WORLD JOURNAL OF MEDICAL INNOVATIONS

PCA3 performance in localized prostate cancer

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Article info

UROLOGY

Review

Article history:
Accepted
October 04, 2024

Published online
November 11, 2024

Keywords:
PCA3, peripheral zone prostate cancer, prostate cancer tumor dominant growth pattern, clinically significant prostate cancer

Abstract

PCa incidence and mortality is rising. It is the fifth most common cause of mortality globally, and it is the most frequently diagnosed cancer in Europe. The PCa screening, diagnosing and treatment keeps being extremely actual. Much more popularity in PCa screening and diagnosing gains biomarkers. In our previous results we described the influence of the tumor zone origin (TZO) and tumor growth dominant pattern (TGDP) on PCA3 urine levels. In this work we try to evaluate performance of the PCA3 urine levels in identifying clinical significant PCa according to the postoperative ISUP class. The study included 130 participants with PCa that underwent extraperitoneoscopic radical prostatectomy (ERP). The control group (CG) included: 40 healthy volunteers, 40 patients with benign prostatic hyperplasia (BHP) and 40 with chronic prostatitis (CP). The PCA3 urine levels ROC-analysis for identifying the pPZ-PCa, as well as, pPZ-csPCa demonstrated excellent AUC model. Conclusion. PCA3 urine levels can be used to identify pPZ-csPCa patients according to the postoperative ISUP-class.

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Introduction

According to the Wang et al., (2022) meta-analysis PCa incidence and mortality is rising [25]. It is the fifth most common cause of mortality globally, and it is the most frequently diagnosed cancer in Europe [3, 4, 5, 24]. So the PCa screening, diagnosing and treatment keeps being extremely actual [1, 5, 9, 10, 11, 17, 18]. On the last decade much more popularity in PCa screening and diagnosing gains biomarkers and according to Lee (2020) PCA3 is one of the best knowns [1, 2, 6, 14]. But the study results and practical utility of the last ones still remains uncertain [6, 12, 14, 19, 20]. In our previous results we described the influence of the tumor zone origin (TZO) and tumor growth dominant pattern (TGDP) on PCA3 urine levels. [21]

Objectives

To evaluate performance of the PCA3 urine levels in identifying clinical significant PCa according to the postoperative ISUP class.

Materials and methods

The study included 130 participants with PCa that underwent extraperitoneoscopic radical prostatectomy (ERP). Inclusion criteria were the presence of the: urine PCA3 level, total PSA, prostate MRI, patho-morphological conclusion after surgery (pISUP). All patients were divided into subgroups depending on the TZO and TGDP PCa (Figure 1, 2, 3): anterior peripheral zone (aPZ-PCa), posterior peripheral zone (pPZ-PCa) and transition zone (TZ-PCa). TZO

were identified with MRI and confirmed by the patho-morphological conclusion after extraperitoneoscopic RP. The control group (CG) included: 40 healthy volunteers, 40 patients with benign prostatic hyperplasia (BHP) and 40 with chronic prostatitis (CP). STATISTICA version 10 (64 bit) and MedCalc's free statistical calculators were used for analysis.

Results

The participants general data are present in Table 1. According to the Mann-Whitney U-test statistically significant difference in PCA3 urine levels and PSA were observed, with no differences in age between the investigating groups, p <0,01 (table 2, figure 4).

Table 1. The participants general data.

Me	PCa (130)	aPZ-PCa (31)	pPZ-PCa (80)	pPZ-csPCa (66)	CG (120)
AGE	66 (63; 71)	66 (64; 69)	65 (62; 70,5)	65,5 (63; 71)	65 (58,5; 73,5)
PSA	11,1 (7,1; 17,6)	16 (9,8; 24,8)	11,1 (7,1; 16,8)	11,9 (7,8; 17,3)	7,3 (5,4; 9,9)
PCA3	57,4 (29,2; 73,2)	40,5 (14,9; 57,6)	68,3 (55,9; 89,8)	70,3 (59,4; 91,2)	15 (8,5; 25,7)

Table 2. The Mann-Whitney U-test of the research parameters

Parameter	aPZ-PCa vs CG			pPZ-PCa vs CG			pPZ-csPCa vs CG		
	U	Z	p	U	Z	p	U	Z	p
AGE	1821,5	-0,18	0,86	4754,5	-0,11	0,91	3782,5	-0,5	0,61
PSA	668,5	-5,5	<0,01	2924,5	-4,7	<0,01	2152,5	-5,1	<0,01
PCA3	956,5	-4,2	<0,01	671,0	-10,3	<0,01	293,5	-10,4	<0,01

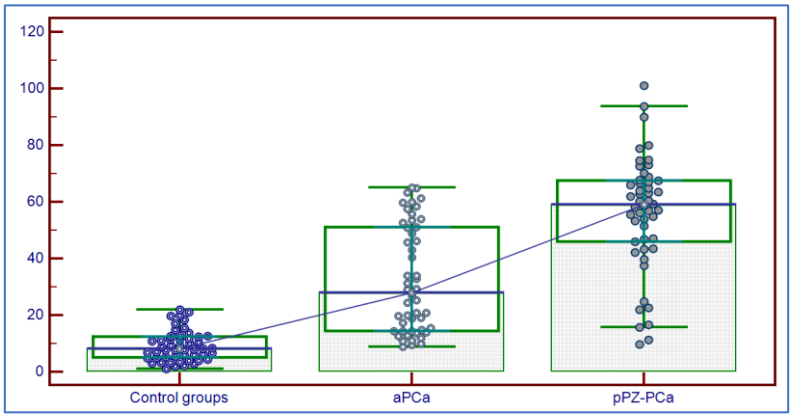

Figure 1. Difference in PCA3 levels between pPZ-PCa vs aPCa and pPZ-PCa vs CG (p<0,01)

The subgroup of the clinically significant pPZ-PCa (pPZ-csPCa) also had statistically significant difference in PCA3 urine levels comparing with the CG (figure 5).

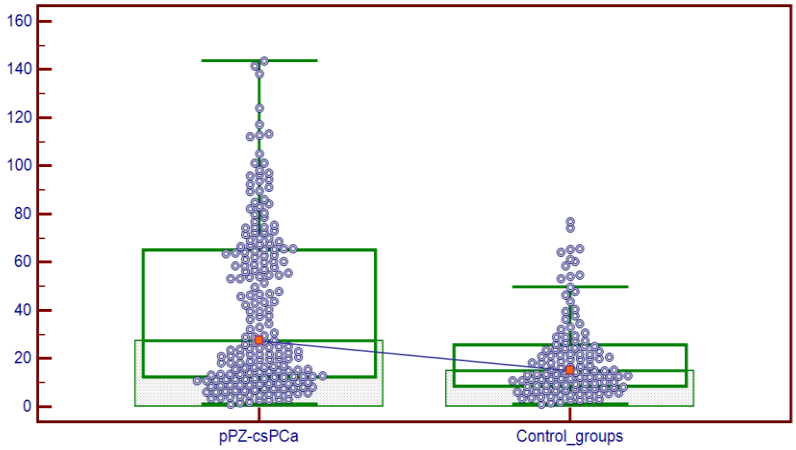

Figure 2. Difference in PCA3 levels between pPZ-csPCa vs CG (p<0,01)

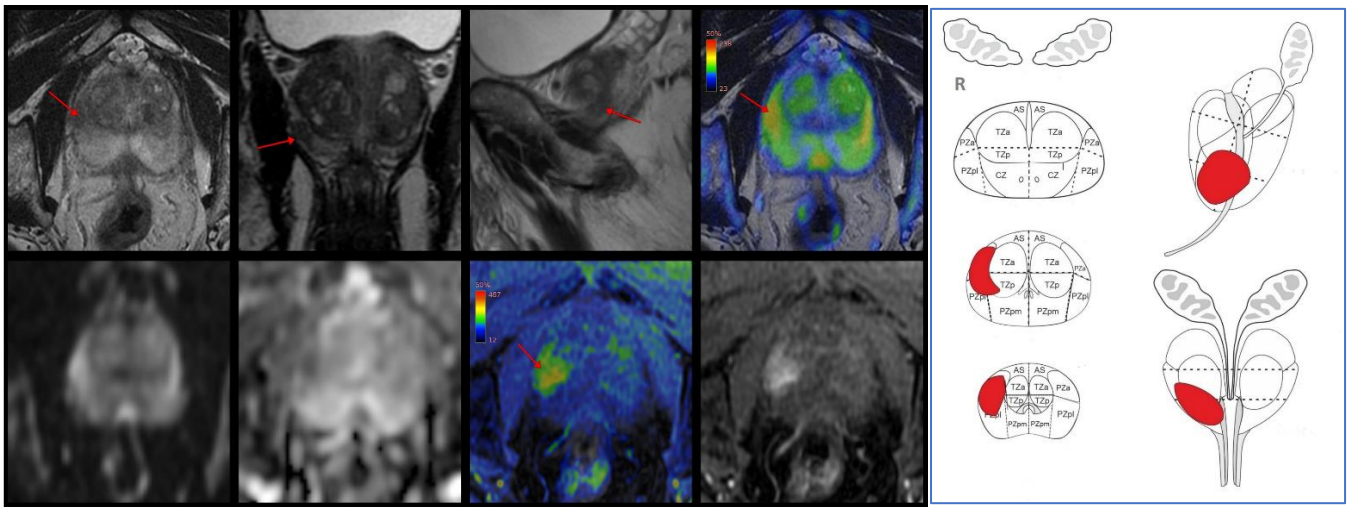

Figure 3. MRI and schematic view of the anterior peripheral zone PCa.

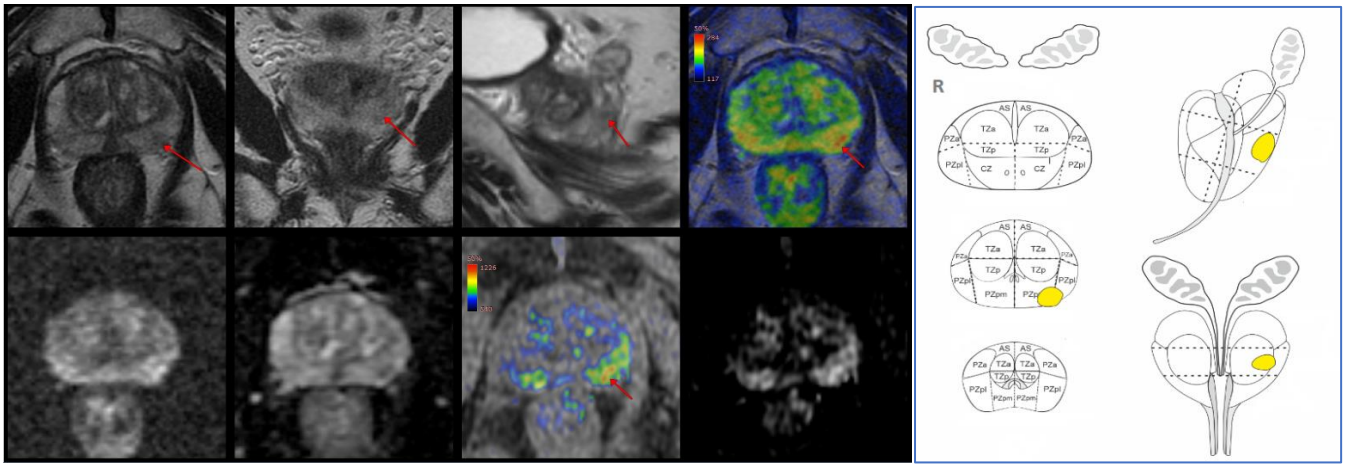

Figure 4. MRI and schematic view of the posterior peripheral zone PCa.

Table 3. The ROC-analysis results of the research parameters and subgroups.

PCA3	AUC 95% CI	OC	p-value	Se 95% CI	Sp 95% CI	+LR 95% CI	-LR 95% CI	+PV 95% CI	-PV 95% CI
aPZ-PCa n=31 vs 120	0,74 [0,67-0,81]	> 40,7	<0,01	48,4 [30,2-66,9]	87,5 [80,2-92,8	3,87 [2,1-7,0]	0,59 [0,4-0,8]	50 [31,3-68,7	86,8 [79,4-92,2]
pPZ-PCa n=80 vs 120	0,93 [0,89-0,96]	> 40,7	<0,01	88,8 [79,7-94,7]	87,5 [80,2-92,8]	7,1 [4,4-11,5]	0,13 [0,1-0,2]	82,6 [72,9-89,9]	92,1 [85,5-96,3]
pPZ-csPCa n=66 vs 134	0,94 [0,9-0,97]	> 46,4	<0,01	93,9 [85,2-98,3]	86,6 [79,6-91,8]	6,9 [4,5-10,8]	0,07 [0,03-0,2]	77,5 [66,8-86,1]	96,7 [91,7-99,1]

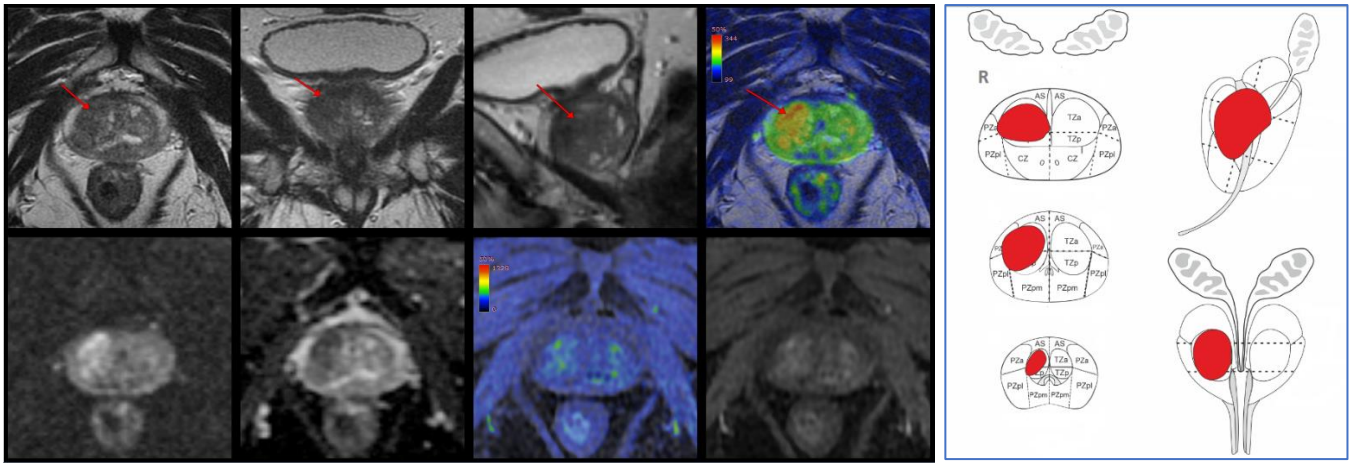

Figure 5. MRI and schematic view of the tranzitional zone PCa.

The PCA3 urine levels ROC-analysis for identifying the pPZ-PCa, as well as, pPZ-csPCa demonstrated excellent AUC model (table 3, figures 7, 8). The aPZ-PCa, as we can see on table 3 and figure 6, had an acceptable AUC model, with very poor sensivity.

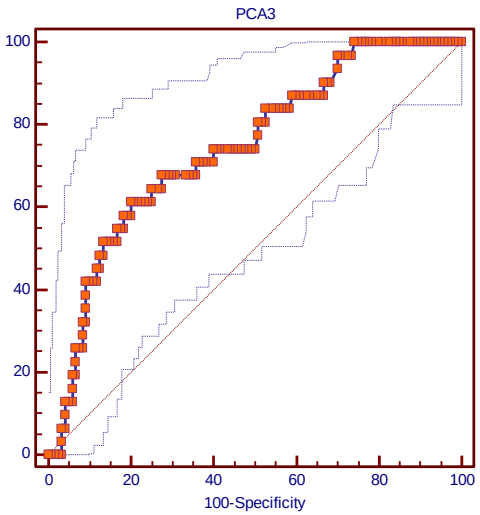

Figure 6. aPZ-PCa

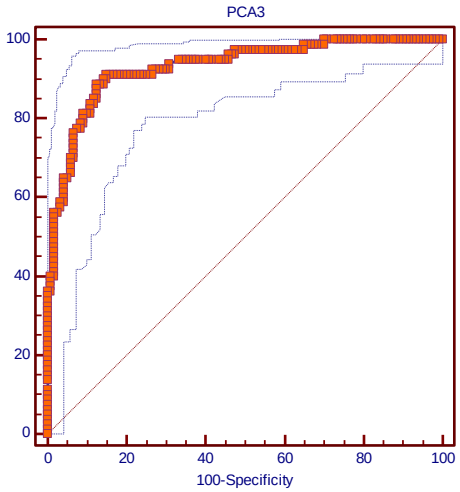

Figure 7. pPZ-PCa

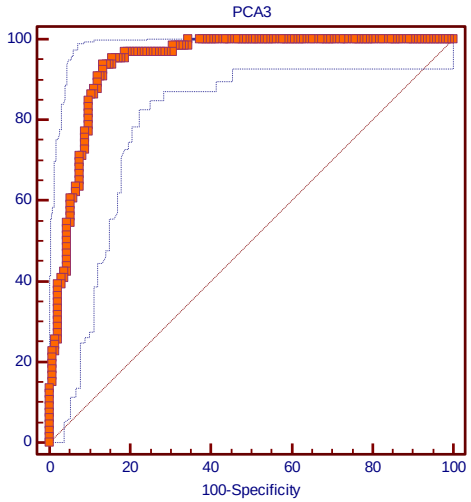

Figure 8. pPZ-csPCa

Discussion

Nowadays the use of biomarkers, especially PCA3, in identification csPCa is actively discussed [1, 2, 6, 14, 19, 20]. L.S. Marks et al. (2008) described the principles of the urine collection for PCA3 test [16]. We suppose that this may be the main limitation in cases with anterior TGDP PCa.

So, in this study design we decided to be in consensus with our colleagues' recommendations in terms of distinguishing TZO and TGDP in PCa patients [7, 8, 22, 23, 26]. The results of our previous work demonstrated differences in PCA3 urine levels between aPZ-PCa and pPZ-PCa, as well as, pPZ-PCa correlations with pISUP [21]. In this work we founnd PCA3 optimal values for identifiying pPZ-csPCa according to the pISUP class. Which can be usefull for choosing the optimal treatment way in patients with localized PCa. PCA3 is well known biomarker, which routinely used for PCa diagnosis [5, 1].

Conclusion

PCA3 urine levels can be used to identify pPZ-csPCa patients according to the postoperative ISUP-class. Further investigations may show a knew PCA3 test performance.

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