategy 3: get an mpMRI alone and biopsy any positive mpMRI, considered as PI-RADS score 4-5; strategy 4: get a SelectMDx test first and if negative do not biopsy; if positive get an mpMRI and do a biopsy only if it is positive (considered as PI-RADS score 3-5); strategy 5: get a SelectMDx test first and if negative do not biopsy; if positive get an mpMRI and do a biopsy only if it is positive (considered as PI-RADS score 4-5); strategy 6: get an mpMRI first and if positive (considered as PI-RADS score 3-5) do a biopsy; if negative get a SelectMDx and do a biopsy only if it is positive; strategy 7: get an mpMRI first and if positive (considered as PI-RADS score 4-5) do a biopsy; if negative get a SelectMDx and do a biopsy only if it is positive.

Since PI-RADS 3 lesions at mpMRI are equivocal by nature and several possible clinical factors have been evaluated as predictors of positive biopsy, we further explored the potential value of SelectMDx as a decision-making tool in this particular scenario (ie, whether a prostate biopsy versus observation should be advised in PI-RADS 3 cases). In our clinical experience, performing a biopsy only in those with a positive SelectMDx would have resulted in the detection of 81.3% of PCa and 85.7% of csPCa diagnosed within this category. Of note, using PSA density with a cutoff value of ≥0.15 to decide on the need for biopsy did not show a clinical benefit for the detection of PCa and csPCa.

It should be noted that our results could be at least partially affected by variability in mpMRI-related factors (ie, inter-reader variability, readers experience, and technical performance) mainly due to the multicentric nature of our study, and that a cost-effectiveness analysis of SelectMDx compared to mpMRI is needed before drawing definitive conclusions. However, several points of interest have emerged from our clinical experience, suggesting that the implementation of SelectMDx can improve the current diagnostic workup for the detection of PCa.

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