COMMENTARY

Re: Clinical utility of multiple secondary combined tests in prostate cancer screening

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Referring to article published on pp. 11538-11544 in this issue.

HEINLEN JE. Re: Clinical utility of multiple secondary combined tests in prostate cancer screening. *Can J Urol* 2023;30(3):11545.

The authors present a series of patients with elevated PSA who underwent testing with two separate panels: the Prostate Health Index (PHI) and ExosomeDx Prostate Intelliscore (EPI). As a retrospective study, the decision to obtain either panel was at the discretion of the surgeon and based on the unknowable factors which go into each patient encounter of this nature. The results bear out significant discordance between the two panels, in particular in the area of specificity and positive predictive value (PPV). The outcomes were analyzed primarily through the lens of the detection rate of clinically significant prostate cancer (csPCA) in cases where either or both tests were positive or negative. As the authors point out, there are very few studies in which the performance of different panels are evaluated within the same cohort and from this perspective, there is value in the data.[1]

Readers should be cautioned in their interpretation. Although the results of the panels did influence the recommendation for biopsy, it is curious that nearly 20% of the patients for whom both panels were positive were not recommended biopsy - and this represents missing information that could be valuable. This highlights a significant problem - that the biases of the clinicians involved are not accounted for in the study design due to its retrospective nature and calls into question other factors that could have contributed to the ultimate end results.

The authors state in the discussion that while EPI had a helpful negative predictive value (NPV), the PPV was actually quite poor. This means that a negative test would rule out need for a biopsy but a positive test would be essentially meaningless. In cases where the EPI was positive but PHI was negative, the rate of csPCA was identical to when both tests where negative. Similarly, when EPI was negative but PHI was positive, the rate of csPCA was similarly as high as when both were positive (40% vs. 54%). These data are hard to interpret given the low number of patients with negative EPI and positive PHI (6) but it does beg the question - why obtain an EPI test at all? If anything, these data may more accurately be seen as proof that the combined panel is not helpful in clinical decision making.

Until a true "liquid biopsy" is developed, debate of this nature will continue and I commend the authors on their willingness to share their experience. □

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References

1. Dudinec JV, Wang SM, Kotamarti S, Morris KE, Polascik TJ, Moul JW. Clinical utility of multiple secondary combined tests in prostate cancer screening. *Can J Urol* 2023;30(3):11538-11545.