A novel mathematical simulation modelling method to predict the probability of finding cancer in prostate biopsy on an individual basis

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Abstract

**Purpose:** To calculate the probability of finding cancer on prostate biopsy, we developed a prostate cancer (PCa) predictive statistical model (PCP-SMART), deriving a novel PCa-predictor (pcrdindex) and a pca-risk mathematical equation.

**Subjects and methods:** A total of 371 men were included. Since PCa-risk relates to tPSA, age, prostate volume[PV], fPSA, f/tPSA-ratio, PSAD and tPSA≥50ng/ml has 98.5% Positive-Predictive-Value(PPV) for PCa diagnosis, we hypothesized that correlating two variables, each consisting of three ratios/values including patient’s-tPSA, PSA50ng/ml, age, prostate volume, f/tPSA ratio, could operate as a “PCa-conditions imitating-simulating model”. Linear regression derived the coefficient-of-determination(R²), termed PCRDindex. Statistics included x² test, multiple logistic regression analysis, test-performance characteristics and AUC/ROC-curve analysis [SPSS-22(p<0.05)].

**Results:** Biopsy was PCa(+) in 45.1% and PCa(-) in 44.2%. PCRDindex signed(+) in 89.82% PCa(+) and negative in 91.46% PCa(-) cases (x²-test: p<0.001-RR: 10.52) [Sensitivity: 89.8%, specificity: 91.5%, PPV: 91.5%, Negative-Predictive-Value(NPV): 89.8%, Positive-Likelihood-Ratio[LR(+)]: 10.5, Negative-Likelihood-Ratio[LR(-)]: 0.11 Accuracy: 90.6%]. Multiple logistic regression and AUC/ROC analysis revealed PCRDindex as independent PCa-predictor strongly (p<0.001) outperforming other clinically established while, the formulated risk-equation predicted 91% accurately the probability of finding cancer.

**Conclusions:** PCRDindex effectively predicted prostate biopsy outcome, identifying correctly 9/10 men who indeed harbored cancer while, correctly ruling out PCa in 9/10 men without disease evidence. It significantly outperformed other established PCa-predictors while, the PCa-risk equation, accurately calculated the individual probability of finding cancer on biopsy.

Key words
prostate cancer; PSA testing; PCP-SMART model; PCRD-Index; prostate cancer risk mathematical equation

Citation

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**Introduction**

In the past few years there has been considerable controversy regarding PSA testing diagnostic performance, based on evidence indicating that currently this biomarker is insufficient for identifying prostate cancer (PCa), mainly due to lack of ideal PSA cut-points that yield both high sensitivity and specificity. Instead, PCa risk varies continuously at all PSA values, with no lower limit existing to safely predict absence of the disease. Nevertheless, absolute PSA thresholds continue to be a central facet for recommending prostate biopsy (PBx), policy resulting in a high percentage of unnecessary biopsies, avoidance of which is crucial because of the risk of potentially severe complications (pain, infections, bleeding, urinary obstruction, emotional distress) not to mention financial cost. To optimally evaluate patients and prevent men with persistent PSA abnormalities and previous negative biopsies from undergoing a vicious cycle of useless repeat biopsies, it is of great clinical importance to assess PCa risk prior to PBx. To this aim, patient stratification techniques, accurately estimating individual risk of finding PCa at biopsy (risk based strategy), are essential for evidence based decision making and patient counselling.

Aiming to develop a clinical method capable of making individualized predictions regarding PBx outcome as well as, of “measuring/weighing the intensity” of follow-up and further interventions (repeat PBx) needed, in cases with negative initial biopsies and abnormal PSA thereafter, we formulated a “PCa mathematical conditions simulating/mimicking” predictive model (PCP-SMART), deriving a novel PCa predictor (PCRD) and a mathematical risk equation, that allows calculation of a single value for estimating the probability of finding cancer on biopsy in an individual basis. Herein, we introduce this novel model and report the results of a prospective, observational study on its clinical validity and applicability. (For further details refer to: http://www.clinical-genitourinary-cancer.com/article/S1558-7673(16)30179-3/fulltext).

**Material and methods**

Our main idea for constructing the PCP-SMART model (Prostate Cancer Predictive Simulation Modeling, Assessing the Risk, Technique), was based on key data such as: 1) Apart from total PSA (tPSA), several other clinical parameters represent established independent predictors (risk factors) of prostate cancer, such as age, age-specific/adjusted PSA, free PSA (fPSA), free/total PSA ratio (f/tPSA), prostate volume and PSA Density (PSAD), serum tPSA values ≥50 ng/ml have a positive predictive value (PPV) of 98.5% (PCa diagnosis considered 98.5% certain) in predicting the presence of prostate cancer on needle biopsy, 2) statistical regression analysis (linear/logistic) is applied to model the probability of prostate cancer more accurately, estimated directly as a function of serum total and free PSA, combined with other key risk factors. Capitalizing on these observations, we developed a linear-regression model incorporating all the aforementioned predictors, mainly hypothesizing that, if we calculated the “strength” of association between the function of a given set of PCa predictors and another set formed by the same parameters projected to function under “mathematical conditions mimicking/simulating” PCa (as when tPSA = 50ng/ml), we would presumably have attained a close estimation/measure of the probability the patient to be diagnosed with the disease. Subsequently, we formulated two variables, [Y- (dependent) / X- (independent)], each consisting of three (3) numerical values (decimal fractions), emerging as follows: 1) Variable (Y): patient tPSA/age, patient tPSA/PV, fPSA/patient tPSA, 2) Variable (X): tPSA50/age, tPSA50/PV, fPSA/tPSA50. Simple linear regression derived the coefficient of determination-R², which we called Prostate Cancer Risk Determinator (PCRDindex), signed (+) / (-) according to the correlation’s equation line slope (ascending = positive / descending= negative) (http://mathbits.com/MathBits/TISection/Statistics2/correlation.html). All calculations were performed using Windows-Excel (see Appendix) and free online calculators.

After receiving institutional board approval, we performed an observational, prospective evaluation of a cohort of 725 men subjected to transrectal ultrasound-guided needle biopsies/ies at Naval-Veterans Hospital of Athens (Nov2006–Dec 2014), because of abnormal serum tPSA-values (2.5–10 ng/ml) and/or suspicious digital rectal examination (DRE). Cases with abnormal DRE and tPSA 10-20ng/ml or <2.5ng/ml were also included. Exclusion criteria were: 1) insufficient patient follow-up, 2) tPSA>20ng/ml, 3) uri-
nary tract infection, 4) medical therapy affecting tPSA (5α-reductase inhibitors), 5) previous benign prostatic hyperplasia (BPH) surgery, recent urethral/prostatic (DRE) manipulations, 6) PCa diagnosis and/or endocrine manipulations. Strictly conforming to criteria, 371 (51.2%) patients were considered eligible for enrollment in the study.

After dividing subjects were into those with confirmed PCa diagnosis and them not harbouring the disease, comparative analysis of the predictive accuracy among input clinical variables as well as PCRDindex was performed. Serum tPSA and f/tPSA ratio were assessed using enzyme immunoassay method, PSAD was calculated dividing tPSA by PV (ng/mL/cc) while, since no significant differences exist between transabdominal / transrectal ultrasound PV measurements, to best approximate prostate volume when given transabdominal ultrasound gland dimensions, the ellipsoid formula \[\frac{\pi}{6} \times \left(\frac{0.52}{x} \times \text{height} \times \text{width} \times \text{length}\right)\] was employed\(^4\).

All patients underwent transrectal ultrasound guided PBx (TRUS/PBx) in the left lateral decubitus position, by using 18-gauge core-biopsy needle and grayscale ultrasonography (7.5 MHz endocavity transducer). A 12-core biopsy protocol was applied and in negative result cases, further biopsies with increasing numbers of cores were performed, based on data showing that in men with suspicion of PCa (abnormal tPSA / High Grade Prostate Intraepithelial Neoplasia (HGPIN) / Atypical Small Acinar Proliferation (ASAP) after initial negative PBx, more aggressive protocols up to saturation biopsy (≥24 cores), obtained the highest cancer detection rates\(^5\). Subjects were classified truly PCa negative if had undergone 2-3 extended biopsies (16-24 cores) followed by prostatic adenomectomy (transurethral [TURP] or open) or, subjected to ≥3 biopsies including saturation schemes (≥24 cores). HGPIN/ASAP cases were excluded from analysis.

Univariate analysis between variables and diagnostic groups (men diagnosed with cancer and those not) was performed using chi-square(x²)-test (Yates-correction), Relative-Risk (+/-) 95% Confidence Intervals [CIs] were derived and differences were compared using Student’s t-test. The predictive efficiency/accuracy of PCRDindex was evaluated by calculating specificity (% cancer cases with positively signed PCRD), sensitivity (% non-cancer controls with negatively signed PCRD), LR(+), LR(-), PPV, NPV and accuracy while, it was quantified by computing the AUC-ROC curves. Multiple logistic regression analysis with binary dependent variable the biopsy result, estimated the influence of each included risk-factor in the PCP-SMART model building set, on the likelihood of PCa positive PBx outcome (identify independent predictors), as well as, derived a logistic regression equation calculating the probability of diagnosing PCa at PBx. Analyses were performed using SPSS-22® (SPSS Inc-Chicago, IL) and INSTAT (GraphPad)® statistical packages. Two-sided hypothesis testing was used, \(p<0.05\) considered statistically significant.

### TABLE 1
Presentation of the logistic regression coefficient (b), Wald test, statistical significance of individual regression coefficients tested using the Wald Chi-square statistic and odds ratio [Exp(B)], for each of the predictors (variables in the equation) in the full model of the multiple logistic regression analysis

<table>
<thead>
<tr>
<th>Variables in the Equation</th>
<th>b</th>
<th>S.E.</th>
<th>Wald test</th>
<th>df</th>
<th>Sig.</th>
<th>Exp(B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.036</td>
<td>0.029</td>
<td>1.529</td>
<td>1</td>
<td>0.216</td>
<td>1.036</td>
</tr>
<tr>
<td>Age-adjusted tPSA</td>
<td>-3.048</td>
<td>6.239</td>
<td>0.239</td>
<td>1</td>
<td>0.625</td>
<td>0.047</td>
</tr>
<tr>
<td>Prostate volume</td>
<td>-0.023</td>
<td>0.011</td>
<td>4.530</td>
<td>1</td>
<td>0.033</td>
<td>0.977</td>
</tr>
<tr>
<td>PSAD</td>
<td>-3.421</td>
<td>4.184</td>
<td>0.668</td>
<td>1</td>
<td>0.414</td>
<td>0.033</td>
</tr>
<tr>
<td>total PSA</td>
<td>0.015</td>
<td>0.194</td>
<td>0.006</td>
<td>1</td>
<td>0.940</td>
<td>1.015</td>
</tr>
<tr>
<td>free PSA</td>
<td>0.166</td>
<td>0.607</td>
<td>0.075</td>
<td>1</td>
<td>0.784</td>
<td>1.181</td>
</tr>
<tr>
<td>f/t PSA ratio</td>
<td>-3.713</td>
<td>5.130</td>
<td>0.524</td>
<td>1</td>
<td>0.469</td>
<td>0.024</td>
</tr>
<tr>
<td>PCRD index</td>
<td>3.198</td>
<td>0.464</td>
<td>47.446</td>
<td>1</td>
<td>0.000</td>
<td>24.489</td>
</tr>
<tr>
<td>Constant</td>
<td>0.220</td>
<td>2.012</td>
<td>0.012</td>
<td>1</td>
<td>0.913</td>
<td>1.246</td>
</tr>
</tbody>
</table>
Results
Among 371 men biopsied, PCa was diagnosed in 167 (45.1%), no evidence of the disease was found in 164 (44.2%) while, HGPIN or/and ASAP lesions were detected in 40 (10.7%). PCa diagnosis was made in 92 (55.1%) patients at initial biopsy, in 52 (31.1%) at second while, 23 (13.8%) at ≥3 repeat biopsies. The median number of tissue cores taken at 1st, 2nd and ≥ 3 repeat biopsy was 11.5 (8-14), 16 (13-19) and 21 (17-32) respectively. Among PBx negative cases, 53 (31.7%) underwent 2-3 extended biopsy protocols (>18-20 cores) and prostatic adenomectomy (transurethral/open) whereas, 112 (68.3%) were subjected to ≥4 biopsy sessions using extended (≥20) or saturation (≥24 cores) schemes.

Comparative univariate analysis (median values) showed that, men with PCa vs controls, were significantly more likely to be older (69 vs. 65.5 years - \(p=0.051\)), have higher tPSA (7.75 vs. 6.69ng/ml - \(p=0.0065\)), lower fPSA (0.92 vs.1.31ng/ml\(\ p=0.0052\)), lower f/tPSA-ratio (0.12 vs. 0.19 - \(p<0.001\)), smaller prostates (36 vs. 67cc – \(p<0.001\)) and higher PSAD (0.20 vs. 0.10 – \(p<0.001\)). Overall, PCRDindex values were positive (positive linear-regression line slope) in 164 (49.55%) cases and negative (negative-slope) in 167 (50.45%) men. In 150 (89.82%) of the 167 patients diagnosed with PCa, PCRD values were signed positive and in 17 (10.18%) signed negative whereas, in 150 (91.46%) of the 164 patients with no evidence of the disease, PCRDindex values were negative and in only 14 (8.54%), had positive values. Chi-square test yielded a value of 215.45, two-sided \(p<0.0001\), Odds-Ratio 94.5 (44.97-198.7 [95% CI]) and Relative Risk 8.98 (5.7-14.1 [95% CI]). PCRDindex sensitivity for predicting PBx outcome was 89.82% ([95% CI]: 83.95-93.78), specificity 91.46% (85.82-95.08), PPV 91.46% (85.82-95.08), NPV 89.82% (83.95-93.78), LR(+) 10.52 (6.36-17.41), LR(-) 0.11 (0.07-0.17) and overall accuracy 90.63%. A test of the full model against a constant (intercept) only model was statistically significant (-2Log-likelihood = 200,798 vs. 444,848 - Omnibus x² test = 244,049, \(p<0.001\)), indicating that after excluding age-adjusted PSA ratio (tPSA/age) found to be insignificantly correlated to biopsy outcome (score=1.05–\(p=0.305\)), all other predictors as a set reliably distinguished between PCa negative/ positive PBx outcome. As such, each independent variable significantly improved the model (scores/significances): age: 7.275 - \(p=0.007\), PV: 64,657 - \(p<0.001\), tPSA: 7.030 - \(p=0.008\), fPSA: 25,147- \(p<0.001\), f/tPSA ratio: 77,339 - \(p<0.001\), PSAD: 75,69 - \(p<0.001\), PCRD: 183,519 - \(p<0.001\) (overall-score = 198,137). PCRDindex exhibited the highest score test (=measure of how much an independent variable would be significant in the model), significantly outperforming other predictors. The model explained...
71.0% (Nagelkerke's-R2= 0.71) of biopsy result variance and correctly classified 90.7% of cases. Table 1 presents logistic regression coefficient (b), Wald-test, statistical significance of individual regression-coefficients (Wald-Chi-square) and odds-ratio [Exp(B)] for each predictor. Employing a 0.05/Wald-test criterion, only PCRDindex and PV made a significant contribution to prediction of cancer (key PCa predictors) while, age, tPSA, fPSA, f/tPSA-ratio and PSAD, had insignificant partial effects. The EXP(b) [Odds-ratio] value for PCRDindex was 24.02 (95% CI: 9.812-58.778) suggesting that, increasing PCRD values are associated with highly increased likelihood (x24-times) of diagnosing PCa. To examine which variables were most strongly associated with the outcome, we ranked them by the probability of the Wald/chi-square test (metric=1 minus Wald-x\(^2\)p-value) coded such that, higher values pointing to greater outcome association strength, in the following order: (1) PCRD: 1.0, (2) PV: 0.961, (3) age: 0.847, (4) f/t PSA ratio: 0.559, (5) PSAD: 0.518, (6) fPSA: 0.265, (7) tPSA: 0.232. Employing logistic regression equation formula:

\[ p = \frac{e^{a + b1x1 + b2x2 + b3x3 + \ldots}}{1 + e^{a + b1x1 + b2x2 + b3x3 + \ldots}} \]

\( p \) = event probability, \( e \) = natural logarithms base(≈2.72), \( a \) = equation constant, \( b \) = predictor variables coefficient, we formulated an equation calculating the probability of finding PCa on biopsy in the form: 

\[ p = \frac{e^{3.199xPCRDindex - 0.023xPV + 0.22}}{1 + e^{3.199xPCRDindex - 0.023xPV + 0.22}} \]

PCRDindex exhibited significantly greater AUC-ROC curve \( [0.926, \ vs. \ tPSAD (0.848-p=0.0015), PV (0.830-p<0.001), f/tPSA-ratio (0.814-p<0.001), fPSA (0.672-p<0.001), age (0.595-p<0.001), tPSA (0.577-p<0.001). (Table 2, Figure 1, Figure 2)\]

Discussion

Main advantage of the PCP-SMART model is that it comprises established and routinely available PCa predictors such as age, PV, fPSA, f/tPSA-ratio and PSAD. First step of model development was simple linear regression of two variables, comprising the above-mentioned key predictors, which derived the coefficient of determination (R\(^2\)), a math-factor that provides a measure of how well future outcomes are likely to be predicted by statistical models [http://mathbits.com/MathBits/TISection/Statistics2/correlation.htm] and which we re-termed PCRDindex. Main hypothesis was that, by identifying patient-subgroups with high/low risk (positively/negative signed PCRD values respectively), our novel index could become potent measure of the probability of finding cancer at biopsy. Subsequently, we logistically modelled this probability and formulated a single-value calculating PCa risk equation that individually measures the probability of finding cancer on PBx. Multiple logistic regression models, quantify the combined contribu-
tion of several risk-factors and provide PBx outcome probability, yielding exact numerical values applying to an individual instead of a risk-group, highly improving predictive accuracy compared to mental physician predictions 14,18,20,24. Noteworthy, all calculations are performed on computer-interface basis without need for specific mathematical knowledge and costly statistical packages, by using common PC programs (Windows Excel) or free online calculators26.

We found a very strong association between the sign of PCRDindex values (positive[+] or negative[-]) and PCa outcome (cancer, no-cancer). In 9 out of 10 (9/10) patients diagnosed with PCa, the calculated PCRD values were positively-signed (positive correlation with cancer diagnosis) whereas, 9/10 men with no evidence of the disease, had negatively signed PCRD-test (negative correlation). Accordingly, PCa diagnosis occurs nine (9) times more often in patients with positive relative to those with negatively signed PCRD index values. Hence, PCRDindex correctly identifies the vast majority of men who will prove to have PCa or, in whom this diagnosis will be excluded.

Sensitivity and specificity of PCRD testing yielded very good-to-excellent values of 89.8% and 91.46% respectively suggesting that, positively-signed PCRD-index values are almost 90% likely to predict presence of PCa in men who indeed have the disease (test correctly predicts PCa in 9/10 cases) whereas, PCRD (-) values correctly rule out carcinoma in 9/10 patients who indeed do not have the disease. In other words, only 1 in 10 men (10.5%) among those diagnosed with PCa would have been missed while, less than 1-in-10 (8.5%) without carcinoma would have been subjected to unneeded biopsies. The high PPV (91.5%) and NPV (89.8%) mean that, men with PCRD(+) values are >90% likely to be diagnosed with PCa while, those with PCRD(-) test are >90% certain not to harbour the disease. Likewise, the high diagnostic accuracy (90.63%) suggests that pre-biopsy estimations based on PCRD-values, are 91% close to the true outcome. The likelihood ratio for PCRD(+) values was 10.5 while, for PCRD(-) 0.11, meaning that individuals with PCa are about 10.5 times more likely to have positively-signed PCRDindex than those without the disease while, PCa negative cases are about 9-times more likely to have negatively signed PCRD test than do individuals with the disease. To remind, likelihood ratios >10 / <0.1 provide strong evidence to rule-in/out diagnoses respectively27.

The formulated logistic-regression model correctly predicted 90.7% of biopsy outcomes, diagnosing 90.4% of those who indeed had PCa and correctly excluding 90.9% of men who didn’t have the disease, yielding low false-positive (9.7%) and false negative (9.1%) values. To examine which variables in the predictor set most strongly associate with biopsy outcome, we computed Wald-$x^2$ according to which, PCRD ranked first followed, in descending predictive ability rank order by PV, age, f/tPSA ratio, PSAD, fPSA and, last, by tPSA. Thus, PCRDindex represents a highly powered univariable PBx outcome predictor, greatly outperforming established risk-factors and highly improving PCa predictive accuracy while avoiding unnecessary biopsies, compared to tPSA10,17. Key product of this model was a logistic regression equation formulated as:

$$p = e^{[3.2 \times \text{PCRDindex} - 0.023 \times \text{PV} + 0.22]} / (1 + e^{[3.2 \times \text{PCRDindex} - 0.023 \times \text{PV} + 0.22]})$$

that calculates a single value determining the probability of finding PCa on biopsy, with accuracy »91% and may offer advantages over multistep algorithms (i.e nomograms) presently used to estimate the need for biopsy [3,12,19,22,26].

PCRDindex yielded an interestingly high AUC-ROC curve value of 0.926, one of the best having been reported for a diagnostic tool for PCa21, discriminating well between patients with/without PCa, exhibiting diagnostic accuracy significantly outperforming that of other predictors as it emerged as the most informative risk factor for predicted cancer at PBx, followed by PSAD (0.848), PV (0.830), f/tPSA-ratio (0.814), fPSA (0.672), age (0.595) and tPSA (0.577), the weakest PCa-predictor among all examined. Overall, AUC-values for tPSA are lower than those of commonly employed predictive tests such as, PCa risk-calculators, PCA3-test, Prostate-Health-Index (PHI), which have shown substantially higher AUCs (0.65-0.88) and predictive ability significantly outperforming tPSA (AUC: 0.52-0.69)3,7,8,10,19,28,29,30. Limitations of our study include:

1) possible bias due to employing a single institution’s experience,

2) intra/inter-observer variability in ultrasound PV measurements, might potentially affect PSAD calculation accuracy1,10,19,
3) lack of external model validation that mandates further confirmatory studies,
4) lack of head-to-head comparison between the model and other PCa predictive tools.

**Conclusion**

The PCP-SMART prostate biopsy outcome predictive mathematical model, exhibited high diagnostic performance, providing significantly improved ability in identifying men at risk for PCa who need biopsy and/or intensive follow-up and equally important, those who may avoid unnecessary interventions. PCRDindex, key derivative of this model, predicted with high accuracy PBx outcome, identifying correctly 9/10 patients with cancer as well as, 9/10 without the disease, emerging as strong PCa-predictor. A multiple logistic regression mathematical equation, deriving a single value for calculating the probability of finding cancer on prostate biopsy in an individual basis, was formulated. We anticipate that, following external validation, our model and it’s derivatives, might become useful clinical tools facilitating proper, prostate biopsy related, management decision making.

**Conflicts of interest**

The authors declared no conflict of interest.

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**Appendix**

To make a XY Scatter Graph with linear regression and equation (Linear Plot) and calculate the coefficient of determination using Microsoft Excel®, complete the following steps:

1. Enter a set of values in column A (X axis values) on the spreadsheet (value-1 = tPSA50 / patient’s age, value-2= tPSA50 / prostate volume, value-3 = patient’s free PSA / tPSA 50 )
2. Enter a set of values in column B (Y axis values) on the spreadsheet (value-1 = patient’s tPSA / patient’s age , value-2 = patient’s tPSA/prostate volume, value-3 = patient’s free PSA/ patient’s total PSA )
3. Set the data range by selecting all the data on the spreadsheet using the mouse (Click in a corner and drag the mouse until all boxes are selected)
4. Press/click on the chart (wizard) button in the toolbar.
5. In the charts menu, click on “XY scatter” plot type.
6. Select the “scatter with data points connected by smoothed lines” or “scatter with data points connected by smoothed lines without markers” option.
7. Press <Finish>.
8. Right click on the line in the chart and select “Add Trendline” to draw a straight line through the data.
9. Press the “Options” tab and check the “display equation on chart” and “Display R-squared value on chart” boxes and then press “OK”, to show the equation \(y=mx+b\) of the line and the R2 value (positive or negative according to the slope [direction: increasing (+) or decreasing (-)]) of the equation line.

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**Περιλήψη**

**Σκοπός:** Στο πλαίσιο προσπάθειας βελτίωσης της διαγνωστικής ικανότητας της δοκιμασίας PSA, αναπτύξαμε μέθοδο εκτίμησης της πιθανότητας ύπαρξης προστατικού καρκίνου σε άνδρες με παθολογικές τιμές PSA καθώς και στάθμισης της «έντασης» των απαιτούμενων προσπαθειών για περαιτέρω διερεύνηση (επαναληπτικές βιοψίες), μετά αρνητική/ές αρχική βιοψία/ές προστάτη. Για τον σκοπό αυτό, εκπονήσαμε προοπτική - μακρόχρονη μετρητική μοντέλο προοπτικής μαθηματικής συνθηκών καρκίνου προστάτη PCP-SMART (Prostate Cancer Predictive - Simulation Modelling, Assessing the Risk, Technique), με κύρια παράγωγο τον δείκτη (index) PCRD (Prostate Cancer Risk Determinator) και την προκύπτουσα μαθηματική εξίσωση λογιστικής παλινδρόμησης, μεσο των οποίων υπολογίζεται εξατομικευμένα η πιθανότητα θετικού για καρκίνο αποτελέσματος, σε ασθενείς που υποβάλλονται σε διορθική βιοψία προστάτη.

**Ασθενείς και μέθοδος:** Σε 371 άνδρες, εφαρμόσαμε το
Περίληψη (συνέχεια)

πρωτόκολλο μελέτης PCP-SMART που επινοήθηκε στην κλινική μας ως μοντέλο «κλινικής προσομείωσης» καρκίνου του προστάτη, με κύριες μεταβλητές: Ηλικία ασθενείς, ύγος του προστάτη (διακοιλικό υπεργιαγγράφημα, ολικό PSA, Free-PSA, PSA ratio, Age-adjusted PSA ratio, PSAD). Με συνδυασμό των κλινικών αυτών παραμέτρων και εφαρμογή στατιστικού μοντέλου γραμμικής παλινδρόμησης (linear regression), υπολογίσθηκε η συντελεστής προορισμού (coefficient of determination) R2, που δειγμάτισε ότι αποτελεί μέτρο εκτίμησης της πιθανότητας το αποτέλεσμα της βιοψίας προστάτη να είναι θετικό (επί θετικής κλίσης [slope]) της εξίσωσης της ευθείας που απεικονίζει (τον συντελεστή) η αρνητική (αρνητική κλίση της ευθείας) ο συντελεστής R2 ονομασθήκε PCRD, και αποτέλεσε την κεντρική υπό μελέτη παράμετρο και το καινοτόμο στοιχείο του προεξοχούς μοντέλου. Ακολούθησε στατιστική ανάλυση της διαγνωστικής (προβλεπτικής) ικανότητας του δείκτη αυτού και σύγκριση του με άλλους κλινικούς προβλεπτικούς παράγοντες, καθώς και υπολογισμός της εξίσωσης της ευθείας της πιθανότητας θετικού αποτελέσματος βιοψίας προστάτη, μέσω εφαρμογής καινοτόμας συντελεστής ευθείας που δημιουργήθηκε με κύριο συντελεστή τον συντελεστή της εξίσωσης της ευθείας (y = mx + b).

Αποτελέσματα:
Από τους 371 ασθενείς, καρκίνος προστάτη (KP+) διαγνωσθήκαν στους 167 (45,1%) ενώ σε 164 (44,2%) το αποτέλεσμα ήταν ναρκιτικό (KP-) και σε 40 (10,7%) διαπιστώθηκαν αλλοιώσεις HGPIN και/ή ASAP. Στους 150 (89,82%) από τους 167 ασθενείς με KP+ (αυτός το δείκτης PCRD είχε θετικό προσόν και στους 17 (10,18%) αρνητικό. Οι 150 (91,46%) ασθενείς KP- είχαν PCRD- και μόνο οι 14 (8,54%) θετικές τιμές PCRD. Εφαρμογή της δοκιμασίας της υπόλοιπης προγνωστικής παραμέτρου (PSAD, free PSA, PSA ratio, όγκος προστάτη) της διαγνωστικής (προβλεπτικής) ικανότητας του δείκτη PCRD (0,916) ακολουθούμενο από διαγνωστική ακρίβεια PCRD του βιοψίαν της προστάτη, με κύριους συντελεστές (ισχυρούς, ανεξάρτητους προγνωστικούς παράγοντες) τον δείκτη PCRD και τον όγκο του προστάτη, και διαγνωστική ακρίβεια αποτελέσματος της διαγνωστικής (προβλεπτικής) ικανότητας του δείκτη PCRD τον συντελεστή της εξίσωσης της ευθείας (y = mx + b).

Λέξεις ευεργετισμού

καρκίνος προστάτη, δοκιμασία PSA, μοντέλο PCP-SMART, δείκτης PCRD, μαθηματική εξίσωση υπολογισμού κινδύνου καρκίνου προστάτη

(95% CI: 83,95 - 93,78), θετικό likelihood ratio ήταν 10,52 (95% CI: 6,36 - 17,41) και αρνητικό [LR-] 0,11 (95% CI: 0,07- 0,17). Εφαρμογή του δείκτη PCRD ως τον ισχυρότερο προβλεπτικό παράγοντα μεταξύ των υπολοίπων, με βάση τον συντελεστή συναξίωσης Pearson ως εξής: PCRD (r = 0,832), PSAD (r = 0,569), ύγος προστάτη (r = 0,355), PSA ratio (r = 0,487), Free-PSA (r = 0,304), ηλικία (r = 0,413) και ολικό PSA (r = 0,142). Ωστόσο, υπολογισμός της περιοχής (AUC) υπό την καμπύλη λειτουργικών χαρακτηριστικών (ROC), κατέδειχθηκε σημαντική υποχροιότητα (p < 0,001) την διαγνωστική ακρίβεια του δείκτη PCRD και τον όγκο του προστάτη, και διαγνωστική ακρίβεια αποτελέσματος της διαγνωστικής (προβλεπτικής) ικανότητας του δείκτη PCRD τον συντελεστή της εξίσωσης της ευθείας (y = mx + b).

ΣΥΜΠΕΡΑΣΜΑΤΑ:
Ο δείκτης PCRD, κεντρικό παράμετρο του καινοτόμου μοντέλου PCP-SMART, εμφανίζει ως παράμετρο πρόβλεψης του αποτελέσματος βιοψίας προστάτη, με κύριους συντελεστές (ισχυρούς, ανεξάρτητους προγνωστικούς παράγοντες) τον δείκτη PCRD και τον όγκο του προστάτη, και διαγνωστική ακρίβεια αποτελέσματος της διαγνωστικής (προβλεπτικής) ικανότητας του δείκτη PCRD τον συντελεστή της εξίσωσης της ευθείας (y = mx + b).

Αναφορές:

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