

Review article:

## ***A variable level of prostate specific antigen and its relative tests and their probable explanatory diagnosis***

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**Abstract:** Prostate specific antigen is a glycoprotein that liquefy the semen normally. It suppose to be in a very low level abnormally and increase in cases of infection of the prostrate, hyperplasia and tumor. Due to increase and decrease in many other cases not only a tumor and due to high percent of existence in many normal fluids and many other tumor, it somewhat reduce its specificity and sensitivity and so it supported by other test. Aim: it to predict whether that tumor marker is sufficient to the diagnosis of the prostate tumor. Nowadays it had been seen that this tumor marker is secreted from many other fluid beside the prostate gland and found in many other tumor beside the prostate tumor and so it is better to be supported by many other assessments and clinical and histological steps for making a definite decision.

**Keywords:** prostate specific antigen, biopsy, prostate carcinoma, hyperplasia, free to total ratio, radiotherapy, glycoprotein

**Introduction:** Prostate-specific antigen is a protein (glycoprotein) that produced by the epithelium tissue of the gland prostate, it used in diagnosis of the prostate illness whether is a prostate carcinoma and benign prostatic hyperplasia. For some countries it regarded as one of the

tumor markers used in the prostate carcinoma, which is common tumor in the male and its percent of incidence increased with age and reached to one hundred in those more than ninety years old. Its molecular weight is about thirty three kilodalton. One of the theories of its rules is that it increase the liquefaction of the sperms and might increase the chance of fertilization. As mentioned, it increased in the prostate infection (porosities), benign prostatic hyperplasia, prostate tumor and increase in rectal examination during palpation of the prostate which could leads to a libratory errors. (1)

Its level usually undetectable but increase with age might be due to prostate enlargement and that's why its level screening should be occurred with age and the laboratory assessment should be performed every six months to every three months. Its used as a marker for might be limited due to that it not only increased in infection but also increase by tumor and BPH and for this reason it's used in diagnosis should be supported by ultrasound and clinical examination to exclude the tumor reason of its increment. Its level should be returned to a very low concentration after total prostatectomy. Its level may also be reduced by prostacare drug (finstride) which is five alpha reductase inhibitor that used to reduce the symptoms of prostate enlargement due to it relaxes the muscles of the prostate and so it facilitate the urination. The PSA is found in a bound or a free (active) form(2). The increase of the level of the bound one might give an indication of the tumor while the high concentration of the free type spark the presence of the benign hyperplasia, and so if the ratio of the bound PSA to the total concentration is increase in the tumor while increase the ratio of the free to the total amount indicate the presence of the benign case of the prostate enlargement(3). As mentioned previously, the increase the ratio of the free to the total PSA diagnose the presence of the BPH and may increase to more than seventeen percent which strengthen the diagnosis of BPH, but if the ratio is less that seventeen percent it indicate that occurrence of the tumor(4).

In general, the concentration of this protein is measured in microgram per milliliter and as this concentration increase to more than ten microgram per milliliter it strongly support the idea of the occurrence of the tumor. Traditionally, the grossly increased concentration (more than the twenty microgram per milliliter) is an indicator that this tumor not only present but might be spread (metastasis) to the surrounding tissue particularly to the bone itself which is more indicator of the malignancy(5,6). Still, its level assay should be accompanied with assessment of

the prostate state by digital examination (the rectal one), ultrasound and even biopsy which should be performed as a programmed screening strategy in those have a genetic risk or under the chance of increase its incidence especially if the level increase more than ten microgram per milliliter (7). Unfortunately, there is a no global protocol for the screening program and it is used widely. The risk of the biopsy and sample withdrawal of prostate for further examination is subside down in concentration between four to ten microgram per milliliter, i.e., the risk of operation ignore the need for the biopsy for a concentration in the shadow area ( an area between the normal level to the high one)(8).

Crucial question should be asked: is the prostate specific antigen efficient of diagnosis of prostate cancer? Another question if its elevated dose it means the presence of only the cancer of the prostate and not any other kinds of tumor or disease?

Some articles revealed that this tumor marker regarded as an excellent and one of the guide line for the diagnosis of tumor of the prostate particularly during the routine checkup of the human body every three to six months and even without the occurrence of the sign and symptoms ant which the tumor could be discovered early and it is much easier to be removed before the metastasis and so decrease the death rate. Although the results might be controversial due to it might loss its sensitivity in the presence of other tumors. And that's why some countries didn't regard this test is mandatory, like England. On the other hand its level variation give some many expectations, i.e, when its level vary from four to ten nanogram per milliliter the diagnosis might be the prostatitis, prostate enlargement, on the other hand a sever elevation might give the hint of the occurrence of the tumor and even hepato-cellular carcinoma . and that's why the biopsy is necessary for the final and crucial diagnosis. But still the death rate of the tumor is very low and might be leveled to four to five death case recorded every one thousand case reported that mean the tumor had a very good prognosis result. (9)

The screening might be used in reduce the mortality rate in to less than twenty five percent of the total. But is it mentioned in the previous question, the accuracy of the screening test is questionable and might give more than one explanation. It might give a false result of high elevation although there is no prostate tumor, and might give a normal value even in the presence of the tumor so we return to the question: is the screening test is sensitive and specific for diagnosis of the tumor of the prostate and not any other kinds of the tumors or disease? Is the

elevation or decrement of its level useful for diagnosis without the need for the other test? We ask this question here because the dissection made about the elevation of the value of the test might push the individual to unnecessary stress of this bad news, might push him to perform unnecessary biopsy and might expose him to infection by instrument used for biopsy and even hemorrhage. The false results of the low value might put the patient under a faked safety of absence of the tumor while the patient have a tumor and could be metastasized to the bone of the other surrounding tissue and so make it very difficult to heal the patient especially that the tumor is very low growing and so difficult to be diagnosed (10).

Prostate carcinoma might have a very rare illness symptoms; of one hundred cases diagnosed, only three cases suffer from erectile dysfunction, two cases might shows a difficult in urination, and vary rare case have a cardiac problem, respiratory problems and thrombotic problems (11).

This screening test should be monitored with a regular intervals ( every three, six till thirty six months) post operatively, post radiation therapy or post treatment and this is more serious in high risk individual. It is due to some of the level of this antigen could be detected even at a very low concentrations. This could be explained as a false laboratory errors, idiopathic and even a recurrence of the tumor. It suppose to reach to undetectable level after total removal of the prostate but the elevated level to about two nanogram per milliliter might give a hit of recurrent of the tumor or a residual tissue of the prostate which it not malignant in nature. Even the radiation treatment is not a sufficient method of treatment of the tumor due to that the screening might shows an increment of its concentration to less than two nanogram per ml and this might give an evidence of not successful treatment and a recurrence of the tumor(12).

Expected serum level of the prostate-specific antigen:

Normally and due to its function in liquefying the sperms and facilitating the fertilization, so its normal level supposed to be very low and might reached to a level that couldn't be detected or even to lower than four nanogram per milliliter, its elevated level (could be reached to twenty to twenty five nanogram per ml) give a good evidence of a tumor but still it is not enough and might required a further test or biopsy or at least US, on the other hand its elevated might not revealed the occurrence of a tumor and its decreased might not indicated the absence of the cancer. Low level may even presented in some people with a body mass index more than thirty.

It is high level may found in some cases of infection of the prostate, some case of benign prostatic hyperplasia, tumor, after ejaculation, and palpitation or digital rectal examination. It also increase with the age increase and the chance of occurrence of the tumor also increase with age and might reach to a level of one hundred percent at the late ninety years old(13-17).

One of the obstacles of diagnosis of the tumor is that there are a free PSA and a protein bound PSA, as the ratio of the free to the total one increase the chance of the tumor is decrease and as the ration of the free to the total decrease less than twenty five percent, the chance of the occurrence of the tumor increased. This ratio is more reliable and more accurate and lower percent or error than measurement the concentration of the PSA. The lower the ratio seen the more expectation of the tumor. This ratio assessment might be helpful in the make a defiant decision about the occurrence of the tumor at which it show a low concentration of the free to the total and so the ratio is low, this assessment is useful at a concentration between four to about ten or nine nanogram per ml. if the concentration of both free and total increased or reduced the percent will remain constant and this occur after intercourse and after twenty four hour respectively.(18,19)

Another ratio had been used is the ration of the active to the total PSA. Both of the previous ration (the ration of the free to the active PSA) and the ration of the active to total PSA have been used synergistically to support the screening test of the PSA and reduce the chance of error and decrease the false positive and negative results and the different probabilities of the high and low level of this tumor marker. Al the strategies that had been mentioned have a goal to reduce the requirement for the biopsy and the complication that may occur after sample intake from the patient. A summary for this strategies is that the PSA normally reached to undetectable level, it may increased in prostate infection, hyperplasia of the prostate, tumor, after intercourse and might be falsely positive increase without a tumor but might be idiopathic. It also reduced in some case of falsely results even if the patient had a tumor and in obesity. To reduce the percent of error especially in the diagnosis of prostate tumor and this tumor should be monitored carefully so it is better to measure the percent of free to the total PS which is reduced in case of the tumor and also we can do the percent or the ratio of the active to the total PSA due to that as the ratio of active increase there is a low chance of growth of new arteries and vein of the tumor,

finally it is could perform the biopsy regardless its risk and unpleasant out come or side effect.(20,21).

Nowadays the term prostate-specific antigen is not correctly used due to that from its name it refer to the source of its existence while it had been found in many other fluids not only a prostatic fluid and not only produced in prostate infection nor a tumor and not even found in men only but also found in women. It found in many fluids like: semen, endometrium, lung, gland of the urethra, amniotic fluid, female urine and serum and breast milk and even in female ejaculation. It is not found in tumor of the prostate only but some other tumors like the tumor of the renal system, and uterine cancer(22).

Conclusion: so many researches showed that the prostate specific antigen might not be such a sensitive and specific test for the follow and diagnosis the tumor of the prostate and so so many techniques should be used to support the diagnosis.

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