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Head-to-head comparison of two online nomograms for prostate biopsy outcome prediction

Mário Oliveira, Vera Marques, António Pedro Carvalho and Américo Santos

Department of Urology, Hospital de Braga, Braga, Portugal

Accepted for publication 17 June 2010

Study Type – Diagnosis (exploratory cohort)
Level of Evidence 2b

What's known on the subject? and What does the study add?
In recent years, several nomograms were developed in an effort to decrease the number of unnecessary prostate biopsies. The European SWOP-PRI and the North American PCPT are among the most popular. However, evidence on the relative predictive accuracy is lacking.

A head-to-head comparison on the diagnostic accuracy of two previously validated prostate cancer risk predictors on biopsy confirmed the superiority of these tools over PSA alone. Moreover, in the studied population, the European SWOP-PRI proved to be more accurate than the North American PCPT-CRC.

OBJECTIVE

- To compare the diagnostic accuracy of two previously validated prostate cancer risk predictors on biopsy.

PATIENTS AND METHODS

- In total, 390 consecutive patients submitted to 10-core systematic transrectal prostate biopsy at our institution were included in this retrospective study.
- External validation of a European (European Randomized Study of Screening for Prostate Cancer derived Prostate Risk Indicator; SWOP-PRI) and a North American (Prostate Cancer Prevention Trial Cancer Risk Calculator; PCPT-CRC) nomogram was performed.
- The predictive accuracy of these online available nomograms was calculated based on the area under the curve derived from receiver–operator characteristic curves and then compared using the DeLong method.

RESULTS

- Both tools were confirmed to be superior to prostate-specific antigen alone. Moreover, the SWOP-PRI (77.9%) displays a 7.96% increase in the predictive accuracy compared to the PCPT-CRC (69.9%) in a statistically significant fashion ($P = 0.002$).

CONCLUSIONS

- The results obtained in the present study confirm the utility of nomograms with respect to biopsy outcome prediction in patients with suspicion of prostate cancer.
- In the current sample of patients, the European-based nomogram appears to be more accurate than the North American nonogram, which lacks information regarding prostate volume and prostatic ultrasonographic lesions.
- To our knowledge, this is the first study to compare the accuracy of these popular risk calculators in a specific population.

KEYWORDS

biopsy, prostate cancer, nomogram

INTRODUCTION

In recent years, several nomograms have become available to the clinician, assisting in the risk stratification of prostate cancer (PCa) at needle biopsy [1–5]. On the basis of data obtained from large populations, these tools were developed for application in the daily clinical practice. However, and despite having shown a better predictive accuracy compared to PSA alone [6], the use of nomograms in the decision to perform prostate biopsy is not yet a standard practice [7].

On the other hand, different variables are considered in the various nomograms that may contribute to their individual predictive accuracy. In addition to increased PSA, several positive predictors of PCa were identified, including a suspicious DRE and TRUS as well as a positive family history, whereas an increased prostate volume was considered a negative predictor [8]. Moreover, the accuracy of such tools may differ according to the characteristics of the target population [9,10].

We considered it of interest to perform an external validation and compare the diagnostic accuracy of two popular online available risk calculators in a specific population: the European Randomized Study of Screening for Prostate Cancer derived Prostate Risk Indicator (SWOP-PRI) [1] and the Prostate Cancer Prevention Trial derived Cancer Risk Calculator (PCPT-CRC) [2].

PATIENTS AND METHODS

PATIENT POPULATION

Retrospective analysis of data from consecutive patients submitted to 10-core systematic TRUS-guided prostate biopsy at our institution between January 2007 and August 2009 was performed. Patients were referred to biopsy as a result of either a suspicious DRE and/or elevated PSA. Analysis targeted subjects with a PSA level <50 ng/mL.

TABLE 1 Characteristics of the patient population submitted to prostate biopsy

Variable	*n*	Cancer	No malignancy	*P*
Number of patients (%)	390 (100)	155 (39.7)	235 (60.3)	
Age (years)				
Mean ± SD	69.2	71.6 ± 8.0	67.6 ± 8.3	<0.001
Range	44–89	44–89	44–87	
PSA (ng/mL), mean ± SD	12.5	17.2 ± 15.75	9.4 ± 7.9	<0.001
Suspicious DRE, *n* (%)	129 (35)	70 (47.0)	59 (26.0)	<0.001
Prostate volume (mL)				
Mean ± SD	65.4	52.0 ± 28.6	73.3 ± 33.9	<0.001
Range	15–200	15–192	15–200	
Hypoechogenic lesion	113 (37%)	53 (48%)	60 (31%)	0.001

Data are also presented according to biopsy outcome.

TABLE 2 Rate of prostate cancer detection according to calculated risk for the European Randomized Study of Screening for Prostate Cancer derived Prostate Risk Indicator (SWOP-PRI) and Prostate Cancer Prevention Trial derived Cancer Risk Calculator (PCPT-CRC) nomograms

	Calculated risk (%)	
Age (years)	SWOP-PRI	PCPT-CRC
<15	14.9	14.3
15–44	31.0	24.0
45–59	47.8	30.8
60–74	62.5	45.9
≥75	87.5	76.8

TRUS-GUIDED PROSTATE BIOPSY

TRUS-guided prostate biopsy was performed using a 7-MHz probe (Prosound SSD-35005v, Aloka co. Ltd., Tokyo, Japan). An automatic biopsy gun (Porgés Laboratories, Le Plessis Robinson, France) with a 18-gauge needle (Coloplast Corporate, Humlebaek, Denmark) was used to obtain 10-core fragments.

RISK CALCULATORS

The European SWOP-PRI was designed based on data obtained from 6288 Dutch males, mostly Caucasian, participating in a study on the viability of a population-based screening and its effect on mortality [1]. On the other hand, the North-American PCPT-CRC was based on data obtained from 5519 males from the placebo group of the study evaluating the possible preventive effect of finasteride in PCa development [2]. In both populations, sextant biopsies were performed.

To obtain risk estimates, predictor variables necessary for each tool were gathered. Predictor variables considered for the SWOP-PRI nomogram included abnormalities on DRE, serum PSA, previous negative biopsy, hypoechogenic lesions on TRUS and prostatic volume determined by ultrasonography. All these parameters have independent value in predicting biopsy outcome [7]. On the other hand, to obtain the risk of the PCPT-CRC nomogram, in addition to the former three predictor variables included for the SWOP-PRI, a family history of PCa was also considered. The formula for the latter is:

$$1/[1+\exp(-\mathrm{PCA})], \text{ being } \mathrm{PCA} = -1.7968 + 0.8488 \times \log(\mathrm{PSA}) + 0.2693 \times \text{Familiar history} + 0.9054 \times \mathrm{DRE} - 0.4483 \times \text{Previous biopsy}\ (1 = \text{yes}, 0 = \text{no})$$

STATISTICAL ANALYSIS

Predictive variables were compared based on the biopsy outcome, either using a *t*-test or chi-squared. Next, an external validation of SWOP-PRI and PCPT-CRC was performed. The predictive accuracy of both tools was assessed by analysis of the area under the receiver–operator characteristic (ROC) curve. The statistical significance of the difference between the areas under the ROC curves was analyzed using the DeLong method [11].

All statistical tests were performed with the use of the MedCalc for Windows, version 11.2.1 (MedCalc Software, Mariakerke, Belgium). $P < 0.05$ (two-tailed) was considered statistically significant.

RESULTS

The characteristics of the study population are shown in Table 1. Among the 390 patients included in the analysis, 121 (31.0%) had history of a previous negative biopsy and 155 (39.7%) were diagnosed with PCa. Age, PSA, DRE, prostate volume and TRUS findings were all significant predictors of PCa.

Table 2 displays the rate of PCa detection according to calculated risk for each

FIG. 1. Receiver–operator characteristic curves for the European Randomized Study of Screening for Prostate Cancer derived Prostate Risk Indicator (SWOP-PRI) and Prostate Cancer Prevention Trial derived Cancer Risk Calculator (PCPT-CRC).

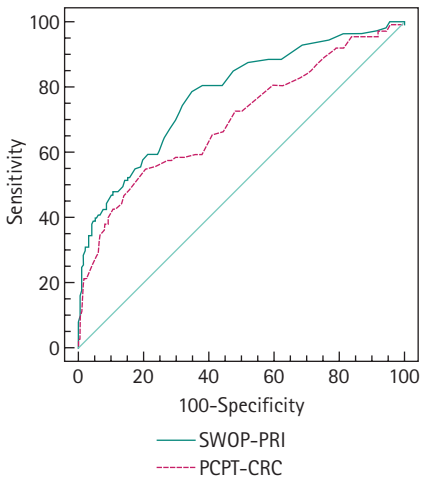

TABLE 3 Head-to-head comparison of the predictive accuracy of the European Randomized Study of Screening for Prostate Cancer derived Prostate Risk Indicator (SWOP-PRI) and Prostate Cancer Prevention Trial derived Cancer Risk Calculator (PCPT-CRC) nonograms and PSA

	SWOP-PRI	PCPT-CRC
PCPT-CRC	0.002	–
PSA	<0.001	0.044

nomogram. Along with rising SWOP-PRI and PCPT-CRC risks, an increase in the rate of PCa detection is observed.

Figure 1 shows the ROC curves for both risk calculators. The accuracy of the SWOP-PRI was 77.9% (95% CI, 0.728–0.823; $P < 0.001$) vs 69.9% (95% CI, 0.645–0.749; $P < 0.001$) for the PCPT-CRC. Comparison of the difference between the areas under the ROC curves using the DeLong method revealed a 7.96% increased predictive accuracy for the SWOP-PRI compared to the PCPT-CRC nomogram in a statistically significant fashion ($P = 0.002$) (Table 3). Moreover, the area under the curve for serum PSA alone was 65.8% (95% CI, 0.602–0.711; $P < 0.001$) and was significantly different from both risk calculators.

DISCUSSION

PCa risk calculators are valuable tools in the process of prostate biopsy decision-making. By incorporating several predictor variables, these tools have already proved to be superior to PSA alone, particularly in patients presenting several risk factors, and thus should be considered in the office-based clinical practice [6,8].

Various predictors of PCa were identified, namely suspicious DRE and TRUS findings and a positive family history [8]. Conversely, increased prostate volume and previous negative biopsy are considered to be negative predictors [2,8].

In the present study population, the areas under the curve for the SWOP-PRI and the PCPT-CRC were 77.9% and 69.9%, respectively, thus reproducing the previewed predictive accuracy in the original populations (79.0% and 70.2%, respectively) [1,2]. Moreover, considering the minimal accepted predictive accuracy of nomograms is 70–80% [12], both risk calculators can be considered as adequate.

Nonetheless, in the present data set, the SWOP-PRI displays a superior accuracy compared to the PCPT-CRC. According to the results obtained in the present study, and in addition to any geographical and ethnical issues that need to be considered, the information concerning prostate volume and hypoechogenic lesions in ultrasonography appears to confer an added value to the tool when predicting the risk of PCa because these variables are not taken into account in the North-American model.

Despite the clinical implementation of these two parameters in all patients often proving difficult, recent data suugest that, even with a relatively approximate estimation of the total prostate volume by DRE, an adaptation of the SWOP-PRI performs better than PSA alone or in combination with DRE [13].

Furthermore, previous studies have shown a discrepancy with respect to accuracy according to the population under study, which, as well as for other reasons, could be justified by racial differences [9,10].

Both risk calculators were initially developed based on a sextant biopsy regimen, which is no longer current practice. Because the extended biopsy regimens that are now commonly applied will probably decrease the effect of prostate volume on PCa detection, an adaptation of these models is necessary [14]. Moreover, nomograms based on extended biopsy regimens have already shown an increased predictive accuracy compared to previously established models based on 6–10-core biopsies [15].

Nonetheless, the obvious limitations of PSA-based tools should be considered when using these nomograms because the inconvenience of PCa over- and under-detection persists [16]. The poor correlation of serum PSA levels with PCa aggressiveness [17] appears to be at least partially responsible for the trend in over-diagnosis and subsequent over-treatment in clinical practice [18]. On the other hand, previous data from the PCPT failed to reveal a PSA threshold with both high sensitivity and specificity when monitoring healthy men [19]. According to that study, to detect more than 80% of PCa cases, the PSA threshold would need to be 1.1 ng/mL, which would mean submitting >60% of men without cancer to biopsy. Furthermore, with a threshold of 2.6 ng/mL, only 40% of PCa cases would be detected.

Thus, the need for alternative PCa biomarkers has lead research, with the PCA3 test emerging as a strong candidate [20]. Recent data suggest that the use of this marker can decrease the number of unnecessary biopsies and possibly contribute to the reduction of over-diagnosis [21]. Evidence also shows that the PCA3 test may result in a preferential detection of higher risk cancers rather than indolent disease [16]. Additionally, several studies of genetic susceptibility to the development of PCa are also in progress [20].

In conclusion, despite their limitations, the risk indicators evaluated in the present study can be of added value when defining a starting point in patient assessment and should be considered in clinical practice. However, improvements regarding the selective identification of men who are susceptible to the development of life-threatening disease are mandatory, and will hopefully contribute to the timely and proper management of these patients.

CONFLICT OF INTEREST

None declared.

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Correspondence: Mário Oliveira, Department of Urology, Hospital de Braga, Apartado 2242, 4701-965 Braga, Portugal.
e-mail: mariooliveira@ecsaude.uminho.pt

Abbreviations: **PCa**, prostate cancer; **PCPT-CRC**, Prostate Cancer Prevention Trial Cancer Risk Calculator; **ROC**, receiver–operator characteristic; **SWOP-PRI**, European Randomized Study of Screening for Prostate Cancer derived Prostate Risk Indicator.