

PROSTATE CANCER GENE 3 (PCA3): DEVELOPMENT AND INTERNAL VALIDATION OF A NOVEL BIOPSY NOMOGRAM

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- This study in 809 men referred for (repeat) prostate biopsy showed that incorporation of prostate cancer gene 3 (PCA3) into a multivariate model predicting the outcome of a biopsy significantly increases the predictive accuracy of the model. Based on this multivariate model a nomogram was developed which may assist patients and physicians in deciding whether a prostate biopsy is necessary.
- Mean and median PCA3 scores were statistically significantly higher in men with a positive biopsy vs. those with a negative biopsy ($P < 0.001$).
- In PCA3 score cut-off analysis for predictive accuracy, a cut-off of 17 was identified as the most statistically significant cut-off.
- In univariate analysis age, digital rectal examination (DRE), prostate specific antigen (PSA) level, prostate volume, previous biopsy, and PCA3 score were statistically significant predictors of a positive biopsy. The PCA3 score had the highest predictive accuracy, regardless of cut-off used. Of the PCA3 scores, the continuously coded PCA3 score had the highest predictive accuracy (0.679). The PCA3 score cut-off 17 had the highest odds ratio for predicting prostate cancer at biopsy.
- In multivariate analysis all above mentioned variables were statistically significantly independent predictors of a positive biopsy. Incorporating PCA3 into a base model including these variables improved its bootstrap-adjusted predictive accuracy with 2.3%-4.6% depending on the cut-off used. The highest increment in predictive accuracy (of 4.6%) was achieved by incorporating PCA3 score cut-off 17; this significantly increased the predictive accuracy from 0.68 for the base model (without PCA3) to 0.73 ($P = 0.04$).
- Based on the multivariate analysis, a nomogram incorporating PCA3 was developed which was superior to the nomogram without PCA3 in diagnostic accuracy and on local regression nonparametric calibration plots.
- It was concluded that PCA3 is a statistically significant independent and informative novel marker capable of increasing the predictive accuracy of multivariate models. The PCA3 nomogram better identifies men at risk of harboring prostate cancer and may assist patients and physicians in deciding whether a prostate biopsy is necessary.
- In the editorial comment to this article, it was discussed that although this study supports the use of PCA3 in the diagnosis of prostate cancer some key questions need to be answered:
 1. Normal ranges of PCA3 in the population;
 2. The optimal cut-off value of PCA3 as an indicator for prostate biopsy. It was recommended that this should be addressed in future larger studies, separately for first- and repeat biopsy situations; and
 3. The role and characteristics of PCA3 according to various PSA strata.
- The author concluded that PCA3 represents a novel and promising marker in the diagnosis and staging of prostate cancer.

Reviewed By: Prof. H. van Poppel

More Information:

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