Prostate Cancer Biomarkers

Marco A. Alvarez, MD

KEYWORDS

- Biomarkers Prostate Screening TRUS PSA PCA3 TMPRSS2:ERG
- Prostate Health Index

KEY POINTS

- Prostate cancer is among the top newly diagnosed cancers in the United States and the rest of the world.
- Its approach has radically shifted because of prostate-specific antigen, transrectal ultrasound-guided biopsy (TRUS), and improvements in medical and surgical options.
- The use of biomarkers for prostate cancer screening helps not only to select which patients will likely benefit from TRUS, thus reducing the need for unnecessary biopsies, but also, once the diagnosis is confirmed, to discriminate between more aggressive and indolent disease, helping to diminish overtreatment.

INTRODUCTION

Prostate cancer (PCa) is among the top newly diagnosed cancers in the United States and the rest of the world. ^{1,2} Its approach has radically shifted in the past 30 years after the introduction and wide use of prostate-specific antigen (PSA), ^{3–5} transrectal ultrasound-guided biopsy (TRUS) (**Figs. 1–3**), ^{6–8} and improvements in the medical and surgical options offered to patients. ⁹

To maximize the benefit for the patient, everyone in the team, from the general practitioner, urologist, and radiologist, to the pathologist, must have the basic knowledge and understanding of the tools available and the current trends.¹⁰

Even despite its current reach and limitations, we believe that the use of biomarkers will revolutionize PCa care. We will move from a one-size-fits-all to a personal tailored approach.

BIOMARKERS

The National Cancer Institute defines a biomarker as "a biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or a condition, or a disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition."¹¹

An ideal biomarker to screen for PCa, or a combination of them, would improve screening by helping in the decision making as to which patients will likely benefit from a biopsy or rebiopsy. It would also help to differentiate between insignificant and aggressive tumors and guide in the selection of treatment in the case of a positive biopsy and in the long-term management of the disease. 4,10,12-14

PCa biomarkers can be obtained from urine, blood, and prostate tissue. There is a wide array of options, with no single all-around solution.¹⁵

PSA

The characteristics of this biomarker (**Fig. 4**) have been widely published and its introduction in the early 1970s resulted in early detection, reducing mortality from PCa.^{4,5} Even though its use as a screening tool has been criticized, ^{16,17} it still has a long future because of many of its characteristics. ^{18–21}

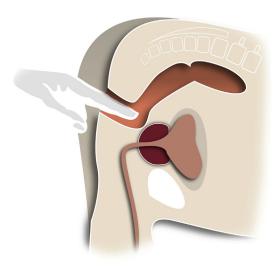


Fig. 1. Digital rectal examination provides information on the state of the peripheral zone of the gland. For centuries, it was the only tool to screen the prostate.

[-2]PROPSA AND PROSTATE HEALTH INDEX

Approved by the US Food and Drug Administration (FDA) in 2012,²² this PSA isoform, produced in the peripheral zone of the prostate (also known as p2PSA), circulates in the blood as a part of the free PSA fraction and has been used in Europe for several years. It has shown a high accuracy in predicting repeat biopsy outcome,²³ and when used during active surveillance programs, it can also help to predict biopsy reclassification.^{24,25} Recent studies have even compared it with other biomarkers, such as PCA3 (Hologic Gen Probe,

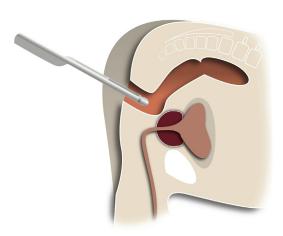


Fig. 2. TRUS was introduced in the 1980s and provides real-time anatomic views of the prostate. Recent advances in sonography, such as the use of contrast and elastography, are being tested to improve its efficacy.

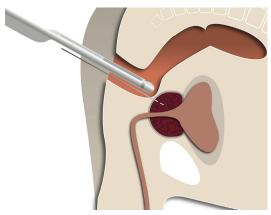


Fig. 3. Prostatic TRUS is the mainstay for diagnosis of PCa.

Bedford, MA, USA), concluding that its use increases both sensitivity and specificity compared with other biomarkers. Its goal is to help reduce the number of unnecessary biopsies.

Through a patented mathematical process, the values of PSA, free PSA, and p2PSA provide the Prostate Health Index (Beckman Coulter, Pasadena CA, USA).²⁶

4KSCORE AND PROSTARIX

Other markers, such as 4Kscore (Opko Health, Miami, FL, USA), aim to predict the result of a prostate biopsy. A panel of 4 kallikreins (a subgroup of serine proteases) have been shown to help predict the result of an initial biopsy in previously screened men with increased PSA levels.^{27,28}

Prostarix is also a genetic examination, which identifies common PCa alleles and aims to provide population risk stratification.²⁹

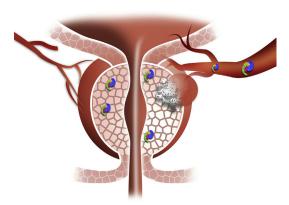


Fig. 4. PSA was introduced in the early 1970s and has been at the forefront for PCa screening. The use of some of its derivatives, such as [-2]proPSA, has improved its value.

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