COMMENTARY

Biomarkers to improve PSA-cancer screening

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Since its discovery in 1979, the prostate-specific antigen (PSA) has become an invaluable tool for screening and detecting prostate cancer. Because of its limited accuracy, especially with values below 10 ng/mL, the widespread use of PSA results in an important increase in the number of unnecessary biopsies and potentially nonlife-threatening disease. Fortunately, new biomarkers such as prostate cancer gene 3 (PCA3) represent a promising tool to improve PSA effectiveness in prostate cancer detection and discrimination between aggressive and indolent prostate cancer.[1] Roobol et al reviewed numerous recent publications on the PCA3 test and concluded that it is not capable of replacing the PSA test in clinical practice and that an appropriate cut off level with acceptable characteristics is hard to define. Nevertheless, its addition to risk assessment tools leads to an increase in predictive capability.[2]

In this issue of *The Canadian Journal of Urology*, Pepe et al intent to evaluate the use of PCA3 score in the accuracy of PCPT (Prostate Cancer Prevention Trial) risk calculator in detection rate of prostate cancer, number of avoided biopsies and missed prostate cancer. The authors present a retrospective, single institution, 1 year assessment of the PCPT risk calculator performance in 100 Caucasian men (median: 66 years old) with PSA < 10 ng/mL undergoing repeat TRUS (transrectal ultrasonography) biopsy for persistant suspicion of prostate cancer with initial negative biopsy using a saturation prostate biopsy (SPBx) (median: 30 cores; range: 24-48 cores) in which PCA3 score done several days prior to SPBx was integrated. Decision curve analysis was used to explore the clinical effects of the calculator. Using various PCA3 score cut off values sush as > 20 missed 7.2 % of prostate cancer and > 35 avoided 22% of biopsies. Pepe et al conclude that PCA3 score improves PCPT risk calculator in prostate cancer diagnosis (100%) and in combination with PSA F/T (Free/ Total) reduces the number of unnecessary biopsies (> 20 %).[3]

Numerous PCA3 studies have been published including that by Crawford et al with a review of 1962 men. In short, traditional PCA3 cut off of 35 reduced the number of false-positives from 1089 to 249, a 77.1% reduction. However, false-negatives (i.e. missed cancers) increased significantly from 17 to 413, an increase of more than 2300%. Lowering the PCA3 cut off to 10 reduced the number of false-positives 35.4% and false-negatives only increased 5.6%. The authors then conclude that PCA3 testing in conjunction with PSA has the potential to significantly decrease the number of unnecessary prostate biopsies.[4]

Goode et al did assess the impact of PCA3 in intial and repeat TRUS biopsy. In a series of 456 men, PCA3 was found to be a better predictor of prostate cancer than PSA in the total population as well as the initial biopsy population (AUC 0.772 versus AUC = 0.552, $p < 0.0001$), but was not superior to PSA in the repeat biopsy population (AUC = 0.605 versus AUC = 0.500, $p = 0.2488$).[5]

Finally, this study has its limitation such as the limited number of patients submitted to repeat SPBx and the lack of data about PSA accuracy (PCPT risk calculator only combined with PSA F/T). Nevertheless, the reported results are meaningful insofar that no previous data was available about computed models accuracy in patients submitted to repeat SPBx and especially in presence of PSA below 10 ng/mL. It also reaffirms the already existing literature in favor of the use of non-invasive urine-based novel biomarkers such as PCA3 to improve PSA accuracy. Currently in Canada, a PCA3 cut-off of 35 is used since it provides the most optimal balance between sensitivity and specificity in guiding repeat biopsy decisions. □

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