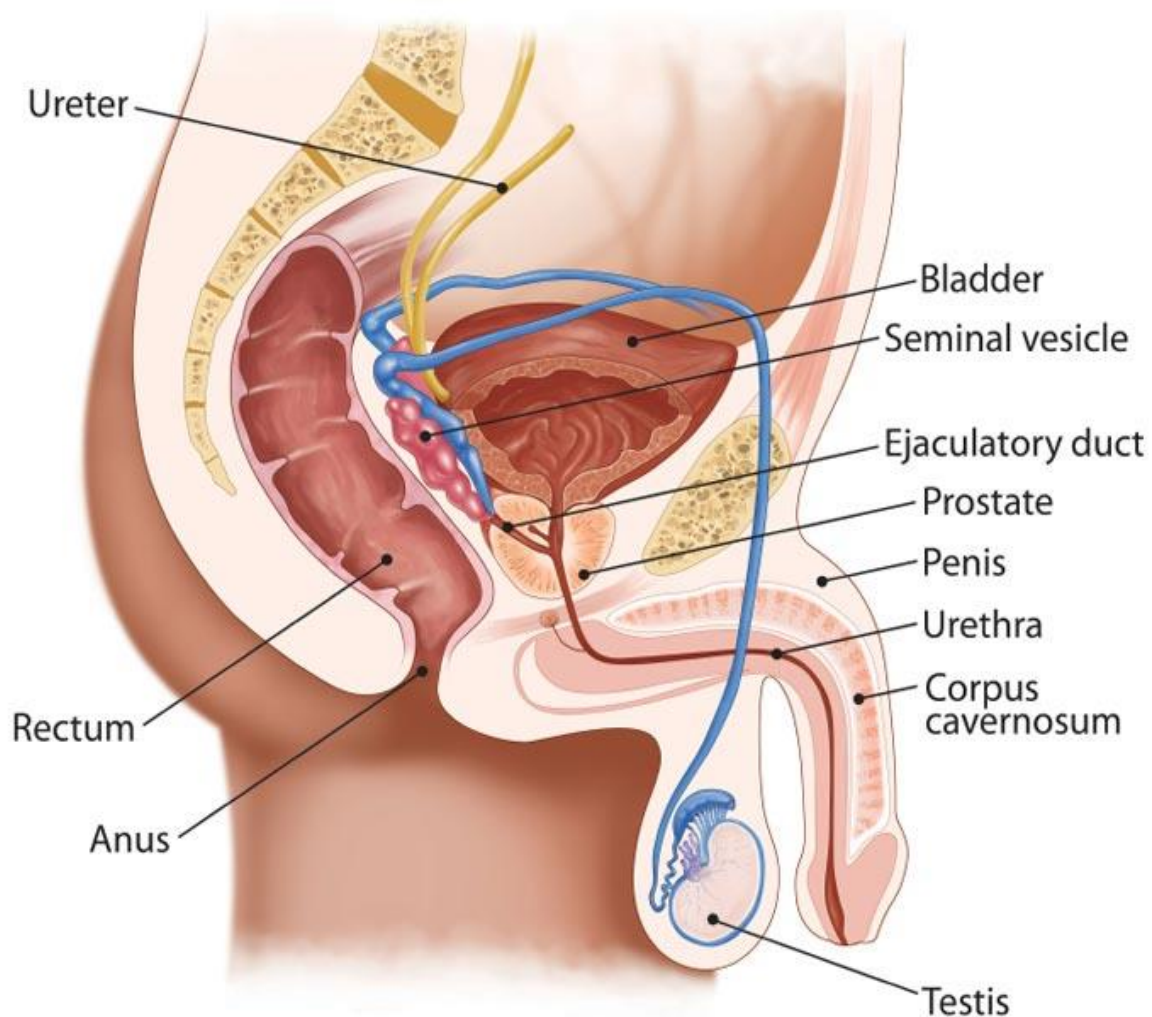


PROSTATE SPECIFIC ANTIGEN (PSA), TOTAL & FREE

INTRODUCTION

Prostate cancer is leading cancer in older men. When detected early (organ confined), it is potentially curable by Radical Prostatectomy. Therefore, early detection is important and Prostate specific antigen (PSA) is widely used for this purpose. It is considered as one of the most promising tumor marker available.

The absolute value of serum PSA is useful for determining the extent of prostate cancer and assessing the response to therapy. Its use as a screening method to detect prostate cancer is limited as it is prostate tissue specific and not a prostate cancer specific marker.



PSA exists in three forms–

- PSA enveloped by protease inhibitor Alpha-2-macroglobulin. This form lacks immunoreactivity.
- PSA enveloped by protease inhibitor Alpha-1-antichymotrypsin (ACT)
- PSA not complexed to any protease inhibitor. This is called ‘Free PSA’

The ACT bound PSA & Free PSA are collectively called ‘Total PSA’.

Free PSA alone has not been shown to be effective in patient management. Both Total and Free PSA concentrations should be determined on the same serum specimen to calculate the percentage of Free PSA as follows –

$$\frac{\text{Free PSA (ng/mL)}}{\text{Total PSA (ng/mL)}} \times 100\% = \text{Free PSA \%}$$

NORMAL RANGE

Total PSA <4 ng/mL	
Probability of Cancer in %	PSA Total in ng/mL
1	0-2
15	2-4
25	4-10
>50	>10
Free PSA >25% of Total PSA	
Probability of Cancer in %	Free PSA %
56	0-10
28	10-15
20	15-20
16	20-25
8	>25

CLINICAL USE

- Monitoring patients with a history of prostate cancer as an early indicator of recurrence and response to treatment.
- Staging of Prostate cancer
- Prostate cancer screening in high risk individuals

INTERPRETATION

Increased Levels

Prostatic diseases	<ul style="list-style-type: none"> • Cancer • Prostatitis • Benign Prostatic Hyperplasia • Acute Urinary retention
Manipulations	<ul style="list-style-type: none"> • Prostatic massage • Cystoscopy • Needle biopsy • Transurethral resection • Digital Rectal Examination • Radiation therapy • Indwelling catheter • Vigorous bicycle exercise
Drugs	Testosterone
Physiological variations	<ul style="list-style-type: none"> • PSA has no circadian rhythm but 6-7% variation occurs between specimens collected on same day & 30% on specimens collected on different days • Ambulatory values are $\geq 50\%$ higher than sedentary values • Ejaculation causes transient increase <1 ng/mL for 48 hours
Analytic factors	<ul style="list-style-type: none"> • Different assays yield different values • Antibody cross reactivity • High titre heterophile antibodies
Diseases of other organs	<ul style="list-style-type: none"> • Cancer of sweat and salivary glands , breast, colon, lung • Acute Renal failure • Acute Myocardial infarction

Decreased Levels

Anti-androgen drugs	Finasteride reduces PSA by 50% after 6 months
Castration	
Radiation therapy	
Prostatectomy	
Hospital stay	PSA falls by 17% in 3 days

HIGH RISK FACTORS FOR PROSTATE CANCER

- Age >50 years
- Change in urinary function e.g frequency, urgency, nocturia, hesitancy, hematuria, hematospermia
- Family history of prostate cancer

EARLY DETECTION OF PROSTATE CANCER

❖ **Suspected Prostate Cancer**

- Digital Rectal Examination (DRE)
- Prostate Specific Antigen (PSA)

Suspicious DRE and / or increased PSA require confirmation by biopsy for definitive diagnosis of Prostate cancer.

Digital Rectal Examination



❖ **Unsuspected Prostate Cancer**

Screening of unsuspected cases of Prostate cancer is controversial because of low specificity of elevated PSA for Prostate cancer versus BPH or Prostatitis.

LABORATORY DIAGNOSIS

To improve the ability of PSA testing to detect early Prostate Cancer and/or prevent unnecessary biopsies following is recommended:

1) Age based reference range

Age in years	PSA in ng/mL
40-49	<2.5
50-59	<3.5
60-69	<4.5
70-79	<6.5

2) PSA density

Determined by: $\frac{\text{PSA concentration}}{\text{PSA volume by USG}}$

PSA density accounts for more PSA in larger prostate as in BPH. Patients with PSA between 4-10 ng/mL, a negative DRE result and elevated PSA density (>0.15) have increased risk of Prostate cancer

3) PSA Velocity

It is an annual rate of change of PSA.

PSA in ng/mL	PSA velocity	Remarks
4-10	>0.75 ng/mL/year	Prostate cancer suspected
<4	0.35-0.4 ng/mL/year	Normal

4) PSA Free versus Total PSA

Risk of Prostate cancer is increased if ratio of Free to Total PSA is <25%

LIMITATIONS

- American Cancer Society recommends use of PSA with DRE for early detection of Prostate cancer starting at age 50 years in men with at least 10 year life expectancy. However patients at high risk may develop cancer at earlier age.
- Biologic variability may lead to an apparent rise in PSA level whereas actual level is normal.
- Different assay methods lead to variability in PSA levels.
- Radiation therapy alters PSA levels & the value may not reach undetectable concentrations.