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Research Article

PCA3 Score Failed to Predict Prostate Cancer and Reduce the Repeat Biopsy

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Abstract

Purpose: To assess whether the urinary PCA3 gene test has proved helpful for diagnosing prostate cancer and reducing biopsy, we searched for pathological features that influence the shedding of PCA3 producing prostate cancer cells in urine.

Methods: We detected 89 patients' urine samples for amplification of PCA3 mRNA and PSA mRNA by transcription media amplification and tested their serum PSA level using ELISA. The type of biopsy was done with a local anesthetic to numb the tissue the needle passed through for Gleason score.

Results: It showed that serum PSA level raised in parallel with Gleason score process and Serum PSA level significantly increased in prostate cancer. Therefore, the PCA3 score in operated patients negatively correlated with patient age. The area under the ROC curve of PCA3 score was smaller than Area under the ROC curve in serum PSA, respectively 0.6008 and 0.836. There was no significant difference in PCA3 score analysis in prostate cancer compared to these in non-prostate cancer. PCA3 score level gradually decreased in parallel with Gleason score process.

Conclusion: Taken together, PCA3 score failed to predict prostate cancer and reduce the repeat biopsy. Serum PSA still was a critical factor for prostate cancer diagnosis. The higher a man's PSA level, the more likely it is that he has prostate cancer.

Keywords: Prostate cancer gene3 (PCA3); Prostate-specific antigen (PSA); PCA3 score; Gleason score; Repeat biopsy; Serum

Introduction

The PCA3 gene, which is over-expressed in up to 95% of tumors, has high specificity for prostate cancer [1], as Bussemakers MJ public the data showed. So far hundreds of papers implicated that PCA3 score can predict prostate cancer and reduce the repeat biopsy outcome [2-4]. The aim of this present study was to evaluate the clinical validity of Prostate Cancer Associated3 (PCA3) gene in the prediction of PCA3 and the correlations between the PCA3 level and prognostic factors. We tried to repeat the experiment and confirmed that PCA3 score failed to predict prostate cancer and reduce the repeat biopsy.

Materials and Methods

Patients

The study population consisted of 89 consecutive men with serum PSA levels of 2.5 ng/mL or greater who had a history of at least one negative biopsy documented by the study site investigator and who had been scheduled for a follow-up biopsy. A urinary PCA3 test was performed in first voided urine after DRE in patients admitted to the Urology departments at Yijishan hospital for the prostate biopsy, based on PSA 2.5 ng/ml or greater, abnormal DRE and/or a family history of PCA. From January 2018 to October 2018, 89 patients were hospitalized in Urology. The mean interval between urine sampling and prostatectomy was 5 months. No patient received neoadjuvant treatment. Urine samples were collected for PSA mRNA and PCA3 mRNA test. The diagnosis age, serum PSA, Gleason score, family history, tumor stage, and prostate cancer were obtained by questionnaire and medical record. All cases were suspected of prostate cancer. Then the prostate biopsy was performed, and the biopsy specimens were confirmed by pathologists. The institutional review board approved this study and all patients provided informed consent to participate.

Serum PSA assay

All serum samples were detected with total serum PSA assay and all standards and samples were run at least in duplicate. And specimens were read absorbance at 450 nm immediately. All operations were performed based on the instruction.

Prostate biopsy

This type of biopsy was done with a local anesthetic to numb the tissue the needle passed through. A Transrectal Ultrasound (TRUS) will be used to guide the placement of the biopsy needle. The healthcare provider used a spring-loaded tool that quickly inserted a needle through the wall of the rectum into the prostate gland. The needle was put in several times to take tissue samples from different parts of the gland. The prostate tissue samples were sent to the lab for an exam.

Urine specimen extraction

Urine samples were harvested after the prostate was massaged. The initial urine was placed on ice. The samples were centrifuged with 2500 rpm at 4°C for 15 min. The supernatant was discarded to

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avoid pouring off cell sediment containing a variety of cells, including prostate cancer cells. RNA template in urine specimens was prepared following Trizol instruction. All samples were quantified and analyzed at the same laboratory.

The urinary PCA3 score test

In separate assays, PCA3 and PSA mRNAs were isolated from the processed urine samples and respectively amplified by transcription media amplification, the products were detected using with eppendorf® biophotometer D30. We optimized the reaction system of amplification in the experiment. Calibrators containing PCA3 or PSA RNA transcripts were included in each assay run and were used to convert the signal to mRNA copies. PSA mRNA levels were used to normalize PCA3 to the total amount of prostate RNA present in the sample and to ensure that the RNA yield was sufficient for analysis. For each processed urine specimen, the quantitative ratio of PCA3 to PSA mRNA was determined as pubic manuscripts described previously [5,6]. The PCA3 score was calculated as PCA3 mRNA/PSA mRNA 1000.

Statistical analysis

The results were expressed as means ± SEM and statistical differences were evaluated by two-way ANOVA and T-test followed, using Graph Pad Prism 7.0. A p-value <0.05 was considered statistically significant.

Results

No potential link was showed between age and PCA3 score in prostate cancer

The average age of 89 patient's was 72.6 ± 7.01 in Urology. The mini age was 55 and the max age was 90. They were separated with three groups according to prostate biopsy, respectively normal people, people with hyperplasia of the prostate gland and prostate cancer people. To analyze their relationship between PCA3 score and age, we compared three groups. As shown, the PCA3 scores of patients with prostate cancer decreased in parallel with age growth (n=42). The PCA3 scores of people with hyperplasia of prostate gland showed no definite regularity, irrespective of the variation of age (n=40). However, the PCA3 score of normal people significantly increased in parallel with age growth in normal people (n=7) (Figure 1).

Serum PSA level significantly raised in prostate cancer

We compared serum PSA level in three groups, respectively normal people as a control, patients with hyperplasia of the prostate gland in non-prostate cancer and patients underwent pathological procedures in prostate cancer. In Figure 1, serum PSA level in prostate cancer significantly increased compared to those in normal people. It implicated that serum PSA level was a crucial parameter for diagnosing prostate cancer.

A PCA3 score in prostate cancer was no significant difference in control

PCA3 score level gradually increased in normal people, hyperplasia of the prostate gland, prostate cancer. A PCA3 score in prostate cancer was higher than those in control. But there was no significant difference in (Figure 2). It indicated that PCA3 score in normal people did not correlate with those in people with hyperplasia of prostate gland and prostate cancer people. To assess the ability of the PCA3 assay to predict the prostate biopsy outcome, receiver operating characteristic (ROC) curve analysis was performed using the biopsy result as the reference method (Figure 3). For comparison, the performance of the serum PSA assay on this subject population was also evaluated. For the PCA3 score, the area under the ROC curve was 0.6008 (95% confidence interval 0.4838 to 0.7178).The serum PSA assay yielded an area under the curve of 0.836 (95% confidence interval 0.7406 to 0.9329), indicating that the serum PSA level has a diagnostic value for this subject population.

Serum PSA significantly raised in parallel with Gleason score growth

The complete analysis revealed many differences of patients in serum PSA level and Gleason score. Serum PSA level raised in parallel with Gleason score in Figure 4. But another observation supported the notion that PCA3 score did not correlate with Gleason score in prostate cancer patients in Figure 5.

Discussion

Current practices for detecting prostate cancer utilize serum PSA and DRE as indications for biopsy and approximately 25% of patients with elevated serum PSA are found to have prostate cancer [7]. This means that 75% of the first biopsies are negative [8]. Men with one or more previous negative biopsies present a clinical dilemma and there is a medical need for additional tests to help physicians and patients make more informed repeat biopsy decisions [9,10]. Prostate cancer gene3 (PCA3) is a promising urinary biomarker of prostate cancer [10]. This specific non coding mRNA is highly over expressed in more

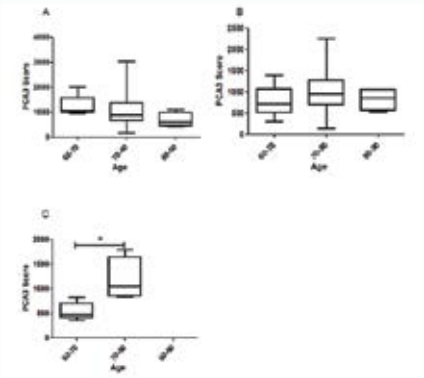

Figure 1: The relationship between age and PAC3 score in normal people, patients with hyperplasia of the prostate gland, patients with prostate cancer. (A) PCA3 score level in prostate cancer decreased in parallel with age growth (n=42). (B) There was no significant difference in three group (n=40). (C) PCA3 score in normal people significantly increased in parallel with age growth (n=7).

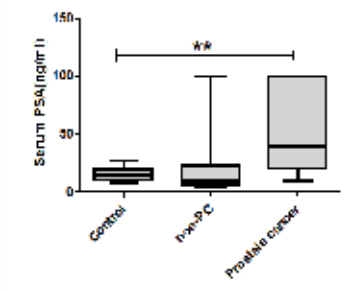

Figure 2: There was the concentration of serum PSA in each group. Serum PSA level in prostate cancer significantly increased compared to those in control (n=48). Normal people in control, patient with hyperplasia of prostate gland in non-Pc and patient underwent pathological procedures in prostate cancer.

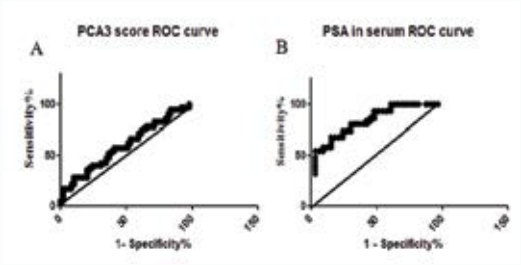

Figure 3: ROC curve analyses and AUC using PCA3 score or serum PSA level as a diagnostic indicator and prostate biopsy as reference method. (A) Area under the ROC curve of PCA3 score was 0.6008. 95% confidence interval is 0.4838 to 0.7178. The P value is 0.09861. (B) Area under the ROC curve in serum PSA is 0.836. 95% confidence interval is 0.7406 to 0.9329. The P-value is less of 0.0001.

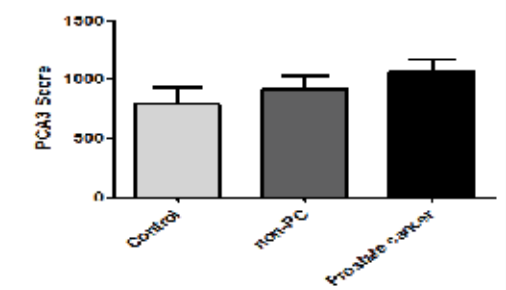

Figure 4: PCA3 score were showed in each group. PCA3 score in Control did not correlate with those in people with hyperplasia of prostate gland and prostate cancer people (n=42). Normal people in control, patient with hyperplasia of prostate gland in non-Pc and patient underwent pathological procedures in prostate cancer.

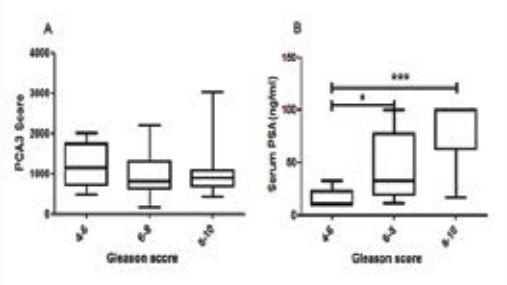

Figure 5: The relationship in PCA3 score and Gleason score and in serum PSA and Gleason score. (A) PCA3 score in 4-6 Gleason score did not correlate with those in 6-8 Gleason score and 8-10 Gleason score (n=22). (B) There were a significant link between serum PSA and Gleason score. Gleason score increased in parallel with serum PSA growth (n=31).

than 95% of primary prostate tumors [11]. Therefore, a PCA3 score is currently being used in some research studies for predicting the prostate cancer [12-14]. Our result confirmed the observation that PCA3 score level increased in parallel with serum PSA raising. We revealed that there was no any link between prostate cancer patient age and PCA3 score. And the PCA3 score of hyperplasia of prostate gland showed no definite regularity, irrespective of the variation of age. In addition, we observed that PCA3 score level gradually decreased in parallel with the Gleason score. It implicated that PCA3 score did not potentially correlate with Gleason score process. Dramatically, serum PSA level raised in parallel with Gleason score enhancing. That means that serum PSA still is a critical factor for prostate cancer diagnosis. The higher a man's PSA level, the more likely it is that he has prostate cancer.

Conclusion

PCA3 score failed to predict prostate cancer and reduce repeat biopsy. Serum PSA still was a critical factor for prostate cancer diagnosis. The higher a man's PSA level, the more likely it is that he has prostate cancer. A continuous rise in a man's PSA level over time still is a sign of prostate cancer.

Conflicts of Interest

We declared that this manuscript is original, has not been published before and is not currently being considered for publication elsewhere. There are no known conflicts of interest associated with this publication.

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