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ORIGINAL RESEARCH

Performance of PCA3 and TMPRSS2:ERG Within the Prostate Cancer Prevention Trial Risk Calculator Version 2 in a Lithuanian Cohort

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Background: Prostate cancer (PCa) remains a significant health concern due to its high incidence and associated mortality. Conventional screening approaches, like PSA testing, often lack specificity, resulting in unnecessary biopsies and overtreatment. This study seeks to overcome these limitations by assessing the integration of novel urinary biomarkers into established risk prediction models.

Objective: This study aimed to evaluate the performance of incorporating urinary biomarkers – prostate cancer antigen 3 (PCA3) and transmembrane serine protease 2 (TMPRSS2) gene and ETS-related gene (ERG) fusion genes (T:E) – into the Prostate Cancer Prevention Trial Risk Calculator version 2 (PCPTRC2) in a Lithuanian cohort to enhance the detection of clinically significant prostate cancer (csPCa).

Materials and methods: A single-centre prospective study included 246 men scheduled for initial prostate biopsy between January 2021 and August 2024 due to elevated total PSA levels or abnormal digital rectal examination (DRE). Following ethical approval and informed consent, urinary samples were collected post-DRE and analysed for PCA3 and T:E. Each patient's risk was calculated using the basic PCPTRC2 and updated versions incorporating biomarkers. Biopsies were performed based on multi-parametric magnetic resonance imaging (mpMRI) findings.

Results: Of 209 biopsy samples analysed, 111 (53.1%) were diagnosed with csPCa. The AUC for PCa detection was 59.6% for the original PCPTRC2, improving to 76.2% with PCA3 and further to 79.5% when both PCA3 and T:E were included. Both updated versions demonstrated significantly higher sensitivity compared to the original ($p<0.001$). However, no significant differences were noted in distinguishing csPCa from non-csPCa.

Conclusion: Incorporating PCA3 and T:E into PCPTRC2 substantially enhances diagnostic accuracy for detecting PCa in biopsy-naïve patients. Despite limitations, these findings underscore the potential for optimizing risk calculators in clinical practice, advocating for larger cohorts to validate these results.

Keywords: prostate cancer, biomarker-based risk assessment, PCA3, TMPRSS2:ERG, multiparametric MRI, risk calculator

Introduction

Prostate cancer (PCa) is the second most commonly diagnosed cancer after lung cancer and the sixth leading cause of cancer-related deaths among men worldwide.[1] Early detection is crucial, yet PSA-based screening has low specificity (20–30%), often leading to unnecessary treatments for clinically insignificant tumours.[2] Efforts are being made to optimize screening practices by using prediction models and risk calculators to improve accuracy and reduce unnecessary medical procedures.

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There are several well-known externally validated calculator models for PCa risk assessment, including the Prostate Cancer Prevention Trial Risk Calculator version 2 (PCPTRC2)[3] These models integrate various factors—such as age, PSA levels, digital rectal examination results, and family history—to estimate the probability of PCa detection through histological examination. Studies have shown that incorporating urinary biomarkers, such as Prostate Cancer Antigen 3 (PCA3) noncoding RNA and the TMPRSS2:ERG (T:E) gene fusion, into PCPTRC2 enhances diagnostic accuracy and may improve the detection of clinically significant prostate cancer (csPCa).[4] The selection of PCA3 and TMPRSS2:ERG for this study is based on their proven potential to improve the specificity and sensitivity of PCa detection, ultimately reducing the rate of unnecessary biopsies and enhancing patient management.[5,6]

The study aimed to assess the performance of incorporating PCA3 and T:E into PCPTRC2 within a Lithuanian cohort, using an alternative urinary biomarkers testing method.

Methods

Study Population

The investigation was approved by the regional Bioethical Commission, Decision no. BE-2-116. In a single-centre prospective study, 246 patients were consecutively enrolled between January 2021 and August 2024. The study was conducted at the Lithuanian University of Health Sciences Kaunas Clinics in Kaunas, Lithuania. Informed consent was obtained from all individual participants. Men who were scheduled for initial prostate biopsy, based on elevated total PSA level (defined in this study as >2 ng/mL and <20 ng/mL) or abnormal digital rectal examination (DRE) were included in the study. Exclusion criteria were a history of PCa or other neoplasms under active treatments and prior prostate biopsy. A total of two patients did not undergo prostate biopsy for personal reasons, while seven patients were excluded due to unsuccessful purifying of urinary test samples. Additionally, 28 patients were excluded due to age restrictions, as PCPTRC2 calculates csPCa risk only for individuals aged 55–90 years, in accordance with the calculator's guidelines.[7] The remaining 209 subjects underwent genetic urinary testing after DRE as well as multiparametric Magnetic Resonance Imaging (mpMRI). (). In this study, genetic urine testing involved analysing the urinary biomarkers PCA3 and TMPRSS2:ERG using a validated assay. This process included collecting first-void urine samples after a DRE, stabilizing them, and quantifying biomarker levels through precise molecular techniques.[8] Following these examinations, targeted cognitive fusion US-guided prostate biopsy and systematic prostate biopsy were performed in

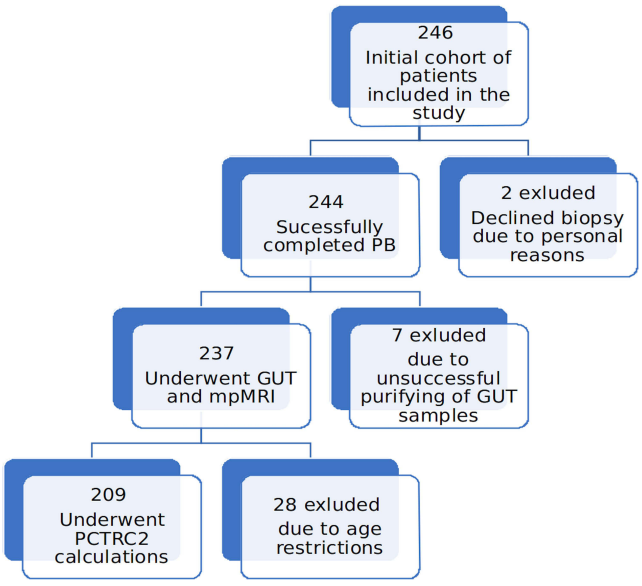

Figure 1 Study Cohort Flowchart: Patient Selection and Data Processing.Abbreviations: mpMRI, multiparametric magnetic resonance imaging; GUT, genetic urinary test; PCPTRC2, prostate cancer prevention trial risk calculator 2.

cases where mpMRI detected PIRADS 3, 4, and 5 lesions. In cases where mpMRI revealed PIRADS 1 or 2 lesions, only systematic US-guided biopsy was conducted, as per the study protocol.

PCTRC2 with and without Biomarkers

A basic version of PCPTRC2 was used in all patients aged 55 to 90 years old (n=209), as required by the calculator.[9] The calculator incorporated the following variables: race, age, PSA level (ng/mL), family history of PCa, DRE result, and prior biopsy. The probability of high-grade PCa was first estimated using basic PCPTRC2 model. Originally, PCPTRC2 integrated biomarkers by calculating their values based on copy numbers determined through the MPS test. The MPS test combines serum PSA, urine T:E, and PCA3 to predict a patient's risk for having PCa detected by standard biopsy after digital rectal examination.[10] In this study, urinary biomarker values of PCA3 and the PCA3/T:E combination, obtained through the Diagnolita urinary test, were incorporated in PCTRC2. First-voided urine samples were collected after a prostate massage and prior to biopsy. Colli-Pee 20 mL devices (Novosanis), prefilled with 10 mL of stabilization media (Diagnolita), were used for immediate sample stabilization. The samples were then transferred to the Diagnolita laboratory for analysis.[8,11]

Additional Tests

All subjects included in the study group underwent mpMRI using either a 1.5T or 3T MR scanner. A standard imaging protocol was applied, incorporating T1-weighted (T1W) images, T2-weighted (T2W) images, diffusion weighted imaging (DWI), and dynamic contrast-enhanced (DCE) sequences. Lesions were graded using PIRADS version 2.1 (v2.1) on a scale from 1 to 5.[12] Finally, all participants underwent US-guided prostate biopsy. In each case, 12 systematic cores were collected. For lesions with a PI-RADS score of 3–5 on mpMRI, additional targeted samples (two cores per lesion) were obtained using a cognitive targeted prostate biopsy technique. Histological grading was performed according to both the Gleason grading system and the Gleason Grade Groups.[13]

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics, including age, family history, serum PSA levels, prostate volume, urinary biomarkers results, and biopsy outcomes. Continuous variables were reported as mean and median [interquartile range (IQR)], while categorical variables were expressed as numbers and percentages. Biopsy outcomes were compared with PCPTRC2 results alone, as well as with models incorporating PCA3 and the PCA3/T:E combination, using mean and median values as numbers and percentages. Patients were categorized into clinically significant prostate cancer (csPCa; GS $\geq$7) or non-clinically significant prostate cancer (non-csPCa) groups based on combined systematic and targeted biopsy results.

To assess the predictive capability of different PCPTRC2 models, we calculated the area under the receiver operating characteristic curve (AUC) for three versions: the original PCPTRC2, the updated version incorporating PCA3, and the model including both PCA3 and T:E. Further analysis focused on csPCa versus no PCa or non-csPCa. Given the importance of high sensitivity in diagnosing csPCa, we examined the portion of the ROC curve ranging from 75% to 100% sensitivity, aligning with methodologies from previous studies.[14]

We evaluated how accurately the predicted probabilities from the PCPTRC2 model correspond to actual biopsy results. The calculated probabilities for PCa, csPCa, non-csPCa, and negative biopsy outcomes were averaged across the three PCPTRC2 models: the basic version, the version including PCA3, and the model incorporating both PCA3 and T:E. These predictions were then with actual biopsy outcomes, providing insights into the detection rates of overall PCa, csPCa, non-csPCa, and negative biopsy results. The findings were organized into a table for a clear comparative overview of each PCPTRC2 model's performance in PCa diagnosis.

All statistical analyses were performed using R version 4.3.2 with a p-value ≤ 0.05 considered statistical significance. Data normality was assessed using the Shapiro–Wilk test. Continuous variables were compared using a two-sided Student's *t*-test for normally distributed data and a two-sided Wilcoxon rank sum test for non-normally distributed data. Categorical variables were analysed using a two-sided Fisher's exact test.

To compare AUC values, a one-sided DeLong test was performed, with the alternative hypothesis stating that the AUC values of PCPTRC2 models incorporating one or both biomarkers would be higher than the PCPTRC2 version without biomarkers. The approach was supported by existing literature demonstrating biomarker-enhanced AUC performance.[3,4,8] Similarly, partial AUC values were calculated and compared using the bootstrap method, limited to a high sensitivity range (75% and 100%). The AUC values, partial AUC values, their 95% confidence intervals, and comparison test results were computed using functions from the R package pROC version 1.18.5.

Results

In total, data from 209 men were analysed. Patient characteristics, PCPTRC2 results before and after incorporating urinary biomarkers, and biopsy outcomes are summarized in Table 1. The median age of participants was 65 years (range 55–87) and the mean PSA level was 6.4 ng/mL. Upon biopsy 111 (53.1%) of patients were diagnosed with csPCa (GS>7).

To evaluate PCa prediction we assessed three versions of the PCPTRC2 risk calculator. The original PCPTRC2 had an AUC of 59.6%, while incorporating PCA3 increased it to 76.2%. Adding both PCA3 and T:E further improved the AUC to 79.5%. The updated calculators demonstrated significantly higher sensitivity compared to the original (p=0.001 and p<0.001, respectively). (Table 2 and Figure 2). However, when distinguishing csPCa form no PCa or non-csPCa, no statistically significant differences were found between the original and updated versions ($p > 0.05$) (Table 3). Since high sensitivity is crucial for diagnosing csPCa,[14] we focused on the ROC curve portion between 75% and 100% sensitivity, mirroring a methodology similar to a previous PCa prediction study.[14] For csPCa prognosis, the updated PCPTRC2 model with PCA3 had a partial AUC of 7.8%, while the version including both PCA3 and T:E achieved 8.6%. The latter demonstrated significantly higher performance (p=0.043). (Table 4 and Figure 3).[14] Table 5 presents a comparison of the average predictions from different PCPTRC2 versions – including the basic version and those incorporating urinary biomarkers – against actual biopsy results. In the basic PCPTRC2 version, the average predicted probability of detecting

Table 1 Patients' Characteristics (Number, %, Mean +-SD, Median, Range)

Parameter	Value
Number of cases, n	209
Age (years)	
Mean ±SD	64.6 ±5.7
Median	64
Range	55–87
Total PSA (ng/mL)	
Mean ±SD	6.4 ± 2.9
Median	5.6
Range	2.1–19.1
PSA density (ng/mL/mL)	
Mean ± SD	0.15 ± 0.12
Median	0.12
Range	0.04–1.2

(*Continued*)

Table 1 (Continued).

Parameter	Value
Prostate volume	
Mean ± SD	52.1 ±23.4
Median	46.8
Range	13.5–148.7
DRE suspicious, n (%)	
Yes	99 (47.4)
No	110 (52.6)
Family history, n (%)	
Yes	21 (10)
No	188 (90)
PCA3	
Mean ± SD	136.5 ± 118.2
Median	99.3
Range	7.58–664.7
T:E	
Mean	37.5 ± 70.9
Median	11.7
Range	0–487.13
Biopsy outcomes, n (%)	
GS <7	98 (46.9)
GS≥7	111 (53.1)

Abbreviations: n, number; SD, standard deviation; PSA, prostate-specific antigen; PSAD, PSA density; DRE, digital rectal examination; PIRADS, prostate imaging reporting and data system version 2.1; PCPTPRC2, prostate cancer prevention trial risk calculator 2; csPCa, clinically significant prostate cancer.

Table 2 AUC Comparisons for Predicting PCa with 95% CI, Given in Brackets.

Model	AUC with CI, %	P value vs PCPTRC2
PCPTRC2	59.6 (50.2–69.1)	NA
PCPTRC2 including PCA3	76.2 (68.3–84.1)	**0.001**
PCPTRC2 including PCA3+T:E	79.5 (71.9–87.1)	**<0.001**

Notes: T:E fusion of TMPRSS2 and ERG gene. Significant Differences (p<0.05) are Highlighted in Bold.
Abbreviations: PCPTRC2, prostate cancer prevention trial risk calculator 2; PCA3, prostate cancer antigen 3.

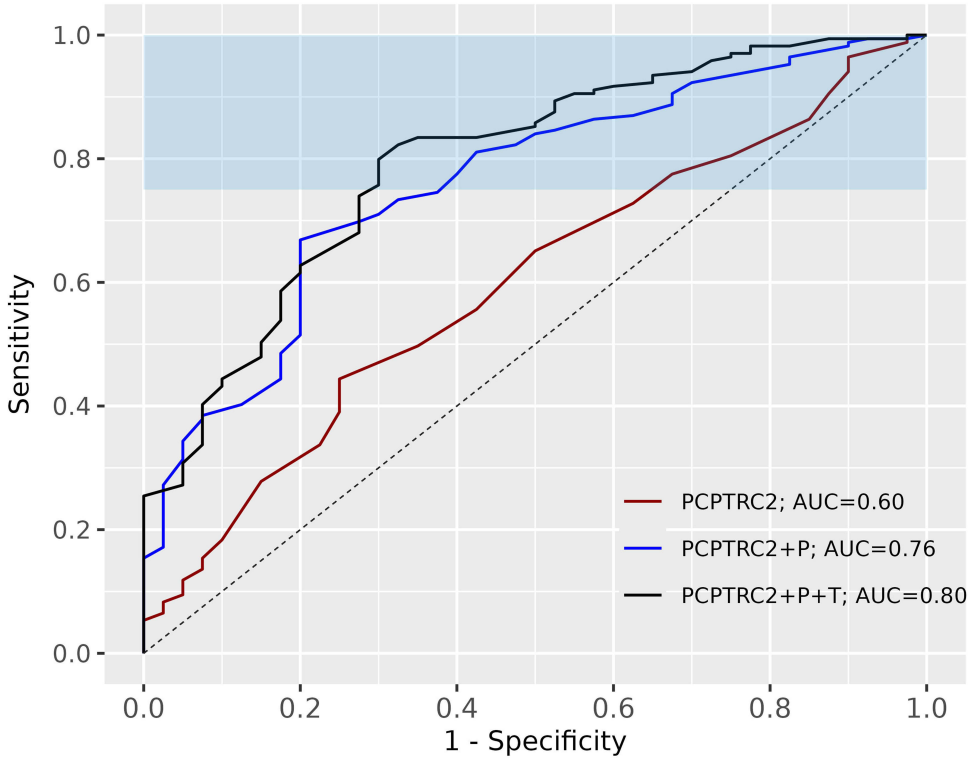

Figure 2 ROC curves and AUC of various PCa risk calculators for predicting PCa. *PCPTRC2* - prostate cancer prevention trial risk calculator version 2.0, *PCPTRC2+P* – PCPTRC2 version including PCA3 scores, *PCPTRC2+P+T* – PCPTRC2 version including PCA3 and TMPRSS2: ERG scores. The blue shaded area indicates a sensitivity range of 75% to 100% that was used for partial AUC calculations.

any PCa was 30%, with csPCa at 11% and non-csPCa at 19%. Negative biopsy results were predicted at 70% on average. Adding PCA3 to the PCPTRC2 increased the predicted probability of detecting PCa to 51%, csPCa to 20%, and non-csPCa to 30%, while negative biopsy results decreased to 49%. Incorporating both PCA3 and T:E further improved average predicted detection rates, with PCa reaching 55%, csPCa at 25%, and non-csPCa remaining at 30%, alongside

Table 3 AUC Comparisons for Predicting csPCa with 95% CI, Given in Brackets

Model	AUC with CI, %	P value vs PCPTRC2
PCPTRC2	61.6 (53.9–69.3)	NA
PCPTRC2 including PCA3	64.9 (57.3–72.6)	0.150
PCPTRC2 including PCA3+T:E	67.8 (60.3–75.3)	0.058

Note: T:E fusion of TMPRSS2 and ERG gene.
Abbreviations: PCPTRC2, prostate cancer prevention trial risk calculator 2; PCA3, prostate cancer antigen 3.

Table 4 Partial AUC (1–0.75 Sensitivity) Comparisons for Predicting csPCa with 95% CI, Given in Brackets.

Model	Partial AUC with CI, %	P value vs PCPTRC2
PCPTRC2	5.8 (3.7–8.5)	NA
PCPTRC2 including PCA3	7.8 (5.4–10.7)	0.063
PCPTRC2 including PCA3+T:E	8.6 (5.7–11.8)	**0.043**

Note: T:E fusion of TMPRSS2 and ERG gene. Significant Differences ($p<0.05$) are Highlighted in Bold.
Abbreviations: PCPTRC2, prostate cancer prevention trial risk calculator 2; PCA3, prostate cancer antigen 3.

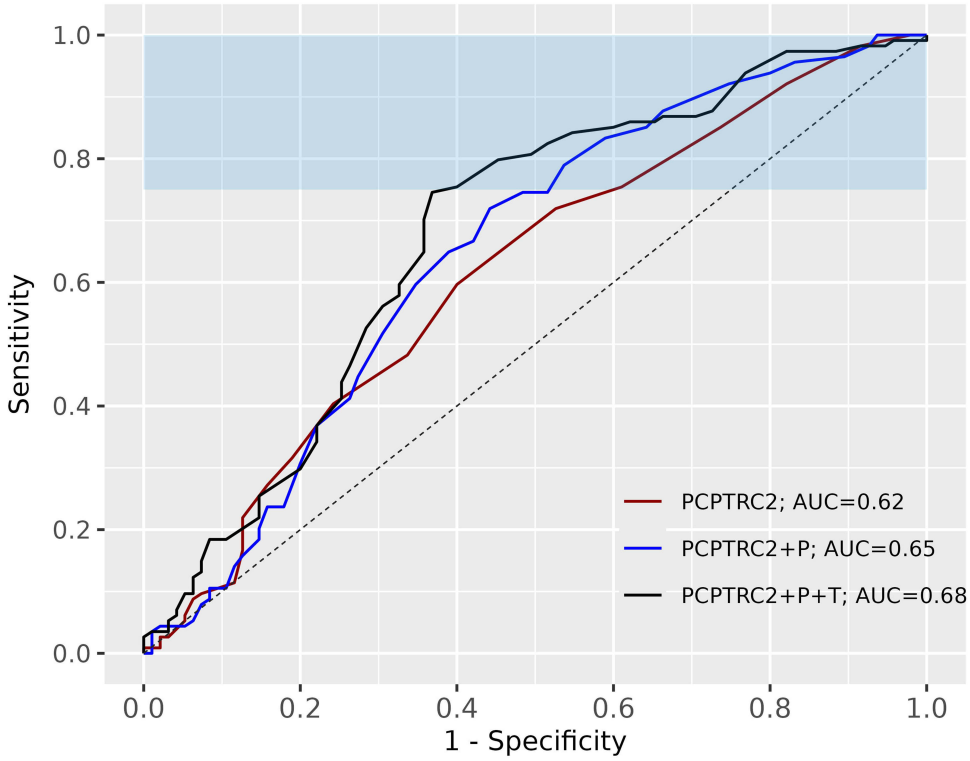

Figure 3 ROC curves and AUC of various PCa risk calculators for predicting csPCa. *PCPTRC2* - prostate cancer prevention trial risk calculator version 2.0, *PCPTRC2+P* – PCPTRC2 version including PCA3 scores, *PCPTRC2+P+T* – PCPTRC2 version including PCA3 and TMPRSS2: ERG scores. The blue shaded area indicates a sensitivity range of 75% to 100% that was used for partial AUC calculations.

a reduction in negative biopsy results to 45%. Regarding biopsy outcomes, PCa was detected in 81.3% of cases, csPCa in 53.1%, and non-csPCa in 28.2%. Negative biopsy results were observed in 18.7% of cases.

Discussion

The currently used biomarker, PSA, exhibits low specificity in detecting csPCa, leading to a high number of unnecessary prostate biopsies.[15] Our study results demonstrate that incorporating additional urinary biomarkers into PCPTRC2 improves csPCa detection.

In a study of Ankerst et al, PCA3 and T:E was incorporated in PCPTRC2, leading to 854 biopsies being performed.[4] The areas under the curve (AUC) for predicting csPCa were 70.0% (66.0–74.0%) for PCPTRC2 alone, 76.4% (72.8–80.0%) with PCA3 added and 77.1 (73.6–80.6%) with both PCA3 and T:E incorporated.[4] Similarly, Tomlins et al evaluated the association of urinary

Table 5 The Average Probabilities of Different Versions of the PCPTRC2 Risk Calculator Compared to Biopsy Outcomes.

Average Probabilities For:	PCa	CsPCa	Non-csPCa	Negative Biopsy
PCPTRC2 basic version	30%	11%	19%	70%
PCPTRC2+PCA3	51%	20%	30%	49%
PCPTRC2+PCA3+T:E	55%	25%	30%	45%
Biopsy outcomes	81.3%	53.1%	28.2%	18.7%

Note: T:E fusion of TMPRSS2 and ERG gene.
Abbreviations: PCPTRC2, prostate cancer prevention trial risk calculator 2; PCa, prostate cancer; csPCa, clinically significant prostate cancer; non-csPCa, non clinically significant prostate cancer; PCA3, prostate cancer antigen 3.

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PCA3 and the T:E with PCPTRC (version 1) in detecting csPCa, using urine samples from 1218 patients.[16] Their findings showed that the AUC for the basic PCPTRC version was 0.707, which increased to 0.752 with PCA3 and further rose to 0.779 when both PCA3 and T:E were included.[16] Our study found Lower AUC values for csPCa across all three scenarios. However, when analysing partial AUC values, PCPTRC2 including both PCA3 and T:E demonstrated significantly higher performance compared to PCPTRC2 alone (p=0.043). For predicting all PCa cases – both csPCa and non-csPCa –Tomlins et al reported that PCPTRC2 alone achieved AUC of 63.9%.[16] Notably, adding PCA3 improved the AUC to 73.9%, and incorporating both PCA3 and T:E further increased it to 76.2%. Our study revealed a lower AUC of 59.6% for PCa detection with PCPTRC2 alone. However, when incorporating additional biomarkers, specifically PCA3, the AUC improved to 76.2%, and with the addition of both PCA3 and T:E, it reached a maximum AUC of 79.5%. Moreover, our study was performed prospectively in a distinct and unique patient cohort. Notably, Lithuania remains the country with an active PCa screening program.[17] Data from cancer registries indicates that, over the past two decades, age-adjusted mortality rates for PCa have significantly declined across most Northern Europe and North America nations.[15] However, Lithuania stands out as an exception, exhibiting a rapid increase in PCa mortality over the same period.[18] This concerning trend underscores the urgent need for developing new diagnostic strategies. Advancements in imaging technologies and biomarker-based diagnostics have the potential to reduce the harms associated with PSA testing while maintaining—or even improving—the sensitivity of PCa and high-risk PCa detection.[18]

The effectiveness of PCA3 testing in detecting PCa and reducing unnecessary biopsies has been demonstrated in previously conducted studies and metanalyses[19,20] Our findings a suggests that incorporating both PCA3 and T:E biomarkers significantly enhances the detection of PCa. However, their addition in PCPTRC2 did not provide significant advantage in distinguishing csPCa from no PCa or non-cs PCa. This limitation is likely due to study's relatively small sample size and the different patient's cohort. Originally, PCTRC2 incorporated urinary biomarkers by quantifying their values based on copy numbers obtained through the MPS test.[10] In this study, we integrated urinary biomarker values obtained through a different urinary test into PCPTRC2.[8] The EAU-EAN guidelines emphasize the importance of using risk calculators that are properly calibrated to reflect the prevalence of PCa in the target population.[2] When applying PCPTRC2 to the Lithuanian population, recalibration may be necessary. This need for recalibration is further supported by our findings, which revealed that the average predicted risks for PCa and csPCa using PCPTRC2 were significantly lower than the actual biopsy-confirmed rates (Table 5).

Our study had several limitations. Firstly, data collection was restricted to a single centre, which could introduce selection bias. To minimize this, patients were included consecutively as they presented with documented suspicion of PCa. Second, the patients sample size was relatively small, highlighting the need for further research with larger cohorts to validate these findings. Third, the assessment of diagnostic performance relied on prostate biopsy results, which may introduce bias due to potential false-negative outcomes. Fourth, MRI combined fusion with transrectal ultrasonography prostate biopsy was not performed in this study, instead, histological results were obtained solely from TRUS guided prostate biopsies. Fifth, the patient cohort did not cover the entire pathological spectrum (ie, Gleason score and stage) and consisted exclusively of men from a single country. Therefore, further investigation in a larger, more diverse prospective cohort is required.

The incorporation of PCA3 and T:E in PCPTRC2 provides significant predictive value to csPCa diagnostics in biopsy-naïve patients. To validate these findings in clinical practice, larger prospective studies involving diverse patient populations are needed.

Data Sharing Statement

Data are available from the authors upon reasonable request.

Ethics Approval and Informed Consent

This study complies with the principles outlined in the Declaration of Helsinki. The investigation was approved by the Lithuanian regional Bioethical Commission, Decision no. BE-2-116. Informed consent was obtained from all individual participants.

Disclosure

The authors declare no conflicts of interest in this work.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209–249. doi:10.3322/caac.21660
2. Cornford P, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-ISUP-SIOG guidelines on prostate cancer—2024 update. part I: screening, diagnosis, and local treatment with curative intent. *Eur Urol*. 2024;86(2):148–163. doi:10.1016/j.eururo.2024.03.027
3. Denijs FB, van Harten MJ, Meenderink JJL, et al. Risk calculators for the detection of prostate cancer: a systematic review. *Prostate Cancer Prostatic Dis*. 2024;27(3):544–557. doi:10.1038/s41391-024-00852-w
4. Ankerst DP, Goros M, Tomlins SA, et al. Incorporation of urinary prostate cancer antigen 3 and TMPRSS2:ERG into prostate cancer prevention trial risk calculator. *Eur Urol Focus*. 2019;5(1):54–61. doi:10.1016/j.euf.2018.01.010
5. Warli SM, Warli MH, Prapiska FF. PCA3 and TMPRSS2: ERG urine level as diagnostic biomarker of prostate cancer. *Res Rep Urol*. 2023;15:149–155. doi:10.2147/RRU.S401131
6. Kemesiene J, Nicolau C, Cholstauskas G, et al. Usefulness of urinary biomarker-based risk score and multiparametric MRI for clinically significant prostate cancer detection in biopsy-naïve patients. *Abdom Radiol*. 2025. doi:10.1007/s00261-024-04727-5
7. Poyet C, Nieboer D, Bhindi B, et al. Prostate cancer risk prediction using the novel versions of the European Randomised Study for Screening of Prostate Cancer (ERSPC) and Prostate Cancer Prevention Trial (PCPT) risk calculators: independent validation and comparison in a contemporary Europe. *BJU Int*. 2016;117(3):401–408. doi:10.1111/bju.13314
8. JSC 'Diagnolita. Prostate cancer biomarker test. Available from: https://www.diagnolita.lt/en/tests/prostate-cancer-biomarker-test//. Accessed March 05, 2024.
9. Ankerst DP, Hoefler J, Bock S, et al. Prostate Cancer Prevention Trial risk calculator 2.0 for the prediction of low- vs high-grade prostate cancer. *Urology*. 2014;83(6):1362–1367. doi:10.1016/j.urology.2014.02.035
10. Lebastchi AH, Russell CM, Niknafs YS, et al. Impact of the MyProstateScore (MPS) test on the clinical decision to undergo prostate biopsy: results from a contemporary academic practice. *Urology*. 2020;145:204–210. doi:10.1016/j.urology.2020.07.042
11. Paliksa S, Gagilas J, Lopeta M, et al. Diagnostic performance of PCA3 and TMPRSS2:ERG biomarkers in prostate cancer patients urine collected with and without prostate massage. *Eur Urol Suppl*. 2019;18(3):e2427–e2428. doi:10.1016/S1569-9056(19)32142-6
12. Weinreb JC, Barentsz JO, Choyke PL, et al. PI-RADS prostate imaging - reporting and data system: 2015, Version 2. *Eur Urol*. 2016;69(1):16–40. doi:10.1016/j.eururo.2015.08.052
13. Baraban E, Epstein J. Prostate Cancer. *Surg Pathol Clin*. 2022;15(4):579–589. doi:10.1016/j.path.2022.07.008
14. Lasko TA, Bhagwat JG, Zou KH, Ohno-Machado L. The use of receiver operating characteristic curves in biomedical informatics. *J Biomed Inform*. 2005;38(5):404–415. doi:10.1016/j.jbi.2005.02.008
15. Hilscher M, Røder A, Helgstrand JT, et al. Risk of prostate cancer and death after benign transurethral resection of the prostate—A 20-year population-based analysis. *Cancer*. 2022;128(20):3674–3680. doi:10.1002/cncr.34407
16. Tomlins SA, Day JR, Lonigro RJ, et al. Urine TMPRSS2:ERG Plus PCA3 for individualized prostate cancer risk assessment. *Eur Urol*. 2016;70(1):45–53. doi:10.1016/j.eururo.2015.04.039
17. Chandran A, van Harten M, Singh D, et al. Risk-stratified approach to implementing population-based prostate cancer screening in five pilot sites in the European Union: a protocol for the PRAISE-U project. *Eur Urol Open Sci*. 2024;70:8–17. doi:10.1016/j.euros.2024.09.003
18. Brawley OW, Thompson IM, Grönberg H. Evolving recommendations on prostate cancer screening. *Am Soc Clin Oncol Educat Book*. 2016;(36):e80–e87. doi:10.1200/EDBK_157413
19. Hu B, Yang H, Yang H. Diagnostic value of urine prostate cancer antigen 3 test using a cutoff value of 35 μg/L in patients with prostate cancer. *Tumor Biol*. 2014;35(9):8573–8580. doi:10.1007/s13277-014-2109-4
20. Qin Z, Yao J, Xu L, et al. Diagnosis accuracy of PCA3 level in patients with prostate cancer: a systematic review with meta-analysis. *Int Braz J urol*. 2020;46(5):691–704. doi:10.1590/s1677-5538.ibju.2019.0360