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ORIGINAL ARTICLE

Urinary PCA3 to predict prostate cancer in a cohort of 1015 patients

Test urinaire PCA3 et diagnostic du cancer prostatique : étude à partir de 1015 patients

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KEYWORDS
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PCA3;
Urinary test

Summary
Aim. — To evaluate the performance of urinary PCA3 test to predict prostate biopsy outcome in a large French cohort.
Patients and methods. — A urine sample was prospectively obtained from 1015 patients undergoing prostate biopsies to determine the PCA3 score. The predictive value of PCA3 was explored using receiver operating characteristic curve analysis (ROC), multivariable logistic regression analysis and decision curve analysis.

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Results. — The median PCA3 score was significantly higher in patients with positive biopsies. The PCA3 score AUC was 0.76 (0.73—0.79), significantly higher than that of PSA (0.55; 0.51—0.58). At the cutoff of 35, sensitivity was 68%, specificity 71%, positive and negative predictive values 67% and 71%, and accuracy 69%. Using multivariate analysis, PCA3 score appeared as an independent predictor of biopsy outcome and its addition to a base model including usual clinicobiological parameters resulted in a significant increase in predictive accuracy. At the cutoff of 20, about 1/2 of the ultimately unnecessary biopsies would have been avoided while ignoring 7% of cancers with Gleason score $\geq$ 7. PCA3 score did not correlate with Gleason score but did correlate with tumor volume (proportion of positive cores).
Conclusion. — Urinary PCA3 is a useful test with high diagnostic performances for early prostate cancer diagnosis. Its correlation with cancer aggressiveness seems rather represented by a link to prostate volume than Gleason score.
Level of evidence.— 5.

MOTS CLÉS
Cancer de la prostate ;
Diagnostic ;
Biopsies prostatiques ;
Prédiction ;
PCA3 ;
Test urinaire

Résumé
But. — Évaluer la capacité du test urinaire PCA3 à prédire le résultat des biopsies prostatiques dans une large cohorte issue du centre hospitalier Lyon Sud.
Patients et méthodes. — Le score PCA3 a été déterminé prospectivement chez 1015 patients adressés pour biopsies prostatiques. La capacité prédictive du score PCA3 a été évaluée par la comparaison des aires sous les courbes ROC, de modèles de régression logistique et une analyse par « decision curve analysis » (DCA).
Résultats. — Le score PCA3 médian était significativement plus élevé chez les patients avec biopsies positives. L'AUC était de 0,76, significativement plus élevée que celle du PSA à 0,55. Au seuil de 35, la sensibilité était de 68 %, la spécificité de 71 %, les valeurs prédictives positive et négative de 67 % et 71 %, et l'efficience de 69 %. En analyse multivariée, le score PCA3 était prédicteur indépendant du résultat des biopsies et son addition à un modèle de base comportant les données clinicobiologiques classiques apportait un gain diagnostique significatif. Au seuil de 20, près de la moitié des biopsies a posteriori inutiles auraient été évitées, tout en ayant ignoré 7 % des cancers avec score de Gleason $\geq$ 7. Le score PCA3 n'apparaissait pas corrélé au score de Gleason, mais était bien corrélé au volume tumoral (évalué par la proportion de carottes envahies).
Conclusion. — Le test urinaire PCA3 présente des performances diagnostiques élevées pour le diagnostic précoce du CaP. Sa corrélation avec l'agressivité du cancer s'exprime à travers le volume tumoral plus que par le score de Gleason.
Niveau de preuve.— 5.

Introduction

The first urine test for the quantitative assessment of prostate cancer gene 3 (*PCA3*) RNA transcripts in patients with suspected prostate cancer (PCa) was published more than 10 years ago [1]. The PCA3 RNA product is almost exclusively expressed in cancerous prostate tissue. It is not expressed in other tissues and only very weakly expressed in healthy prostate tissue or in non-malignant prostatic diseases [1—3]. The discovery and diagnostic use of PCA3 came about in response to the lack of specificity of serum prostate-specific antigen (PSA) testing for the diagnosis of PCa.

To date, approximately 100 studies, involving cumulatively close to 30,000 patients, have been conducted to evaluate urinary PCA3 RNA measurement (PCA3 test) in clinical practice [4—6]. The PCA3 test was approved for diagnostic purposes by the United States Food and Drug Administration in 2012, as a decisional aid for repeat prostate biopsy in patients aged at least 50 years who have had one or more previous negative biopsies. In France, as of this writing, the PCA3 test is only available for clinical research studies or in the setting of a voluntary, patient-payed diagnostic process. Published clinical studies, variable in scientific quality, tend to show that the urinary PCA3 test can be of significant value when deciding whether or not to perform prostate biopsy. In contrast to the serum PSA, which is affected by prostate volume, the PCA3 score does not increase in the presence of a non-malignant prostatic disease [7]. It does however correlate with the risk of positive biopsy and its use may reduce the number