Actas Urol Esp. 2017;41(4):234–241

Actas Urológicas Españolas

www.elsevier.es/actasuro

ORIGINAL ARTICLE

A comparison of 3 on-line nomograms with the detection of primary circulating prostate cells to predict prostate cancer at initial biopsy☆

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Received 11 August 2016; accepted 21 October 2016
Available online 31 March 2017

KEYWORDS
Prostate cancer;
Circulating prostate cells;
Prostate biopsia;
Nomograms

Abstract

Introduction: The use of nomograms which include the PSA may improve the predictive power of obtaining a prostate biopsy (PB) positive for cancer. We compare the use of three on-line nomagrams with the detection of primary malignant circulating prostate cells (CPCs) to predict the results of an initial PB in men with suspicion of prostate cancer.

Methods and patients: Consecutive men with suspicion of prostate cancer underwent a 12 core TRUS prostate biopsy; age, total serum PSA, percent free PSA, family history, ethnic origin and prostate ultrasound results were used for risk assessment using the online nomograms.

Mononuclear cells were obtained by differential gel centrifugation from 8 ml of blood and CPCs were identified using double immunomarcation with anti-PSA and anti-P504S. A CPC was defined as a cell expressing PSA and P504S and defined as negative/positive. Biopsies were classified as cancer/no-cancer. Areas under the curve (AUC) for each parameter were calculated and compared and diagnostic yields were calculated.

Results: 1223 men aged >55 years participated, 467 (38.2%) had a biopsy positive for cancer of whom 114/467 (24.4%) complied with the criteria for active observation. Area under the curve analysis showed CPC detection to be superior ($p < 0.001$), avoiding 57% of potential biopsies while missing 4% of clinically significant prostate cancers.

☆ Please cite this article as: Murray NP, Fuentealba C, Reyes E, Jacob O. Comparación de 3 nomogramas en línea con la detección de las células primarias circulantes de la próstata para predecir el cáncer de próstata en la biopsia inicial. Actas Urol Esp. 2017;41:234–241.

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Conclusions: The CPC detection was superior to the nomograms in predicting the presence of prostate cancer at initial biopsy; its high negative predictive value potentially reduces the number of biopsies while missing few significant cancers, being superior to the nomograms in this aspect. Being a positive/negative test the detection of CPCs avoids defining a cutoff value which may differ between populations.

PALABRAS CLAVE
Cáncer prostático;
Células prostáticas circulantes;
Biopsia prostática;
Nomogramas

Comparación de 3 nomogramas en línea con la detección de las células primarias circulantes de la próstata para predecir el cáncer de próstata en la biopsia inicial

Resumen

Introducción: Los nomogramas que incluyen el PSA para predecir los resultados de una biopsia prostática son de utilidad en la clínica diaria. En este estudio de hombres con sospecha de cáncer prostático comparamos el uso de 3 nomogramas *online* con la detección de células prostáticas circulantes (CPC) para predecir los resultados de la biopsia prostática.

Métodos y pacientes: Una serie de varones con sospecha de cáncer fueron sometidos a una biopsia prostática de 12 muestras. Se registraron la edad, APE total, porcentaje de APE libre, historia familiar de cáncer prostático, origen étnico y resultados de una ecografía transrectal. Se calculó el riesgo de cáncer prostático utilizando 3 nomogramas.

Se separaron las células mononucleares por centrifugación diferencial de 8 ml sangre venosa e identificaron las CPC utilizando inmunocitoquímica con anti-APE y anti-P504S. Una CPC fue definida como una célula expresando APE y P504S y el test como positiva/negativa. La biopsia fue clasificada como cáncer/no-cáncer. Por cada parámetro el área bajo la curva fue calculada y los rendimientos diagnósticos comparados.

Resultados: Un total de 1.223 hombres > 55 años participaron, 467 (38,2%) tuvieron una biopsia positiva para cáncer, de los cuales 114/467 (24,4%) tuvieron un cáncer no-significativo. El análisis del área bajo la curva mostró que la detección de las CPC fue superior ($p < 0,001$), evitando el 57% de las biopsias prostáticas, mientras que no detectó el 4% de los cánceres significativos.

Conclusiones: La detección de CPC fue superior a los otros modelos para predecir los resultados de la biopsia prostática inicial, reduce potencialmente el número de biopsias innecesarias y no detecta solo una pequeña fracción de los pacientes con cáncer clínicamente significativos. Fue superior a los otros modelos en este aspecto, cuando considerados negativos los nomogramas no detectaron un número significativo de cánceres agresivos. De ser un test positivo/negativo, la detección de CPC evita la definición de un punto de corte, lo cual podría variar entre poblaciones diferentes.

Introduction

Today, a new diagnosis of prostate cancer (PC) nearly always occurs following a patient referral for prostate biopsy (PB) as a result of an increased PSA. PSA is currently the only biomarker used for prostate cancer screening; of men aged 50–70, 10–20% will have an increased PSA, and of men with a PSA of 4–10 ng/ml, the probability of a positive initial biopsy is approximately 25%. This probability varies with age, race, family history, PSA level, PSA kinetics, prostate volume, and digital rectal examination (DRE). The ability to incorporate these parameters into risk prediction may decrease the rate of unnecessarily performed biopsies with a decrease in healthcare costs and side effects.

There is an increasing number of predictive tools based on statistical models[1]; however, many have not been externally validated. The Montreal (Canada) predictive tool has been externally validated,[2] it uses simple readily available markers, age, DRE, PSA, and percent free PSA to give a percent risk calculation in an individual patient. The European Randomized Study of Screening for Prostate Cancer derived Prostate Risk Indicator (SWOP-PRI) uses DRE, prostatic ultrasound findings, prostate volume, and total serum PSA,[3] and the North American Prostate Cancer Prevention Trail derived Cancer Risk Calculator (PCPT-CRC) uses ethnic origin, age, serum PSA, DRE, and a family history of prostate cancer to calculate the risk of a positive biopsy.[4] A direct comparison of the three nomograms in a European population of 667 patients the Montreal tool proved to be superior.[5] However, due to the potential discrepancy in predicted outcomes with regard to the study population, genetic differences, differences in the incidence of benign hiperplasia or chronic prostatitis, a nomogram may not be applicable in all geographical zones.

The detection of malignant primary circulating prostate cells (CPC) could be one candidate for the early detection of PC. In men with prostate cancer, there is, at least, one subpopulation of cancer cells that disseminate early, firstly to