

SERUM PSA – LET’S THINK WHAT TO DO?

Prostate specific Antigen, a glycoprotein with MW – 28400 Da, serine protease secreted into prostatic duct helps to liquefy seminal coagulum. It was used by the forensic scientists as a marker of semen.¹ Serum level of PSA increases in CaP, Prostatitis, BPH, DRE, Prostatic Biopsy, Cystoscopy and physical activity and decreases in surgical or medical castration, finasteride.²

PSA is prostate specific but not cancer specific. Decreased expression is seen in poorly differentiated carcinoma prostate. Clinical utility value of serum PSA is found in screening /early detection of CaP, staging and determining the prognosis after surgery, RT, and androgen ablation for CaP.³

Due to the improvement of health facilities and awareness average increase in longevity of Bangladeshi population there is increasing trend of CaP needs early detection and treatment to avoid disease specific mortality and morbidity. Therapeutic options for metastatic disease are only palliative in nature. In the pre PSA era, only 30 – 40% of CaP patients presented with localized and potentially curable disease.

PSA has been used as a marker of advanced CaP but remain controversial. But reduction of PSA level 50% or more after treatment (Surgery or Chemo) significantly increases the survival of patient. Median survival of these group is 91 weeks as opposed to 38 weeks who have <50% reduction in PSA in HRPCC.⁴

So PSA has a good predictive value for prognostic evaluation. But the question is how much predictive it is for diagnosis of CaP?

In a study it is seen that normal PSA with normal DRE there is 15% risk of harboring CaP and normal PSA with abnormal DRE there is 20% risk of CaP. In a range of 4 – 10 ng/ml with abnormal DRE there is 30% risk and PSA>10ng/ml with abnormal DRE has 60% - 70% risk of CaP.

Total PSA level of >4ng/ml prompted further evaluation with DRE, TRUS and biopsy was then recommended if either was abnormal.⁵

PSA based screenings led to CaP detection at earlier and more curable stage.⁶ Organ confined prostate cancer detection increased through PSA based screening.

Nevertheless a considerable proportion of men having total PSA level<4 ng/ml have histologic evidence of CaP.

In a study done by Thompson et al it was seen that PSA<4ng/ml with normal DRE empiric end of study biopsy showed CaP in 6.6 – 26.6% of cases.⁷

Free serum PSA level may predict the incidence of CaP. A large multi-institutional study showed 56% of men with <10% free PSA had CaP where as only 8% of man had CaP who have >25% free PSA.

PSA density is significantly higher in CaP than BPH.⁸ PSAD is a surrogate marker for prostate cancer aggressiveness. In a study it is seen that 74% of patient with PSAD<15 had favorable pathology compared with only 36% of men with higher PSAD.⁹

The challenge to the urologist about over diagnosis and under diagnosis of CaP has become increasingly resonant.

PSAD and percent free PSA may be used to estimate possible confounding from BPH. Moreover, in cases of sudden rise in PSA, sub clinical prostatitis can be ruled out by empirical use of antibiotic and repeat PSA measurement.

PSAV help distinguish the more aggressive tumor that need to be diagnosed and treated from indolent tumor.¹⁰ PSAV of >0.4 ng/ml per year goes more in favour of CaP than other conditions of rising PSA.¹¹

PSA and its derivatives are useful predictors of prostate cancer risk and aggressiveness. With regard to screening, men with a PSA >2.5 ng/ml and suspicious DRE, or a PSAV > 0.4 ng/ml per year have a significantly higher risk in CaP and prostate biopsy should be considered. In terms of prognosis a PSAD >0.15 ng/ml per gram and PSAV > 0.4ng/ml per year are more suggestive of more aggressive disease and are of greater risk of adverse outcomes after definitive therapy.

Recently it is seen that serum PSA measurements have some paucity of sensitivity and specificity to determine the aggressiveness of the diseases and to identify appropriate treatment. Additional biomarkers are extensively on research program to have a more correct answer to the problem of which PCA-3 is going to meet the demand.¹²

Bangladesh J. Urol. 2012; 15(1): 1-2

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Bangladesh Journal of Urology

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