Zagazig University Medical Journal
www.zumj.journals.ekb.eg

https://doi.org/10.21608/zumj.2024.234154.2873 Volume 30, Issue 1.6, September 2024, Supplement Issue
Manuscript ID ZUMJ-2312-3070 (R1) DOI 10.21608/ZUMJ.2024.258419.3070

ORIGINAL ARTICLE

Serum and Urinary Prostatic Cancer Antigen 3 as Diagnostic Biomarkers for Prostate Cancer

Shimaa Refaat Ahmed[1], Nahla Ibrahim Elattar[1], Aref Mohamed Maarouf[2], Azza Moustafa Ahmed[1]
[1]Clinical Pathology Department, Faculty of Medicine, Zagazig University,Eygpt
[2]Urology Department, Faculty of Medicine, Zagazig university,Eygpt

Corresponding author*
Shimaa Refaat Ahmed

Email:
Shimaa.sakr2012@gmail.com

Submit Date 26-12-2023
Revise Date 15-01-2024
Accept Date 19-01-2024

ABSTRACT

Background: TheProstatic cancer antigen 3 (PCA3) is extensively over-expressed in the malignant prostatic tissues more than normal or benign adjacent ones. Clinical diagnosis and targeted therapy are two areas where this biomarker shows a promising value. The present work aimed to evaluate the role of serum and urinary PCA3 as a diagnostic marker in prostatic cancer cases in Zagazig University Hospitals.

Subjects and methods: In a case-control study, we included 44 patients who were divided into two groups: 22 patients with benign prostatic hyperplasia (BPH) as a control group and 22 patients with prostate cancer. Cases were subjected to full history taking, clinical evaluation, and determination of total Prostate-specific antigen (PSA), free PSA, serum, and urinary PCA3.

Results: Both serum and urinary PCA3 were significantly higher in the cancer group than in the BPH group (P=0.007 and P<0.001, respectively). The best cutoff of serum PCA3 to diagnose prostate cancer is ≥5.985pg/ml with the area under curve 0.739, sensitivity 86.3%, specificity 54.5%, positive predictive value 65.5%, negative predictive value 80%, and overall accuracy 70.5% (p=0.007). The best cutoff of urinary PCA3 to diagnose cancer prostate is ≥9.775pg/ml with area under curve 0.965, sensitivity 95.5%, specificity 95.5%, positive predictive value 95.5%, negative predictive value 95.5% and overall accuracy 95.5% (p<0.001).

Conclusion: When compared to PSA, urinary PCA3 had the better diagnostic specificity and sensitivity, making it a promising biomarker and noninvasive test for prostate cancer diagnosis. It could be used in the diagnosis of PCA either alone or in combination with total PSA.

Keywords: Serum, Urinary, Prostatic cancer antigen 3, Prostate Cancer

INTRODUCTION

Among male cancers, prostate cancer (PCA) ranks highest. It was estimated that 248,530 new cases occurred in Western countries in 2021. Most people will get a full recovery, but a sizeable minority of men will have the disease worsen or metastasize to other parts of the body [1]. Once metastasis has begun, there is no turning back; only 30% of patients survive five years after diagnosis. Beyond that, it appears that metastatic prostate cancer has been more common in the last decade across all age groups and racial/ethnic categories [2].

The average age of diagnosis is 66 years, and both the incidence and death of prostate cancer correspond with increasing age globally. Furthermore, 158.3 new cases per 100,000 males are African American men, and their mortality rate is around double that of White men. This is in marked contrast to the lower incidence rates experienced by White men [3].

It is challenging for clinicians to effectively differentiate PCA from benign prostatic

hyperplasia (BPH) because the clinical signs of the two conditions are quite similar. The general prognosis of PCA was bad because there were no quick and accurate ways to diagnose the disease. To lower PCA mortality, improve survival rates, and maximize the potential of effective medical therapies, early detection is crucial for physicians [4]

The majority of prostate cancer screenings still make use of serum prostate-specific antigen (PSA). Although a high PSA level is likely to be related to PCA, the low specificity of PSA limits its utility as a screening test and unnecessary biopsies. However, raised PSA levels may be connected with other disorders, such as BPH, prostatitis, and PCA [5].

A combined research effort discovered prostate cancer antigen 3 (PCA3) around 1995. At first, it went by the name differential display clone 3 (DD3). The expression of PCA3 is significantly higher in prostate cancer tissue as compared to neighboring benign or normal tissue. When it comes to clinical diagnosis and focused treatment, PCA3 is an encouraging biomarker [6].

Overexpression of the prostate cancer antigen 3 genes has been found in numerous investigations. This gene is a segment of noncoding messenger ribonucleic acid (mRNA) located on chromosome 9q21-22. Using PCA3 determination, normal prostate cells can be distinguished from cancerous ones with accuracy close to one hundred percent at the cellular level. Gene levels in prostate cellular material-containing tissues or fluids have been utilized for diagnostic purposes due to the overexpression of PCA3 by cancer cells. The first 20 to 30 mL of voided urine after a digital rectal examination (DRE) must be collected for the PCA3 test. In cases where the DRE is not performed, the test yields correct results in only about 80% of cases, but with the DRE, this yield jumps to over 98% of cases [6].

Serum PCA3 levels are unaffected by variables such as prostate volume, age, or prostatic disease, in contrast to serum PSA levels. Regarding prostate cancer, it is considerably more specific. It detects prostate cancer better than the PSA [7]. The PCA3 also can be measured in urine, and low false-positive rates are associated with this noninvasive diagnostic method [5].

The present work aimed to evaluate the role of serum and urinary PCA3 as a valuable, promising diagnostic marker in prostatic cancer patients in Zagazig University Hospitals.

SUBJECT AND METHODS

Subject:

Thiscase-control study was conducted on individuals who were attending the clinical pathology department and Urology department in Zagazig University hospitals during the period from July 2022 to October 2022. Subjects enrolled included 44 patients divided into two groups: 22 patients with benign prostatic hyperplasia as a control group and 22 cases who had prostate cancer. The mean age of patients was 60 ± 13, with a median of 55 years.

Verbal and written informed consent was obtained from all participants after an explanation of the procedure and medical research. The study was carried out after the approval of the Institutional Review Board (IRB), with approval number (#6737/31-3-2021). The research was conducted as per the World Medical Association's Code of Ethics (Helsinki Declaration) for human research.

Cases with the following criteria were included: adult patients above 50 years old and proved to be PCA or BPH by prostatic biopsy. Exclusion criteria: Patients with symptoms of acute or chronic prostatitis, patients who had a history of other cancer, alcohol use, those who had any history of chronic physical illness, and patients who refused to enroll in the study.

Methods:

Full clinical assessment, which includes complete history taking, clinical examination (by urology specialists) & anthropometric measurements, was performed for all patients. Estimation of tumor grade was done according to Epstein et al. [8]. Estimation of

Gleason score was done according toBostwick et al. [9]

Laboratory tests were performed, including the estimation of serum total and free PSA by using the Electro Chemo _ Luminescence method with the automated analyzer Cobas 6000 (Roche Diagnostics Switzerland). Calculation of PSA density was estimated as total PSA (ng/ml) divided by prostate volume (ml) [10].

Serum and urinary PCA3 were measured by *ELIS*A according to the instructions of the manufacturer. The kits were provided by SunRed biotechnology company (China) Catalogue No. 201-12-5328. Kit specifications were as follows: Sensitivity: 1pg/ml, Assay range: 1pg/ml→40pg/ml.

Statistical analysis

Statistics were applied to the data using IBM SPSS, version 28.0. (IBM Corporation, Armonk, New York). The underlying assumptions of the parametric tests were checked using the Kolmogorov-Smirnov and Levene tests, which measure distribution type and homogeneity of variances, respectively.We utilized the independent sample t-test (for normally distributed data) and the Mann-Whitney test (for non-normally distributed data) to compare quantitative data between the two groups. Two continuous, non-normally distributed variables were evaluated for association and strength of correlation using the Spearman rank correlation coefficient.

RESULTS

Statistically significant differences were found between the studied groups as regards age, history of UTI, total, free PSA, PSA density, serum, and urinary PCA3, which were significantly higher in the cancer group (Table 1).

The free/total PSA ratio was significantly lower in the cancer group (P value was <0.001).

Regarding serum PCA3, a significant negative correlation was found between serum PCA3, prostate volume, and free/total PSA ratio (p=0.009 and <0.001 respectively), and statistically significant positive correlations between serum PCA3 and total PSA, PSA density, grade, Gleason score, and urinary PCA3 (p<0.001, <0.001, 0.048, 0.046, and 0.005 respectively), among the factors that were significantly correlated to serum PCA3, only total PSA (unstandardized β=0.299, p<0.001) significantly independently associated with it. (Table 2).

Also, a statistically significant negative correlation was found between urinary PCA3, free/total PSA ratio, and prostate volume (p<0.001 for each). Statistically significant positive correlations were found between urinary PCA3 and age, total PSA, PSA density, and serum PCA3 (p=0.002, <0.001, <0.001, <0.005 respectively); among factors significantly correlated to urinary PCA3, we found that only prostate volume (unstandardized β=-1.001, p<0.001) significantly independently associated with it (Table 3).

The Gleason score and urinary PCA3 were found to be significantly correlated with significant differences between groups with score six and both scores 7 and 8 (p<0.001).There was a significant relation between PCA grades and urinary PCA3, with the difference being significant between the group with grade I and both grades IV and V (P=0.024) (Table 4).

The best cutoff of serum PCA3 to diagnose cancer prostate is ≥5.985pg/ml with the area under curve 0.739, sensitivity 86.3%, specificity 54.5%, positive predictive value 65.5%, negative predictive value 80% and overall accuracy 70.5% (p=0.007) (table 4) and (Figure 1A), the best cutoff of urinary PCA3 to diagnose cancer prostate is ≥9.775pg/ml with the area under curve 0.965, sensitivity 95.5%, specificity 95.5%, positive predictive value 95.5%, negative predictive value 95.5% and overall accuracy 95.5% (p<0.001) (table 4) and (Figure 1B).

Having serum PCA3 ≥5.985 and urinary ≥9.775 could diagnose prostate cancer with 95.5% sensitivity, 50% specificity, 65.6% positive predictive value, 91.7% negative predictive value, and overall accuracy of 72.7%.Having serum PCA3 ≥5.985 and total PSA ≥4.0 could diagnose prostate cancer with

100% sensitivity, 50% specificity, 66.7% positive predictive value, 50% negative predictive value, and overall accuracy of 75%. Having total PSA ≥4.0 and urinary PCA3 ≥9.775 could diagnose prostate cancer with 100% sensitivity, 81.8% specificity, 84.6% positive predictive value, 100% negative predictive value, and overall accuracy of 90.9% (Table 6).

Table (1): Comparison between the studied groups regarding demographic data, PSA level, PSA density, serum and urinary PCA3.

Parameter	Groups		Test	
	Cancer group N=22 (%)	BPH group N=22 (%)	t/χ^2	P
Age (year): Mean ± SD	73.36 ± 7.17	65.18 ± 10.16	3.085	0.004*
UTI: No Yes	7 (31.8%) 14 (68.2%)	14 (63.6%) 8 (36.4%)	4.463	0.035*
Total PSA(ng/mL) Median Range	10.1 0.5 – 92.9	2.33 0.5 – 4.76	-4.953	<0.001**
PSA density Median Range	0.3 0.01 – 2.9	0.035 0.01 – 0.08	-5.225	<0.001**
Free PSA(ng/mL) Median Range	1.09 0.09 – 1.43	0.7 0.2 – 1.4	-3.389	<0.001**
Free/total PSA ratio:(%) Median Range	10.5 1 – 31%	29 25 – 46%	-5.304	<0.001**
PCA3 Serum level (pg/ml) Median Range	8.75 4.46 – 39.25	5.68 0.8 – 21.67	-2.711	0.007*
PCA3 Urinary level (pg/ml) Median Range	36.02 21.13 – 40	4.98 1.02 – 9.9	-5.681	<0.001**

PSA:prostate specific antigen, PCA3:Prostatic cancer antigen 3, UTI: Urinary tract infection

***p<0.05 is statistically significant** **t independent sample t test**

χ^2 Chi square test.

Z Mann Whitney test ****p≤0.001 is statistically highly significant**

Table (2): Correlation between serum PCA3 and the studied parameters in PCA group, and Linear stepwise regression analysis of factors significantly correlated to serum PCA3

	R	P
Age	0.29	0.056
Prostate volume	-0.388	0.009*
Total PSA	0.599	<0.001**
Free/Total PSA ratio	-0.616	<0.001**

	R	P
PSA density	0.608	<0.001**
Grade	0.426	0.048*
Gleason score	0.429	0.046*
Urinary PCA3	0.415	0.005*

Linear stepwise regression analysis of factors significantly correlated to serum PCA3.

	Unstandardized coefficient		Standardized coefficient	T	P	95% CI	
	B	Std. error	B			Lower	Upper
Constant	8.316	2.376		3.5	0.002*	3.359	13.272
Total PSA	0.299	0.072	0.679	4.131	<0.001**	0.148	0.45

PSA:prostate specific antigen, PCA3:Prostatic cancer antigen 3
r Spearman rank correlation coefficient
****p≤0.001 is statistically highly significant** ***p<0.05 is statistically significant**

Table (3) Correlation between urinary PCA3 and the studied parameters in PCA group, and linear stepwise regression analysis of factors significantly correlated to urinary PCA3.

	R	P
Age	0.453	0.002*
Prostate volume	-0.731	<0.001**
Total PSA	0.599	<0.001**
Free/Total PSA ratio	-0.588	<0.001**
PSA density	0.634	<0.001**
Grade	0.395	0.068
Gleason score	0.383	0.078
Serum PCA3	0.415	0.005*

Linear stepwise regression analysis of factors significantly correlated to urinary PCA3.

	Unstandardized coefficient		Standardized coefficient	T	P	95% CI	
	B	Std. error	B			Lower	Upper
Constant	66.818	4.117		16.06	<0.001**	57.81	74.426
Prostate volume	-1.001	0.086	-0.874	-11.657	<0.001**	-1.175	-0.828

PSA:prostate specific antigen, PCA3:Prostatic cancer antigen 3
r Spearman rank correlation coefficient
****p≤0.001 is statistically highly significant** ***p<0.05 is statistically significant**

Table (4): Relation between Gleason score, PCA grades, total PSA, serum and urinary PCA3 among case group

Gleason Score	Total PSA	P	Serum PCA3	P	Urinary PCA3	p
	Mean±SD		Median (range)		Mean±SD	
6	37.0 ± 7.07	0.288	14.34(6.03 – 32.44)	0.08	25.28 ± 5.88	0.01*
7	35.17 ± 3.19		6.18 (4.46 – 37.78)		33.69 ± 5.29	

8	33.5 ± 3.21		7.77 (5.79 – 18.99)		36.91 ± 2.82	
9	32.33 ± 2.25		21.13 (7.89 – 39.25)		36.41 ± 3.14	
Grade	**Total PSA**	**P**	**Serum PCA3**	**P**	**Urinary PCA3**	**p**
GradeI	37.0 ± 7.07		14.47 (6.03 – 32.44)		25.28 ± 5.88	
GradeII	34.5 ± 3.32		6.18 (4.46 – 37.78)		33.29 ± 5.16	
GradeIII	36.5 ± 3.54	0.386	7.6 (5.84 – 9.37)	0.149	34.5 ± 7.63	0.024*
GradeIV	33.5 ± 3.51		7.77 (7.79 – 18.99)		36.91 ± 2.82	
GradeV	33.23 ± 2.25		21.13 (7.89 – 39.25)		36.41 ± 3.14	

***p<0.05 is statistically significant**

Table (5): Performance of serum and urinary PCA3 in diagnosis of prostate cancer.

Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	p
Serum PCA3 ≥5.985(pg/ml)	0.739	86.3%	54.5%	65.5%	80%	70.5%	0.007*
Urinary PCA3 ≥9.775 (pg/ml)	**0.965**	**95.5%**	**95.5%**	**95.5%**	**95.5%**	**95.5%**	**<0.001****

PCA3:Prostatic cancer antigen 3

****p≤0.001 is statistically highly significant**

***p<0.05 is statistically significant** **AUC area under curve**

PPV positive predictive value **NPV negative predictive value**

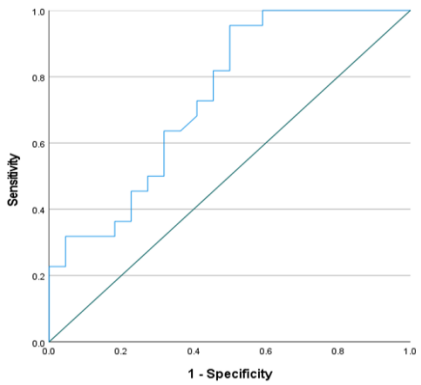
Table (6): Performance of both serum and urinary PCA3, total PSA with serum PCA3, andtotal PSA with urinary PCA3 in diagnosis of cancer prostate.

	Sensitivity	Specificity	PPV	NPV	Accuracy
Serum≥5.985 + urinary PCA3≥9.775	95.5%	50%	65.6%	91.7%	72.7%
Serum PCA3 ≥5.985 + total PSA≥4.0	100%	50%	66.7%	50%	75%
urinary PCA3≥9.775 +Total PSA≥4.0	100%	81.8%	84.6%	100%	90.9%

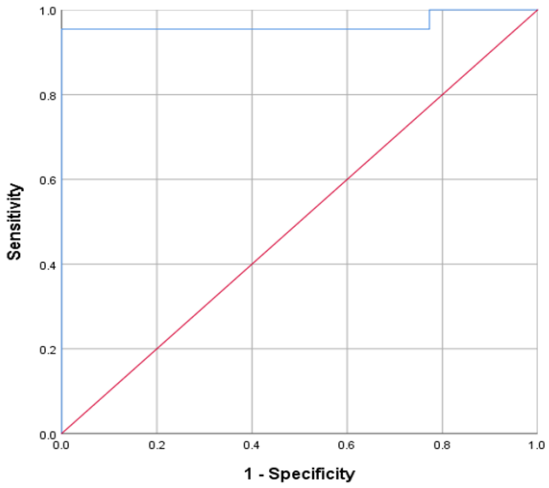
PSA:prostate specific antigen, PCA3:Prostatic cancer antigen 3

Figure(1): Roc Curves showing: (A) performance of serum PCA3 in diagnosis of prostate cancer, (B) performance of urinary PCA3 in diagnosis of prostate cancer

A



B



DISCUSSION

In terms of detecting prostate cancer, PCA3 outperforms PSA. Research indicates that PCA3 can be utilized as a valuable biomarker for the diagnosis of prostate cancer since it is expressed two to three times higher in cancer cells compared to normal cells in over 95% of prostate cancer cases. Patients diagnosed with prostate cancer often have this marker detected in their urine [11].

As regards demographic data of the studied patients, we found that age was significantly higher in the cancer group, with a mean age of 73.36 ± 7.17 years in the cancer group and 65.18 ± 10.16 years in the BPH group; this was in agreement with Yazdani et al. [14] who revealed that there was no statistically significant difference between the groups in terms of age(P=0.087), with the malignant cases having an average age of 67.07 ± 4.85 years and the BPH patients having an average age of 62.81 ± 8.06 years.

The present study showed that prostate volume was significantly higher in the BPH group compared to PCA patients. These results agreed with the study ofYazdani et al. [14] as they demonstrated that in cases of benign prostatic hyperplasia, the prostate volume was significantly larger than in patients with prostate cancer (p<0.001).

The present study revealed a statistically significant difference between the studied groups as regards the total, free PSA, and PSA density, which were significantly higher in the cancer prostate group (p<0.05). Also, the Free/total PSA ratio was significantly lower in the cancer group (p<0.05). The finding was corroborated by Askari et al. [15], who found that patients with prostate cancer had a considerably higher mean total PSA than those with BPH (P<0.05).However, there was no statistically significant difference in PSA level (P=0.172) or PSA density (PSAD) (P=0.055) among the individuals who were screened in the study by Yazdani et al. [14].

We evaluated both serum and urinary PCA3 in the studied groups. The comparison between the studied groups showed that there was a statistically significant difference regarding both serum (p =0.007) and urinary (p<0.001) PCA3, which were significantly higher in the case group.

These results agreed with Askari et al. [15], who reported that mean serum and urinary PCA3 in cases of prostate cancer were significantly higher than patients with BPH (P<0.05). However, the studied population of Yazdani et al. [14] was not statistically different in urine PCA3 levels (P=0.199).

Regarding serum PCA3, the present study

revealed significant negative correlations between serum PCA3 and free/total PSA ratio with prostate volume, and statistically significant positive correlations were found between serum PCA3 and total PSA, PSA density, grade, Gleason score, and urinary PCA3. Among the factors that were significantly correlated to serum PCA3, only PSA (unstandardized β=0.299, p<0.001) was significantly independently associated with it.

These results agreed with Chunhua et al. [16], who found a statistically significant positive correlation between serum PCA3 and total PSA and Gleason score.

Also, we found a statistically significant negative correlation between urinary PCA3, free/total PSA ratio, and prostate volume. Statistically significant positivecorrelations were found between urinary PCA3 and all of age, total PSA, PSA density, and serum PCA3. However, among factors significantly correlated to urinary PCA3, we found that only prostate volume (unstandardized β=-1.001, p<0.001) was significantly independently associated with it.

These results agreed with Askari et al. [15], who revealed a non-significant relationship between Gleason score and urinary PCA3 (P>0.05).Shen et al. [17] carried out research on Chinese subjects and demonstrated that Gleason scores in prostate biopsies taken from cancer patients did not correlate significantly with urine PCA3 levels. However**,** Askari et al. [15] showed a non-significant relationship between urinary PCA3 with age and total PSA level.

Our results regarding increased urinary PCA3 in advanced tumor grade and Gleason score suggest that urinary PCA3 increase is associated with advanced disease.

PSA is a powerful predictor of future prostate cancer risks in addition to being a diagnostic tool for the disease [18]. Additionally, men with low PSA can safely extend test intervals due to the slow growth rate of prostate cancer. Men whose PSA levels are low are statistically very unlikely to acquire aggressive prostate cancer within the next eight to ten years [19].

The present study showed that the best cutoff of serum PCA3 to diagnose prostate cancer is ≥5.985pg/ml with the area under curve 0.739, sensitivity of 86.3%, specificity of 54.5%, positive predictive value of 65.5%, negative predictive value of 80%, and overall accuracy 70.5% (p=0.007). The diagnostic performance of serum PCA3 was much lower than that of PSA.

These results were in line with Chunhua et al. [16], who determined the expression level of PCA3 in the blood of patients with PCA and BPH. They indicated that its expression in the blood PCA was much higher than that of the BPH. When PCA3 was applied as a diagnostic parameter, its sensitivity for PC diagnosis was 86.5%.

The present study showed that the best cutoff of urinary PCA3 to diagnose prostate cancer is ≥9.775pg/ml with area under curve 0.965, sensitivity 95.5%, specificity 95.5%, positive predictive value 95.5%, negative predictive value 95.5% and overall accuracy 95.5% (p<0.001). The diagnostic performance of urinary PCA3 is better than that of total PSA and f/tPSA ratio.

Results from an evaluation of the urine PCA3 assay by Ochiai et al. [20] showed that a cut-off value of 35pg/ml was useful for detecting prostate cancer, with a specificity of 71.6% and a sensitivity of 66.5% in distinguishing malignant masses from benign prostatic hyperplasia, respectively.

Also, at a cut-off level of 27.75 pg/ml, urinary PCA3 had a sensitivity of 72.7% and a

specificity of 69.2% in predicting prostate cancer, according to the research of Yazdani et al. [14].

In addition, a study by Adam et al. [21] found that African males had the highest values of urine PCA3 at a threshold of 60pg/ml, with a specificity of 68.9% and a sensitivity of 66.7%. The different PCA3 cut-offs of our study and different studies are explained by using different immunoassays with different antibody specificities.

In cases of urogenital malignancies, including prostate, bladder, and kidney tumors, urinary markers like PCA3 have the potential to be reliable and extensively utilized [22]. The present study showed that having serum PCA3 ≥5.985pg/ml and urinary ≥9.775pg/ml can diagnose prostate cancer with 95.5% sensitivity, 50% specificity, 65.6% positive predictive value, 91.7% negative predictive value and overall accuracy of 72.7%**.** Using combined urinary and serum PCA3 did not increase diagnostic sensitivity when using urinary PCA3 alone.

Also, it was shown that having serum PCA3 ≥5.985pg/ml and total PSA ≥4.0ng/ml can diagnose prostate cancer with 100% sensitivity, 50% specificity, 66.7% positive predictive value, 50% negative predictive value, and overall accuracy of 75%. Although diagnostic sensitivity was increased, diagnostic specificity was decreased.

The present study showed that having urinary PCA3 ≥9.775 pg/ml and total PSA ≥4.0ng/ml can diagnose prostate cancer with 100% sensitivity, 81.8% specificity, 84.6% positive predictive value, 100% negative predictive value, and overall accuracy of 90.9%. All cases of PCA3 were diagnosed using combined PSA and urinary PCA3 determination.

Various research lines have examined serum PSA and urine PCA3 in this class. Various prostatic indicators, such as PSA and PCA3, were examined and contrasted in a study conducted by Stephan et al. [23]. They demonstrated that urine PCA3 could be just as reliable as serum PSA and yield the same outcomes. This led them to suggest testing for urine PCA3 as a potential prostate cancer screening tool.

These results agreed with Chunhua et al. [16], who proved the efficacy of PCA3, PSA, and fPSA in urine as diagnostic tools. Compared to PSA andfree PSA (fPSA), PCA3 had a higher area under the curve (AUC) for sensitivity and specificity. There was no significant difference in AUC between PCA3 mRNA and PSA, according to ROC curve analysis (P = 0.067). Compared to PSA, fPSA had a greater area under the curve (AUC) (P =.039), but it was not greater than PCA3.

Results for the urinary PCA3, total PSA (tPSA), and free total PSA (f/tPSA) tests were 0.865, 0.505, and 0.607, respectively, when comparing the area under the ROC curve, as validated by Merola et al. [24]. According to the statistics that are currently available, PCA3 is the most reliable method for diagnosing PCA.

This is why there have been a plethora of studies looking at PCA3 as a potential alternative to PSA for detecting prostate cancer. Results on the cut-off values of this biomarker may be more accurately produced with a more diversified study group, potentially including multi-centric participants, leading to higher predictive power [12, 13].

No potential conflict of interest was reported by the authors.

CONCLUSION

When compared to PSA, urinary PCA3 has

better diagnostic specificity and sensitivity, making it a promising biomarker and noninvasive test for prostate cancer diagnosis. It could be used in the diagnosis of PCA either alone or in combination with total PSA. A further exciting finding is that there is a correlation between increased urine PCA3 and tumor aggressiveness, as measured by Gleason score and tumor grades. Future studies are recommended to study its ability to predict cancer prognosis and staging.

REFERENCES

1. **Bernard B, Burnett C, Sweeney CJ, Rider JR, Sridhar SS**. Impact of age at diagnosis of de novo metastatic prostate cancer on survival. *Cancer*. 2020; 126(5):986-93.
2. **Siegel RL, Miller KD, Fuchs HE, Jemal A.** Cancer Statistics, 2021 [published correction appears in CA Cancer J Clin. 2021;71(4):359]. *CA Cancer J Clin*. 2021; 71(1):7-33.
3. **Panigrahi GK, Praharaj PP, Kittaka H, Mridha AR, Black OM, Singh R,et al.** Exosome proteomic analyses identify inflammatory phenotype and novel biomarkers in African American prostate cancer patients. *Cancer Med*. 2019;8(3):1110-23.
4. **Daniyal M, Siddiqui ZA, Akram M, Asif HM, Sultana S, Khan A.** Epidemiology, etiology, diagnosis and treatment of prostate cancer. *Asian Pac J Cancer Prev*. 2014; 15(22):9575-8.
5. **Litwin MS, Tan HJ.** The Diagnosis and Treatment of Prostate Cancer: A Review. *JAMA*. 2017; 317(24):2532-42.
6. **Schalken J**. Interview with Jack Schalken. PCA3 and its use as a diagnostic test in prostate cancer. Interview by Christine McKillop. *Eur Urol*. 2006; 50(1):153-4.
7. **Hessels D, Schalken JA.** The use of PCA3 in the diagnosis of prostate cancer. *Nat Rev Urol*. 2009; 6(5):255-61.
8. **Epstein JI:** Pathology of prostatic neoplasia. In: Partin AW, Dmochowski RR, Kavoussi LR, Peters CA, eds. Campbell-Walsh-Wein Urology. 12th ed. Philadelphia, PA: Elsevier; 2021, chap 151.
9. **Bostwick DG and Cheng L**: Neoplasms of the prostate. Urologic Surgical Pathology. 4th ed. Philadelphia, PA: Elsevier; 2020, chap 9.
10. **Nordström T, Vickers A, Assel M, Lilja H, Grönberg H, Eklund M**. Comparison Between the Four-kallikrein Panel and Prostate Health Index for Predicting Prostate Cancer. *Eur Urol*. 2015; 68(1):139-46.
11. **Mikhaylenko DS, Perepechin DV, Grigoryeva MV, Zhinzhilo TA, Safronova NY, Efremov GD, et al.** PCA3 and TMPRSS2: ERG genes expression in biopsies of BPH ,intraepithelial neoplasia and prostate cancer. *Urologiia*. 2015 ;(5):46-50.
12. **Wang FB, Chen R, Ren SC, Shi XL, Zhu YS, Zhang W,et al.** Prostate cancer antigen 3 moderately improves diagnostic accuracy in Chinese patients undergoing first prostate biopsy. *Asian J Androl*. 2017; 19(2):238-43.
13. **Farha MW, Salami SS**. Biomarkers for prostate cancer detection and risk stratification. *Ther Adv Urol*. 2022; 14:17562872221103988.
14. **Yazdani A, Namdari F, Gorganifiruzjaee S, Niroomand H**. Evaluation of the urine mRNA-PCA3 expression level in prostate patients; comparison between benign prostatic hyperplasia and cancer. Immunopathol Persa. 2022;8(2):15207.
15. **Askari M, Yazdani A, Yazdani M, Izadpanahi MH**. Serum levels of total and urine level of PCA3 in patients with benign prostatic hyperplasia and prostate cancer. *Am J Clin Exp Urol*. 2020;8(1):43-7.
16. **Chunhua L, Zhao H, Zhao H, Lu Y, Wu J, Gao Z, et al**. Clinical Significance of Peripheral Blood PCA3 Gene Expression in Early Diagnosis of Prostate Cancer. *Transl Oncol*. 2018; 11(3):628-32.
17. **Shen M, Chen W, Yu K, Chen Z, Zhou W, Lin X, et al.** The diagnostic value of PCA3 gene-based

analysis of urine sediments after digital rectal examination for prostate cancer in a Chinese population. *Exp Mol Pathol*. 2011; 90(1):97-100.

18. **Vertosick EA, Häggström C, Sjoberg DD, Hallmans G, Johansson R, Vickers AJ, et al.** Prespecified 4-Kallikrein Marker Model at Age 50 or 60 for Early Detection of Lethal Prostate Cancer in a Large Population Based Cohort of Asymptomatic Men Followed for 20 Years. *J Urol*. 2020; 204(2):281-8.
19. **Carlsson S, Assel M, Sjoberg D, Ulmert D, Hugosson J, Lilja H,et al**. Influence of blood prostate specific antigen levels at age 60 on benefits and harms of prostate cancer screening: population based cohort study. *BMJ*. 2014; 348:2296.
20. **Ochiai A, Okihara K, Kamoi K, Oikawa T, Shimazui T, Murayama S,et al.** Clinical utility of the prostate cancer gene 3 (PCA3) urine assay in Japanese men undergoing prostate biopsy. *BJU Int*. 2013; 111(6):928-33.
21. **Adam A, Engelbrecht MJ, Bornman MS, Manda SO, Moshokoa E, Feilat RA**. The role of the PCA3 assay in predicting prostate biopsy outcome in a South African setting. *BJU Int*. 2011; 108(11):1728-33.
22. **Mlcochova H, Hezova R, Stanik M, Slaby O.** Urine microRNAs as potential noninvasive biomarkers in urologic cancers. *Urol Oncol*. 2014; 32(1):41.41.419.
23. **Stephan C, Ralla B, Jung K.** Prostate-specific antigen and other serum and urine markers in prostate cancer. *Biochim Biophys Acta*. 2014; 1846(1):99-112.
24. **Merola R, Tomao L, Antenucci A, Sperduti I, Sentinelli S, Masi S, et al.** PCA3 in prostate cancer and tumor aggressiveness detection on 407 high-risk patients: a National Cancer Institute experience. *J Exp Clin Cancer Res*. 2015; 34(1):15.

Citation:

Ahmed, S., Elattar, N., Maarouf, A., Ahmed, A. Serum and Urinary Prostatic Cancer Antigen 3 as Diagnostic Biomarkers for Prostate Cancer. *Zagazig University Medical Journal*, 2024; (3089-3099): -. doi: 10.21608/zumj.2024.258419.3070