

# PROSTATE CANCER RISK CALCULATOR COMPARISON: IPCRC vs KPCRC vs PCPT-RC vs ERSPC-RC IN PREDICTING PROSTATE CANCER AT HASAN SADIKIN HOSPITAL

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## ABSTRACT

**Objective:** To compare the validated calculators of Indonesian Prostate Cancer Risk Calculator (IPCRC) vs Korean Prostate Cancer Risk Calculator (KPCRC) vs Prostate Cancer Prevention Trial Risk Calculator (PCPT-RC) vs European Randomized Study of Screening for Prostate Cancer Risk Calculator (ERSPC-RC) in predicting prostate cancer in our patients at Hasan Sadikin Hospital Bandung. **Material & methods:** This study is a prospective study conducted from August 2014 – December 2015 at Urology Clinic at Hasan Sadikin Hospital that included all patients with BPH or suspected PCa who have been undergoing prostate biopsy. Variables such as age, PSA level, prostate volume (transabdominal or transrectal ultrasound) and digital rectal examination (DRE) finding were recorded. Risk calculation was generated using each risk calculator. Data were analyzed using Chi-square analysis, Kolmogorov-Smirnov, and finally receiver operating characteristic (ROC) curve. All statistical analyses were performed with SPSS version 20. **Results:** There were 89 BPH and 43 PCa patients between August 2014 – December 2015. The mean age, PSA and prostate volume are  $65.78 \pm 8.33$  years;  $121.16 \pm 375.76$  ng/ml;  $55.86 \pm 31.9$  ml respectively. Abnormal DRE was found in 27 PCas and 4 BPHs. Receiver operator curve analysis of IPCRC showed AUC 0.861 vs KPCRC (AUC=0.779) vs ERSPC-RC (AUC=0.745) vs PCPT-RC (AUC=0.794) vs PSA (AUC 0.794), sensitivity 81.4% and specificity 71.9% with cut-off point 19.67 for the IPCRC in predicting the prostate cancer in our center. **Conclusion:** IPCRC is better than KPCRC, PCPT-RC and ERSPC-RC in predicting prostate cancer in our center.

**Keywords:** Prostate cancer; calculator; screening.

## ABSTRAK

**Tujuan:** Untuk membandingkan kalkulator yang telah tervalidasi yaitu Indonesian Prostate Cancer Risk Calculator (IPCRC) vs Korean Prostate Cancer Risk Calculator (KPCRC) dengan Prostate Cancer Prevention Trial Risk Calculator (PCPT-RC) vs European Randomized Study of Screening for Prostate Cancer Risk Calculator (ERSPC-RC) dalam memprediksi kanker prostat pada pasien kami di RS Hasan Sadikin Bandung. **Bahan & cara:** Penelitian ini merupakan penelitian prospektif yang dilakukan pada Agustus 2014 – Desember 2015 di Klinik Urologi, RS Hasan Sadikin. Penelitian ini menggunakan semua pasien dengan benign hyperplasia of prostate (BPH) atau kecurigaan kanker prostat yang telah menjalani pemeriksaan biopsi prostat. Dilakukan pencatatan variabel usia, kadar PSA, volume prostat (ultrasonografi transabdominal atau transrektal) dan hasil pemeriksaan digital rektal. Data dianalisis dengan Chi-kuadrat, Kolmogorov-Smirnov dan kurva Receiving Operating Characteristic (ROC). Semua analisis dilakukan dengan SPSS versi 20. **Hasil:** Terdapat 89 kasus BPH dan 43 kasus kanker prostat pada periode Agustus 2014 – Desember 2015. Rerata usia, kadar PSA dan volume prostat secara berurutan adalah  $65.78 \pm 8.33$  tahun;  $121.6 \pm 375.76$  ng/mL;  $55.86 \pm 31.9$  mL. Hasil abnormal pemeriksaan digital rektal ditemukan pada 27 kasus kanker prostat dan 4 kasus BPH. Analisis ROC dari IPCRC menunjukkan AUC 0.861 vs KPCRC (AUC=0.779) vs ERSPC-RC (AUC=0.745) vs PCPT-RC (AUC=0.794) dengan sensitivitas 81.4%, spesifisitas 71.9% dan ambang atas 19.67 bagi IPCRC dalam memprediksi kanker prostat pada pusat studi kami. **Simpulan:** IPCRC lebih baik dibandingkan KPCRC, PCPT-RC dan ERSPC-RC dalam memprediksi kanker prostat pada pusat studi kami.

**Kata kunci:** Kanker prostat, kalkulator, screening.

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## INTRODUCTION

Prostate cancer is the second most common cancer and the sixth cause of deaths from cancer of men, about 14% (903.500) from all cases of new cancers in men in 2008.<sup>1</sup> The causes of prostate cancer initiation and progression are still unknown today. Studies suggest genetic, ethnicity, diet, and environmental factors play significant roles in the development of the disease.<sup>2,3</sup>

In the last 20-30 years, development of science and technologies have enabled factors to be identified, which would further classify risk of having prostate cancer.<sup>4</sup> Prostate Specific Antigen (PSA) is one of them, which is the first prostate cancer screening indicator.<sup>5</sup>

The decrease in incidence of prostate cancer from 1992 to 1995 occurred after PSA screening have been applied as a screening tool.<sup>2</sup> However, the usage of PSA for screening prostate cancer is still controversial due to high cost, bias, over diagnosis and over treatment that make it impossible to make proper decisions.<sup>5,6</sup> Yang JB et al. found that the use of PSA as a screening tool was ineffective in detecting prostate cancer.<sup>7</sup>

In the last decade, several monograms have been developed to predict and to guide decision making whether to perform biopsy in patients with suspected prostate cancer. In general, some predictive factors that are used are total PSA value, rectal toucher, and age, but other predictive factors may be added, such as ethnicity, family history, prior prostate biopsy, prostate volume, negative prostate biopsy history, count of biopsy cores, and percentage of free-PSA.<sup>8</sup>

Two types of calculator that are being used in predicting prostate cancer namely: Prostate Cancer Prevention Trial-Risk Calculator (PCPT-RC) and European Randomized Study of Screening for Prostate Cancer-Risk Calculator (ERSPC-RC). These calculators were made based on factors that may determine whether or not a patient should be treated with a biopsy. These factors include, total PSA content, PSA velocity, PSA density, rectal toucher examination, family history, ethnicity, age, prostate volume, abnormality Magnetic Resonance Imaging (MRI) and ultrasonography, use of  $\alpha$ -reductase inhibitors, and prior biopsy history. These calculators are helpful for Urologists, Specialists, and General Practitioners in determining further better measures, possibility of biopsy, and follow-up frequency.<sup>1,6,9</sup>

Several studies revealed ERSPC-RC has a better and more accurate predictive capacity in predicting risk of suffering prostate cancer than PCPT-RC.<sup>1,3,9,10</sup> However, no study shows the validation of the tool in Asia. Lee DH found that ERSPC-RC has a stronger prostate cancer predicting capacity than both PCPT-RC and PSA in a co-hort research in Korea. The difference is statistically insignificant and thus there is no specific advantage gained from using both calculators for clinical practices in Korea.<sup>3</sup>

The weakness of the aforementioned calculators is that they are population specific. The sensitivity of these calculators decreases if used in different populations. Therefore, we proposed to make a calculator specifically for predicting prostate cancers in Indonesia.

Yuri et al., based on a Multicenter Study, invented Indonesian Prostate Cancer Risk Calculator (IPCRC) at sensitivity and specificity levels of 92% and 89.2%, respectively, in predicting prostate cancers in Indonesia's population.

## OBJECTIVE

Considering the aforementioned predicament, we compared validated prostate cancer calculators (IPCRC vs. KPCRC vs. PCPT-RC vs. ERSPC-RC) in predicting prostate cancer patients at Hasan Sadikin Hospital (RSHS) Bandung.

## MATERIAL & METHODS

A prospective study was carried out in the time period of August 2014 – December 2015 at Urological Clinic of RSHS, involving patients that underwent prostate biopsy with benign prostate hyperplasia (BPH) or suspected prostate cancer. The variables of age, PSA value, prostate volume (transabdominal and transrectal ultrasonography) and digital rectal examination (DRE) were recorded.

Criteria of inclusion were 1). Prostate cancer patient and have complete medical record data (age, prostate volume, total PSA content, DRE), 2). Benign hyperplasia prostate patient and have complete medical record data (age, prostate volume, total PSA content, DRE), 3). Patient with an abnormal DRE, 4). Patient have histopathology finding of BPH. Criteria of exclusion were prostate biopsy not been performed.

Risk calculation was obtained by entering the variables to each type of risk calculator. The data

was analyzed by Chi-square, Kolmogorov-Smirnov, and Receiver Operating Characteristic (ROC) curve analyses. The data was processed with SPSS version-20 software.

**RESULTS**

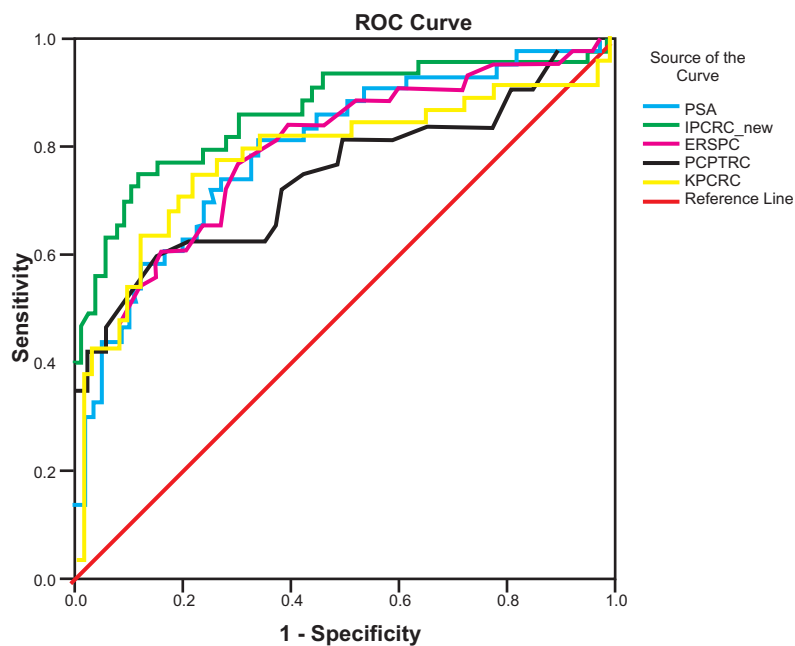
Within August 2014 – December 2015, we found 89 patients with BPH and 43 with prostate cancer. Average age, PSA, and prostate volume were

65.78 ± 8.33 years, 94.95 ± 231.78 ng/ml, and 55.86 ± 31.9 ml, respectively. DRE abnormality was found in 27 prostate cancer patients and 4 BPH patients.

ROC curve shows the superiority of IPCRC in predicting prostate cancer at our hospital (AUC 0.861) vs. KPCRC (AUC=0.779) vs. ERSPC-RC (AUC=0.745) vs. PCPT-RC (AUC=0.794) vs. PSA (AUC 0.794), with sensitivity and specificity levels of 81.4% and 71.9%, respectively, at a bound value of 19.67.

**Table 1.** Descriptive data of BPH and prostate cancer patients at RSHS in August 2014 – December 2015.

Variable	Average	SD	Min	Max
Age	65.78	8.33	46	89
PSA	94.95	231.78	4.66	1438
Prostate volume	55.86	31.9	16	282



Diagonal segmenys are produced by ties

**Figure 1.** ROC Curve of IPCRC vs other calculator.

**Table 2.** Result of AUC IPCRC vs that of other calculator.

Test Result Variable(s)	Area Under the Curve				
	Area	Std. Error <sup>a</sup>	Asymptotic Sig. <sup>b</sup>	Asymptotic 95% Confidence Interval Lower Bound	Asymptotic 95% Confidence Interval Upper Bound
PSA	.794	.043	.000	.710	.879
IPCRC new	.861	.039	.000	.784	.937
ERSPC	.745	.051	.000	.645	.845
PCPTRC	.794	.044	.000	.708	.880
KPCRC	.779	.050	.000	.681	.877

## DISCUSSION

Prostate risk cancer calculator with nomogram based have been formulated to increase the risk prediction and to solve the unnecessary biopsy problem, overdiagnosis and overtreatment. Publication showed that the risk calculators have been more accurate to predict prostate cancer possibility rather than PSA value and digital rectal examination only.<sup>11,12</sup>

Risk calculator is an important prediction tool to solve the problems that come from PSA examination which become redundancy. Ideally, the risk calculator is expected to avoid unnecessary biopsy and the incidence of complication and emotional stress due to biopsy.<sup>13</sup> Moreover, risk calculator is expected to be reliable in predicting the risk of being diagnosed by prostate cancer and accurate prediction whether the diagnosis will give significant influence to the patient. The implementations of this calculator in patient counseling and decision making can decrease prostate cancer overdiagnose and overtreatment.

Two prostate cancer risk calculators that already known are European Randomized Study of Screening Prostate Cancer (ERSPC-RC) and Prostate Cancer Prevention Trial-Risk Calculator (PCPT-RC).<sup>14</sup> ERSPC-RC using DRE as the variable and more easy to use clinically. PCPT also have more data that is added in calculation formulation, but Poyet, et al. say this is not optimal.<sup>15</sup>

ERSPC-RC is formulated from 6.288 patients which are Dutch nationality in 2006. Logistic regression analysis shows DRE abnormality variable, prostate volume from DRE and PSA value associate with prostate cancer diagnosis significantly.

PCPT-RC published in 2006 is the result from the risk calculator development of 5.519 patients with PSA value below 3 ng/mL and have been followed up for 7 years with PSA examination and DRE every years. In the end of follow up, the patients are advised to undergo prostate biopsy regardless of DRE abnormality or PSA value. The result of logistic regression analysis by Thompson, et al. shows that the variables of race, age, PSA value, family history with prostate cancer, DRE abnormality and prostate biopsy are associated with prostate cancer diagnosis significantly.

Poyet, et al. did the first external validation and compared the newest ERSPC-RC and PCPT-RC with cohort study in 2.000 patients. We can conclude

from the study, that both risk calculator are better than PSA only.<sup>15</sup>

The implementation of both risk calculator in Asian population, especially Korean, have been validated by Lee, et al. the result of the study showed AUC in ERSPC-RC and PCPT-RC are 77.4% and 64.5%, with the conclusion that those calculators are not superior in predicting prostate cancer in Korean patient population.<sup>5</sup> In 2011, Park, et al. published Korean Prostate Cancer Risk Calculator (KPCRC) with AUC 0.91 compared with PSA examination only, which is 0.83 ( $p < 0.005$ ).<sup>16</sup>

KPCRC development by logistic regression analysis shows that variables of prostate volume, DRE abnormality, PSA value and transitional zone of prostate volume are associated with prostate cancer diagnosis. Unlike other prostate cancer risk calculators, KPCRC calculates transitional zone volume, with consideration that transitional zone volume is inversely proportional with prostate cancer risk.

The difference results among prostate cancer risk calculators can be caused by population difference which is included in the study. Threshold difference also plays role in the calculator performance.

Demographic data is available from the external validation result in population of urology patients of RSHS/FK Unpad, as listed in the table 1. There is no significant differences with the data from Yuri, et al. that is collected from Indonesian Prostate Cancer Risk Calculator (IPCRC) from 5 urology centers in Indonesia.<sup>17</sup>

We compare the validated prostate cancer risk calculator (IPCRC Vs KPCRC Vs PCPT-RC Vs ERSPC-RC). ROC analysis has been done and shows the IPCRC excellence in predicting prostate cancer in our hospital (AUC 0.861) Vs KPCRC (AUC=0.779) vs ERSPC-RC (AUC=0.745) vs PCPT-RC (AUC=0.794) vs PSA (AUC 0.794), with sensitivity 81.4% and specificity 71.9% in threshold 19.67. As conclusion, our study shows that IPCRC is more excellence than KPCRC, PCPT-RC and ERSPC-RC in predicting prostate cancer in our center.

## CONCLUSION

IPCRC is more excellence than KPCRC, PCPT-RC and ERSPC-RC in predicting prostate cancer in our center.

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