PATHOLOGISTS LANCET KENYA
Key to diagnostic excellence

Maabara ya Kisasa

Main Laboratory / Headquarters
5th Avenue Office Suites Opp.
Traffic HQ - Upper Hill
5th Ngong Avenue, Ngong Road
Switchboard: 0703 061 000
Landlines: 020 273 5123, 271 6701, 271 6697
Mobile: 0729 111110, 0736 493100
Wireless: 020 2508456
Email: info@lancet.co.ke

Website: www.lancet.co.ke

sanas Medical Laboratory
M0462
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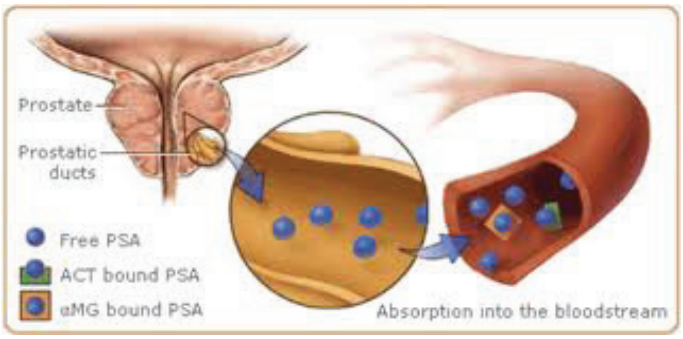
Free PSA: Improving the discrimination between BPH and prostatic carcinoma

"The ratio of free/total PSA improves the discrimination between BPH and prostatic CA, particularly in the intermediate or "grey zone" range of 3-10 ng/ml of total PSA."



Total PSA (prostate specific antigen) assays have been widely used in recent years in the evaluation of patients with prostatic carcinoma (CA) and benign prostatic hypertrophy (BPH).

More recently the ratio of free PSA to complexed PSA has been found by several groups to be superior in differentiating raised levels of total PSA due to prostatic CA from raised levels due to BPH.

PSA, which is a serine protease with chymotrypsinogen-like activity, occurs in different molecular forms in serum. Most of the immunodetectable PSA found in serum is complexed to a serine protease inhibitor called alpha-1- antichymotrypsin (PSA-ACT). Free PSA or uncomplexed PSA is the other immunodetectable form in serum.

Several groups have now found that the proportion of free PSA in serum is significantly higher in patients with BPH than in patients with prostate cancer.

The ratio of free/total PSA improves the discrimination between BPH and prostatic CA, particularly in the intermediate or "grey zone" range of 3-10 ng/ml of total PSA.

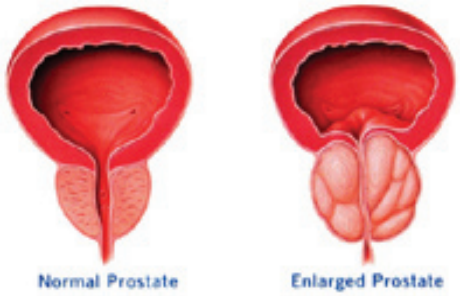
In one of the largest series [Apoorva et al (Oesterling) Urology, 49: 19, 1997] a total PSA level of between 3-4 ng/ml with a free to total ratio of less than 0.19 is regarded as an indication for ultrasound biopsy. In this situation the sensitivity is 90% and the specificity 48%, indicating that 48% of unnecessary biopsies would be eliminated and 10% of cancers would be missed. Lowering the cut point to 0.15 decreases sensitivity to 80% and increases specificity to 62%.

At levels of 4.1-10 ng/ml using a cut off ratio of 0.24 or less, the sensitivity is 95%, and the specificity is 13%, i.e. 13% of unnecessary biopsies would be eliminated and 5% of cancers missed. Using a cut off point of 0.22, sensitivity was 90% and specificity 19%.

In two other series (Partin et al, Urology 48:55,1996 and Alivizatos et al, Urology, 48:71,1996) using a cut off point of 0.20 in the 4-10 ng/ml total PSA range, sensitivities were 95% and 77% respectively and specificities 29% and 65% respectively. From this it can be seen that the results vary in different series.

The free/total cut off point is also dependent on the clinician, depending on whether he desires increased sensitivity of detection of cancer (i.e. raising the cut point), or increased specificity (i.e. decreasing the biopsy rate) by lowering the cut off point.

These recommendations are summarized in a testing algorithm for PSA recommended by Oesterling. July 2003



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