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THE ROLE OF PSA BIOMARKERS IN EARLY DETECTION OF PROSTATE CANCER: CLINICAL SIGNIFICANCE, LIMITATIONS, AND FUTURE DIRECTIONS

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Suyunov Og'abek Oybek o'g'li
Student of EMU University

Abstract

Prostate-specific antigen (PSA) has enabled the early detection of prostate cancer worldwide, significantly improving diagnosis and treatment. However, since PSA is expressed in both benign and malignant cells, prostate cancer screening based solely on single cutoff values provides imperfect diagnostic performance and has led to the detection and overtreatment of low-grade prostate cancer.It has become evident that PSA results are affected by substantial inter- and intra-individual variability, as well as differences related to age and prostate volume, creating challenges in interpretation.Therefore, new approaches have been proposed to refine the interpretation of PSA. These include age-specific cutoff values, adjustments based on age and genetic factors, PSA density, percentage of free PSA, and PSA velocity.

Keywords

Prostate cancer, PSA, biomarker, early detection, screening, diagnosis, personalized medicine, urology, risk stratification.

Introduction

The widespread use of prostate-specific antigen (PSA) has had a significant impact on the diagnosis, treatment, and outcomes of prostate cancer. PSA is considered one of the most important cancer biomarkers, primarily because it is widely available, inexpensive, and clinically easy to interpret. As a result, PSA has enabled prostate cancer screening and detection on a global scale.Before the discovery of PSA, prostate cancer was most often diagnosed at locally advanced or metastatic stages. According to statistics, in the 1970s and 1980s, the 5-year survival rate of patients diagnosed with prostate cancer was 69.3% and 76.3%, respectively. Thanks to early detection and effective treatments, current survival rates have risen to approximately 97.1%, and for patients with localized disease, nearly 100%. Since the introduction of PSA testing in the 1990s, prostate cancer mortality has decreased by 45%–70%.Diagnostic approaches for patients with abnormal PSA

results have also advanced, shifting from traditional sextant biopsies to image-guided and risk-adapted strategies.

The Gleason grading system, developed by Dr. Donald Gleason in the 1960s, remains an important prognostic indicator of prostate cancer to this day. The Gleason grade is scored from 1 (normal) to 5 (most abnormal) based on histological examination of prostate tissue obtained through biopsy. The Gleason score ranges from 2 to 10 and is the sum of the two most frequently observed Gleason grades. However, evaluating the Gleason grade requires an invasive tissue biopsy. Prostate cancer biopsies are painful and invasive procedures, with potential complications such as bleeding and infection.

Detecting prostate cancer at earlier stages has accelerated the development of local treatments, including refinements in radical prostatectomy, radiotherapy, and ablative therapies.However, because PSA is produced by both benign and malignant prostate cells, it has also been a source of controversy. The widespread use of PSA has contributed to the overtreatment of cancers that lacked metastatic potential or sufficient biological aggressiveness to impact long-term survival.

PSA is a serine protease associated with kallikrein and produced by prostatic epithelial cells; it is normally present in prostatic secretion and is often elevated in prostate cancer.PSA screening has been shown to improve the detection of prostate cancer at any stage, increase detection at stages I and II, and slightly reduce detection at stages III and IV. Moreover, it does not affect overall mortality but may slightly reduce prostate cancer–specific mortality. In men with persistently elevated PSA levels, a transrectal core biopsy under ultrasound guidance is usually performed to diagnose prostate cancer. Compared to the general population, PSA screening significantly enhances cancer detection at any stage in patients with prostate cancer.

The Prostate Health Index (PHI) was developed based on p2PSA. PHI is a formula that combines p2PSA, fPSA, and tPSA, and studies have shown that it increases diagnostic accuracy in the detection of prostate cancer.

PSA velocity (PSAV) and doubling time (PSADT) have prognostic significance. PSAV is the annual rate of change in PSA concentration, with higher PSAV being strongly associated with prostate cancer and increasing the risk of prostate cancer death ninefold after prostatectomy. PSADT is the time required for PSA levels to double. A rise in PSA after radiotherapy or prostatectomy indicates residual tumor. Studies have shown that a PSADT of less than 10 months is associated with reduced survival. Nevertheless, neither PSAV nor PSADT is superior to standard PSA measurement in prostate cancer screening.

In recent years, methods for detecting prostate-derived exosomes have been developed. Exosomes are small vesicles formed from the cell membrane and released into the bloodstream, urine, or semen. In patients with prostate cancer, the number of exosomes is elevated, and this has also been found to be associated with the Gleason score.

The relatively small sample size limits the ability to apply these research findings on a broader scale. The use of the PSA test alone has proven insufficient, as physicians should incorporate the advantages of the 4Kscore testing system into their analysis.

So far, many novel and promising prostate cancer biomarkers have been studied, but none of them has been able to replace the PSA test in detecting this malignancy, which highlights the challenges of translating scientific discoveries from the laboratory into clinical practice. However, encouraging results have been obtained with several new biomarkers, and they may have the potential to meet important clinical needs.

New approaches may help reduce overdiagnosis and overtreatment, while at the same time allowing physicians to focus on patients with high-risk, localized prostate cancer who are more likely to benefit from radical intervention.

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