PSA

Dr. Jad AlSmadi, MD.,

Assistant Professor,

faculty of medicine,

The Hashemite University

PSA

- PSA is a glycoprotein produced primarily by the epithelial cells that line the acini and ducts of the prostate gland.
- PSA acts physiologically like a serine protease and an arginine esterase with chymotrypsin-like and trypsin-like activity.
- One of the structural proteins of the seminal fluid, *semenogelin*, causes the ejaculate to clot. One possible biologic role of PSA is to lyse the clot in the ejaculate
- PSA is concentrated in prostatic tissue, and serum PSA levels are normally very low.

PSA

- Disruption of the normal prostatic architecture, such as by prostatic disease, inflammation, or trauma, allows greater amounts of PSA to enter the general circulation.
- Elevated serum PSA level has become an important marker of many prostate diseases – including benign prostatic hyperplasia (BPH), prostatitis, and prostate cancer.
- Prostatic intraepithelial neoplasia (PIN) does not appear to raise serum PSA levels.

PSA

- The ectopic expression of PSA has been reported in smaller concentrations in the tissue of malignant breast tumors, normal breast tissue, breast milk, female serum, and adrenal and renal carcinomas;
- however, for practical and clinical purposes, **PSA is an androgen-dependent and prostate organ-specific** (but not a cancer-specific) **marker**.
- A limitation of PSA as a tumor marker is demonstrated in the substantial overlap in values between benign and malignant prostate disease

PSA

- The concentrations found in seminal plasma range from 0.5 to 5.0 mg/mL, whereas normal serum concentrations in men aged 50 to 80 years without prostatic disease range from **1.0 to 4.0 ng/mL**.
- A small proportion of active PSA diffuses into the circulation, where it is rapidly bound or complexed by covalent attachment to protease inhibitors (most commonly, α1-antichymotrypsin (ACT))
- Inactive PSA can also enter the bloodstream, where it circulates in an unbound state as free PSA (fPSA).

PSA

- Inactive PSA can also enter the bloodstream, where it circulates in an unbound state as free PSA (fPSA).
- PSA expression is strongly androgen dependent: = bimodal peaks between 0-6 months and after 10 years of age
- In the absence of prostate cancer, serum PSA levels vary with age, race, and prostate volume

PSA

- In prostate cancer, the loss of gland architecture and basal cells results in a decrease in the luminal processing of proPSA to active PSA (and thus an increase in proPSA) thus decreasing the amount of fPSA.
- Clinicl application of PSA derivatives such as **PSA density**, **PSA velocity**, **age-adjusted values**, and, more recently, molecular derivatives may be used to improve clinical decisions.

PSA Velocity

- In normal men, the rate of change in PSA is 0.04 ng/mL per year, compared with 0.07 to 0.27 ng/mL per year in men with **BPH** who are between the ages of 60 and 85 years.
- PSA velocity is of minimal use for prostate cancer **screening**.
- PSA velocity should not be used as a trigger for biopsy.
- The main benefit in Active Surveillance.

PSA Density

- Total PSA divided by prostate volume.
- Proposed cutoffs for biopsy in the early detection setting have ranged from 0.08-0.15 ng/mL2.
- PSAD cutoff of 0.150 is the classical one.
- PSAD at a cutoff of ≤0.08 averts 13% of biopsies, while missing 2.7% of all cancers and only 0.47% of potentially clinically significant cancers.

Free PSA

- PSA produced from malignant cells appears to more frequently escape proteolytic processing, resulting in a greater fraction of serum PSA complexed to ACT and a lower percentage of total PSA that is free compared with men without prostate cancer.
- fPSA testing: improve the accuracy of PSA as a prostate cancer screening biomarker, and the FDA has approved its use in men with a serum total PSA level of 4-10 ng/mL and a negative DRE.

Free/Total PSA Ratio

- Within the tPSA range of 4 to 10 ng/mL;
- Proposed cut points generally range from 15% to 25%
- 20% to 65% of unnecessary biopsies may be avoided, while maintaining sensitivity rates of 70% to 95%
- Positive predictive rate of total PSA greater than 10 ng/mL has been demonstrated to be as high as 80%

Causes of elevated PSA

1. Prostate disease (BPH, prostatitis, prost ca)
2. Prostatic inflammation (acute and chronic)
3. Urinary retention
4. prostate manipulation (prostate massage, Cystoscopy)
5. Ejaculation: only >50 y.o (returens to NL within 24 hr
6. Prostate trauma: Biopsy, bicycling

Causes of low PSA

1. Low testosterone levels
2. Anti-androgen therapy (ADT)
3. Finasteride/ dutasteride treatment
4. Prostatectomy
5. Infiltrative diseases replacing prostatic tissues
6. Malignant diseases replacing prostatic tissues

Summary

- TPSA <4 is generally normal.
- TPSA between 4-10 use: f/T ratio, density, or velocity.
- TPSA >10 is generally considered abnormal.

Thank You