# Serum testosterone as predictor of pathological stage in prostate cancer

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## Abstract

**Aim:** The aim of our study is - To assess whether parameter as serum testosterone can be used to predict the pathological stage of the disease. To determine whether serum testosterone can be used as prognostic marker for the carcinoma prostate. To evaluate the efficacy of serum testosterone as a rapid tool in the diagnosis and prognosis of prostate carcinoma.

**Materials and Methods:** A total of 30 patients of carcinoma prostate as a case and 30 patients of BPH as a control. Clinical staging done by CT/MRI. Pathological staging done after radical prostectomy. Serum, testosterone analyzed by radioimmunoassay. Statistical analysis was done using statistical software SPSS version 10.0. Data was found to be normally distributed. Statistical analysis was performed using student's 't' test with statistical significance at <0.05.

**Results:** All patients included in this study were in age group of 50-80 years. Mean age of patients was 66.60 $\pm$ 8.06 years. Mean PSA for all patients was 26.49 $\pm$ 12.34 ng/ml. Minimum PSA was 8 ng/ml and maximum 89 ng/ml. 40% patients have serum testosterone > 400 ng/dl and 30% patients have serum testosterone < 200 ng/dl. Remaining 30% have serum testosterone in between 200-399 ng/dl. Mean preoperative serum testosterone level in study group were 315.30±49.66 ng/ml and in control group the mean preoperative *serum* testosterone level were 369.83±51.12 ng/dl. The mean serum testosterone concentration is lower in carcinoma prostate patients as compared to the BPH patients. The mean difference in both the group were statistically significant (p=0.018). In organ confined disease, the mean preoperative serum testosterone level were 411.14±11.50 ng/ml and in non-organ confined disease the mean preoperative serum testosterone level were 329.33±71.57 ng/dl. The mean serum testosterone level is lower in non-organ confined as compared to the organ confined disease. The mean difference in both organ and non-organ confined disease were statistically significant (p=0.008).

**Conclusion:** We conclude that patients with carcinoma prostate have statistically significant correlation between pretreatment total testosterone level and pathological stage. In our study total testosterone emerged as an independent predictor of extra prostatic disease We also analyzed patients with carcinoma prostate have low serum testosterone level as compared to BHP patients.

**Keywords:** Prostate; prostatic neoplasm; prostatectomy; testosterone

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## Introduction

Prostate cancer is the most common malignancy in men and the second leading cause of cancer death in the Western world (Badalament et al, 1991; Hanchette et al, 1992; Greenlee et al, 2001). Cancer of prostate is a disease of men over age 50. Only 1% of the prostate cancer is diagnosed before 50 years of age.

The role of testosterone in the pathophysiology of prostate cancer remains elusive and the conundrum is yet to be solved. After Huggins and Hodges proved that testosterone reduction by castration or oestrogen treatment caused regression of metastatic disease, the detrimental effect of testosterone administration in patients at risk of or with prostate cancer was inferred (Huggins C et al, 1941). (The relationship of testosterone level and prostate cancer is complex and is implicated in different clinical scenarios in our daily practice.

It has long been acknowledged that androgens are vital to the growth and maintenance of the prostate (Prehn RT, 1999). In vitro androgens have caused the proliferation of most human prostate cancer cell lines that are well differentiated. In vivo androgens also stimulate the induction and promotion of prostate tumors and prostate tumor xenografts in rodent models, whereas androgen ablation causes tumor regression (Lucia MS et al, 1998; Bladou F et al, 1996).

There is substantial controversy in the literature regarding the association between pretreatment testosterone and disease outcome in patients with prostate cancer. Numerous epidemiological studies have attempted to determine a relationship between androgens and prostate cancer risk with varied results. A recent study suggested a significant decrease in the risk of prostate cancer with increasing total testosterone (Stattin P et al, 2004). Other investigators have noted a moderate decrease in risk in men with high levels of serum sex hormone-binding globulin, resulting in lower free, active testosterone, (Gann PH et al, 1996; Dorgan JF et al, 1998). Consistently reports associate lower pretreatment testosterone with a significantly poorer treatment response and worse prognosis in metastatic cases. Specifically pretreatment testosterone less than 300 ng/dl is associated with shorter survival (Chodak GW et al, 1991), suggesting more aggressive disease (Ribeiro M et al, 1997). However, this relationship has been more difficult to establish in men with clinically localized prostate cancer.

Currently the established preoperative predictors of pathological stage and prostate specific antigen (PSA) progression are clinical stage, tumor grade and serum PSA. When combined, these factors predict extraprostatic extension with an area under the curve of 0.79 (Ohori M et al, 2004). Finding reliable preoperative markers that allow us to understand the disease more accurately would certainly be useful in disease management.

## Material & Method

The study was conducted from May 2011 to July 2014 in Bundelkhand region. 30 patients of carcinoma prostate attended General surgery ward/OPD were included, for study and to identify serum testosterone as predictor of pathological stage in prostate cancer.

Patients with already receiving androgens ablation therapy in form of GnRh agonist anti androgens and patient who have ready received radiotherapy were excluded in the study.

All patients underwent basic initial evaluation (history, physical examination, external genetalia examination, digital rectal examination, urine analysis and renal function assessment). All patients also underwent USG/CT/MRI of the abdomen to assess the kidney, ureter, bladder, prostate size and post void residual urine volume.

Estimation of serum testosterone, preoperative PSA estimation, Gleason grade and Gleason score estimation, Pathological staging from specimen, correlation of preoperative serum testosterone with pathological stage and univariate and multivariable ordinal logistic regression analysis was done to examine whether pretreatment testosterone is associated with Pathological stage.

Estimation of serum testosterone – Serum testosterone was analyzed by radioimmunoassay. 3-5 ml blood (specimen) sent in the plain vial (without anticoagulant), time of collection noted and separation of serum by centrifugation. Sample may be stored at 2-8 °C for 7 days and upto 2 months at -20 °C.

Statistical analysis was done using statistical software SPSS version 10.0. Data was found to be normally distributed. Statistical analysis was performed using student's 't' test with statistical significance at $<0.05$.

## Results

The study was conducted from July 2011 to May 2014 in Bundelkhand region thirty patients of carcinoma prostate as a case and 30 patients of benign BPH as a control taken following observations were made.

**Table 1: Age distribution**

| Age group (years) | No. of Patients | Percentage | Mean ± SD |
|---|---|---|---|
| 50-59 | 5 | 16.7 | 53.40 ± 3.43 |
| 60-69 | 13 | 43.3 | 64.49 ± 2.71 |
| 70-79 | 11 | 36.7 | 73.63 ± 3.29 |
| More than 80 | 1 | 3.3 | 80.0 |

Overall mean: 66.60 ± 8.06

Mean age for all patients was 66.60 ± 8.06 years (range 50-80 years). Maximum number (43.3%) of cases were in between 60-69 years age group. Minimum age was 50 years and maximum age 80 years.

**Table 2: Serum PSA (ng/ml)**

| Serum PSA (ng/ml) | No. of Patients | Percentage | Mean ± SD |
|---|---|---|---|
| 4.1 – 10 | 4 | 13.3 | 9.50±1.00 |
| 10.1 -20.0 | 15 | 50.0 | 15.15±3.30 |
| More than 20.0 | 11 | 36.7 | 48.12±24.69 |

Overall mean: 26.49±12.34

Mean PSA for all patients was 26.49+12.34 ng/ml. maximum number (15 cases, 50.0%) were having their serum PSA value between 10.1-20.0 ng/ml. four cases had their PSA levels <10 ng/ml.

**Table 3: Gleason score**

| Gleason score | No. of Patients | Percentage | Mean ± SD |
|---|---|---|---|
| Less than 6 | 15 | 50.0 | 5.73±0.45 |
| More than 6 | 15 | 50.0 | 7.33±0.48 |

Overall mean: 6.53.±0.93

Fifteen cases were of gleason socre <6 with mean Gleason score of 5.75±0.45 and another 15 cases were of Gleason score >6 with mean score of 7.33±0.48.

**Table 4: Serum Testosterone (ng/dl)**

| Serum testosterone (ng/dl) | No. of patients | Percentage |
|---|---|---|
| Less than 200 | 9 | 30.0 |
| 200-299 | 2 | 6.7 |
| 300-399 | 7 | 23.3 |
| More than 400 | 12 | 40.0 |

Table shows preoperative serum testosterone of 30 patients. Out of 30 patients. 12(40%) patients have serum testosterone > 400 ng/dl. 9(30%) patients have serum testosterone < 200 ng/dl and remaining 9 patients have serum

testosterone in between 200-399 ng/dl.

**Table 5: Clinical stage**

| Clinical stage | No. of patients | Percentage |
|---|---|---|
| T1 | 5 | 16.7 |
| T2 | 11 | 36.6 |
| T3 | 5 | 16.7 |
| T4 | 9 | 30.0 |

In our study clinical staging was done by CT/MRI. Eleven (36.6%) patients were in stage T2, 9(30.0%) in T4 and 5 cases both in stage T1 and T3.

**Table 6: Pathological state**

| Pathological stage | No. of patients | Percentage |
|---|---|---|
| Organ confined | 7 | 23.3 |
| Non-organ confined | | |
| • Extraprostatic extension | 7 | 23.3 |
| • Seminal vesicle extension | 4 | 13.3 |
| • Pos node | 4 | 13.3 |
| Clinical stage 4 (non operated) | 8 | 26.7 |

In present study pathological staging was done in patients who underwent radical prostatectomy, 15(49%) patients have non organ confined disease (extraprostatic extension in 7, seminal vesical extension in 4 and Pos node in 4 patients). 7 (23.3%) have organ confined and remaining 8 (26.7%) patients undergone bilateral orchidectomy, hence pathological staging in those patient not done and kept in category of T4 disease.

**Table 7: Comparison of testosterone values in study and control group**

| Group | Mean ± SD | 't' value | 'p' value |
|---|---|---|---|
| Study group | 315.30 ± 49.66 | 2.432 | 0.018 |
| Control group | 369.830 ± 51.12 | | |

The mean preoperative serum testosterone level in study group were 315.300 ± 49.66 ng/ml and in control group the mean preoperative serum testosterone level were 369.830 ± 51.12 ng/dl. The mean serum testosterone concentration is lower in study group compared to the control group. The mean difference in both the group were statistically significant (p=0.018).

## Discussion

Our study was based on 30 patients of carcinoma prostate. We studied prognostic factors including serum PSA, serum testosterone, Gleason grade, clinical stage, pathological stage.

When age group was taken into consideration in the present study maximum number of patients i.e. 43.3% were in between 60-69 years. 36.7% were in 70-79 years and 16.7% belonged to 50-59 years and 3.3% patients in more than 80 years age group. Highest incidence of carcinoma was seen in the middle age group (43.3%). Mean age for all patient was 66.60±8.06 years. Similar findings have been reported by others IHankey et al, 1986). So, any screening programme should lay ample stress over the middle age group apart from the elderly.

Present study thus reveals that increasing Gleason score correlated ^ well with increasing PSA value. However, the increasing PSA value was not statistically

significant. Similar findings have been reported by Stamey et al (2002) and Aihara M et al (1994) who concluded that increasing serum PSA though correlated with tumor volume but it did not directly correlates significantly with Gleason score or grade, PSA density which is an important version of PSA specificity which is a quotient of serum PSA divided prostate gland volume when corroborated with the Gleason score, it was observed that increasing PSA density did not correlated with Gleason score similar was the observation by Brawer MK et al (1993).

Huggen and Hodges (1941), proved that testosterone reduction by castration, or estrogen treatment caused regression of metastatic disease.' Carter et al (2000) analyzed harmone level up to 15 year before diagnosis of BPH and Ca prostate but failed to demonstrate and significant difference in serum testosterone in disease state.

In our study we did not observe any correlation of total testosterone with PSA ultrasound volume, Gleason grade and clinical stage. We found a statistically significant association between pretreatment testosterone and pathological stage in patient of carcinoma prostate.

As testosterone decreases patients have an increased likely hood of non-organ confined disease. Results indicate that low pretreatment total testosterone may be marker of more aggressive disease in prostate cancer. Similar results were found in a recent study in a large cohort of patients also treated with radical prostectomy our study validates these result.

Monda et al (1995) performed similar study and found that total testosterone had no clinical value in predicting pathological stage.

Hoffman et al (2000) also performed similar study and found that lower levels of pretreatment free testosterone were associated with more aggressive disease. However, they did not any association with total testosterone level.fin our study total testosterone was a predictor of extra prostatic disease in univariate analysis.

Our study revealed result opposite to those of several recent studies they proposed that high level of testosterone associated with worse disease. Their study relied on clinical stage and primary treatment was radiation and hormonal therapy. Actual status of disease in their patient not confirmed by pathological assessment of radical prostectomy so that conclusion about pathological stage not reliable, while we show that low testosterone was an independent predictor of pathological stage.

Ginger Isom-Batz et al (2005) retrospectively review the records of consecutive patient with clinically localized prostate cancer treated with radical prostectomy between June 1990 to July 2003 they find a statistically significant association between pre treatment testosterone and pathological stage in patients treated with radical prostectomy for localized prostate cancer. They concluded that as serum testosterone decreased the likelihood of organ confined disease decreased, similar result found in our study.

We found that patient with organ confined disease have more mean serum testosterone (411.14 $\pm$ 11.50) as compared to non-organ confined (329.33 $\pm$ 71.57) mean difference in both organ and non-organ confined disease were statistically significant (p=0.008).

## Conclusion

We conclude that patients with carcinoma prostate have statistically significant correlation between pretreatment total testosterone level and pathological stage. In our study total testosterone emerged as an independent predictor of extraprostatic disease We also analyzed patients with carcinoma prostate have low serum testosterone level as compared to BHP patients.

## References

1. Dorgan JF, Albanes D, Virtamo J, Heinonen OP, Chandler DW, Galmarini M, McShane LM, Barrett MJ, Tangrea J, Taylor PR. Relationships of serum androgens and estrogens to prostate cancer risk: results from a prospective study in Finland. Cancer Epidemiol Biomarkers Prev. 1998 Dec;7(12):1069-74. Erratum in: Cancer Epidemiol Biomarkers Prev 1999 May;8(5):485. PubMed PMID: 9865423.
2. Foti AG, Cooper JF, Herschman H, Malvaez RR. Detection of prostatic cancer by solid-phase

radioimmunoassay of serum prostatic acid phosphatase. *N Engl J Med.*1977 Dec 22;297(25):1357–1361.

3. Fowler JE, Whitmore WF. the response of metastatic adenocarcinoma of the prostate to exogenous testosterone. j urol 1981;126:372-375.
4. Gann PH, Hennekens CH, Ma J, Longcope C, Stampfer MJ. Prospective study of sex hormone levels and risk of prostate cancer. J Natl Cancer Insst 1996;88:1118.
5. Ginger Isom - Batz. Fernando J. Bianco JR., Michael W. Kattan, John P et al. Testosterone as a predictor of pathological state in clinically localized prostate cancer J Urol. 2005;173(6):1935-1937.
6. Hankey D, Todd B, Soloway MS. pretreatment testosterone levels: significance in androgen deprivation therapy. j urol 1986;136:1038-1040.
7. Hoffman MA, De Wolf WC and Morgentaler A. Is low serum free testosterone a marker for high grade prostate cancer/ J Urol 2000;163:824.
8. Huggins C, Hodge GB. Studies on prostatic cancer, I; the effect of castration, of estrogen and of androgen injection on serum phosphates in metastatic carcinoma of the prostat. Camcer Res. 1941;1:293-297.
9. Humphrey PA. Gleason grading and prognostic factors in carcinoma of the prostate. Mod Pathol 2004:17(3):292-306.
10. Imamoto T, Suzuki H, Akakura K, Komiya A et al. Pretreatment serum level of testosterone as a prognostic factor in Japanese men with hormonally treated stage D2 prostate cancer. Endocr J. 2001;48(5):573-8.
11. Kuhn JM, Billebaud T, Navratil H, et al. Prevention of the transient adverse effects of a gonadotropin-releasing hormone analogue (buserelin) in metastatic prostic carcinoma by administration of an antiandrogen (nilutamide). N Engl J Med. 1989;321L:413-418.
12. Massengill JC, Sun L, Moul JQ, QuH, McLeod DG et al. Pretreatment total lestosterone level predicts pathological stage in patients with localized prostate cancer treated with radical prostatectomy, J Urol.2003;169(5):1670-5.
13. Moggentaler A. Tesosterone and prostate cancer; an historical prespective on a modern myth. Eur Urol. 2006;50:935-393.
14. Partin AW, Kattan MW, Subong ENP, el al. Combination of prostatespecific antigen, clinical stage, and Gleason score to predict pathological stage of localized prostate cancer. A multi-institutional update. JAMA 1997;277:1445-1451.
15. Peehn RT. On the prevention and therapy of prostate cancer by androgen administration. Cancer Res 1999;59:4161.
16. Ribeiro M, Ruff P, Falkson G. Low serum testosterone and a younger age predict fro a poor outcome in metastatic prostate cancer. 1:Am J Clin Oncol. 1997;20(6):605-8.
17. Severi G, Morris HA, MAclnnis RF, et al. Circulating steroid hormones and the risk of prostate cancer. Cancer Epidemiol Biomarkers Prev. 2006;15:86-91.
18. Teloken C, DA Ros CT, Caraver F, Weber FA, Cavalheiro AP, Graziottin TM, Low serum testosterone levels are associated with positive surgical margins in radical retropubic prostatectomy: hypogeonadism represents bad prognosis in prostate cancer. J Urol. 2005; 174:7178-2180.
19. Yano M, Imamoto T, Suzuki H, et al. The clinical potential of pretreatment serum testosterone level to improve the efficiency of prostate cancer screening. Eur Urol. 2007;51:375-380.
20. Zagars GK, Pollack A, vol Eschenbach AC. Serum testosterone- a signigacnt determinant of metastatic relapse for irradiate localized prostate cancer. Urology. 1997;49(3):327-34.
21. Zhand PL, Rosen S, Veeramachaneni R, Kao J et al. Association between prostate cancer and serum testosterone levels. Prostate 2002;53:179.