BRITISH JOURNAL OF HOSPITAL MEDICINE

EDITORIAL

Prostate Specific Antigen (PSA) Testing and Cancer Detection: Guidance Notes for the Non-Urologist

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Abstract

Prostate cancer is the most frequently diagnosed cancer in men and is a leading cause of cancer-related deaths. Prostate specific antigen (PSA) is one of the key tests that can aid in making such a diagnosis. It is, however, a test with both advantages and disadvantages. Despite having been a part of clinical practice for over 40 years, its use still represents many challenges. Clinicians across all specialties can benefit from gaining deeper insight into how it can be effectively integrated into their practice.

Key words: prostate cancer; screening; prostate specific antigen

Submitted: 18 December 2024 Accepted: 10 January 2025

Introduction

As early as the 1960s, scientists were searching for a tumour biomarker that was specific to the prostate (Rao et al, 2008). While there were many different research groups involved in the development of prostate specific antigen (PSA), it was T. Ming Chu and colleagues at the Roswell Park Memorial Institute in Buffalo, New York who gained approval from the Food and Drug Administration Agency (FDA) in 1984 (Catalona, 2014). As a result, it is usually this group who are credited with making the key step from translational research to clinical practice. At this time, around one third of new prostate cancer (PCa) diagnoses had bone metastases and an even higher number were dying due to PCa (Van Poppel et al, 2022). The years that followed and especially from the 1990s onwards, saw a dramatic uptake in its clinical use with a resultant decrease in PCa specific mortality accordingly. However, if we fast forward to the present day, PCa is still the most frequently diagnosed cancer in men, albeit with fewer cases of metastatic disease at presentation. Nonetheless, it still represents one of the leading causes of cancer-related deaths in the United Kingdom (Sung et al, 2021). To this end, it represents a major health concern, and it is therefore of relevance to all clinicians, regardless of speciality, to have a basic understanding of how prostate specific antigen (PSA) testing should be implemented and interpreted.

How to cite this article:
Juliebø-Jones P, Beisland C. Prostate Specific Antigen (PSA) Testing and Cancer Detection: Guidance Notes for the Non-Urologist. Br J Hosp Med. 2025. https://doi.org/10.12968/hmed.2024.1035

PSA as a Stand-Alone Diagnostic Tool

A good example of a single blood test that can reliably make a specific diagnosis is the one for pregnancy. While there was initial hope that PSA could serve a similar purpose in the setting of PCa, this was not the case. PSA, a protein produced by the prostate, and which serves to liquify semen, is organ specific and not cancer specific. Significant overlap in PSA values can therefore occur between PCa, benign prostate hyperplasia and prostatitis. While a higher result is associated with an increased risk of PCa, even a normal or low value cannot rule out PCa (Polascik et al, 1999). For this reason, it is not employed as a stand-alone diagnostic tool but interpreted alongside other patient factors. This includes the age, family history and ethnicity among others. Of note, men of African descent are disproportionately affected and twice as likely to die from PCa (Wei et al, 2023). What has allowed for the diagnostic pathway to be improved considerably, has been the introduction of multi-parametric magnetic resonance imaging (MRI) and improvements to prostate biopsy. The latter can now be performed using a transperineal rather than transrectal approach. This is associated with a lower complication profile and antibiotics can be routinely omitted (Honoré et al, 2024). Performing the MRI before the biopsy, can allow for a targeted approach to be taken and thus reducing the total number of biopsies required. Research is ongoing to develop new tests such as the Stockholm 3 (STHLM3) test that combine multiple protein biomarkers and genetic markers combined with clinical data such as age that can provide a more accurate risk assessment for patients (Ström et al, 2018).

To Screen or not to Screen?

The implementation of a national screening programme for asymptomatic men based solely on PSA testing has been a widely debated topic and this is still the case. The current prevailing consensus among European countries is that it should *not* be adopted. While it would lead to an overall reduction in mortality, rather than identify men at risk of harbouring clinically significant disease, it would be associated with overdiagnosis of low-grade cancers and overtreatment (Albertsen, 2020). Current recommendations therefore promote an individual based approach where PSA is offered to men who are aged 50 years and over (or 45 if have African ethnicity), who have been adequately counselled (Harding et al, 2024). Different countries have adopted their own implementations of this such as Sweden that initiated a strategy for men aged 50 to enter a regionally led organised PCa testing (OPT) programme (Bratt et al, 2024).

PSA as a Marker for Disease Recurrence

It is in the setting of identifying PCA recurrence post-treatment, that PSA holds true strengths. In contrast to other urological cancers, such as bladder cancer where follow up often consists of cross-sectional imaging and endoscopy at regular intervals, patients who have, for example undergone radical prostatectomy, will only require follow up regular PSA testing to monitor for recurrence.

Does the PSA Replace the Rectal Exam in Clinical Practice?

The short answer is no. Medical school textbooks list the digital rectal examination (DRE) as a traditional step in a full clinical examination. Indeed, the British Urologist Professor Blandy once wrote, 'Mistakes are easy to make when performing a rectal examination, but the worst mistake is not to do one at all'. Nonetheless, much like the full cranial nerve examination, the time-pressured junior clinician may sometimes forego this step (Blandy and Kaisary, 2009). A focused approach of this kind is understandable for many presenting complaints in medicine. However, clinicians of all hospital specialities will encounter patients with concomitant urological issues. In males with urinary retention, DRE should be performed. It is such, that cases of advanced PCa do go unnoticed despite long inpatient stays. While the sensitivity for DRE findings for localised disease is relatively poor as a test by itself, although still recommended, in cases of locally advanced disease and beyond, the findings on palpation of a hard and craggy prostate with effacement at the lateral border are quite distinctive (Hamdy and Eardley, 2017). These palpatory findings are also quite noticeable to a non-urologist and allow for prompt urological referral and avoiding treatment delays.

Practical Advice in the Hospital Setting

It is not unusual for PSA to be requested as part of an inpatient blood panel and often it may have been done unwittingly. In these cases, the clinician should be aware of possible reasons for a potentially false positive result. Key factors to consider include ongoing urinary tract infections and/or urinary retention. It can also be elevated transiently by recent instrumentation such as cystoscopy (as well as catheterisation) and rectal exam although to a much lesser degree. If the PSA is normal and there is another plausible explanation (e.g., urinary tract infection), then it should be repeated a few weeks later. Two PSA results, and preferably more, give much more information on the risk of PCa and the need for subsequent intervention than a single result. A persistently elevated PSA will trigger the criteria for further investigation in the form of MRI and potentially a subsequent prostate biopsy.

Conclusion

PSA is a core blood test that can provide key information on prostate health. Understanding its advantages and limitations allows for its more appropriate application in the clinical setting.

Key Points

- PSA is organ specific and not cancer specific.
- High-risk groups for PCa include men with a positive family history and African ethnicity.
- Serial PSA values that reveal a trend give much more information than a single value alone.
- National screening programmes based solely on PSA testing are not currently recommended.

Availability of Data and Materials

Not applicable.

Author Contributions

PJJ and CB conceived the project and wrote all steps of the project together. Both authors contributed to important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgement

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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