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# Could Serum Testosteron Level and Body Mass Index Predict Psa Relaps in Prostate Cancer Patients undergoing Radical Surgery?

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## Abstract

**Purpose:** It is well-known that indicators such as biopsy and prostatectomy Gleason score , clinical and pathological stage and preoperative PSA level can be utilized in predicting PSA recurrence in cases who underwent radical prostatectomy (RP) with the diagnosis of organ-confined prostate cancer. The purpose of this study was to investigate the predictability of postoperative PSA recurrence by serum total testosterone levels as well as body mass index (BMI).

**Materials and methods:** Fourty-eight patients in whom RP was planned with the diagnosis of prostate-confined cancer were enrolled in this study. The data recorded included the patient's preoperative testosterone levels and BMI as well as age, serum PSA level, clinical stage, Gleason score on biopsy, the presence of PIN and surgical margin positivity. After operation, the patients were kept under follow up according to the guidelines. During the follow-up, the analysis of the selected markers was performed using T-test, Mann-Whitney U test, Chi square test, Anova and Roc analysis in cases with documented PSA recurrence.

**Results:** Serum total testosterone level, BMI, surgical margin positivity and Gleason score and preoperative PSA level are independent variables that affect PSA recurrence. On Roc analysis, a testosterone level of less than 2,81 ng/dL was found to be significant for the prediction of PSA recurrence (p=0.04).

**Conclusion:** From this study, we concluded that, besides proven risk factors for PSA recurrence (Pre op. PSA level, Gleason score, surgical margin positivity and stage), preoperative low testosterone levels and high BMI can also be predictive.

**Keywords:** Prostate; Adenocarcinoma; Testosterone; Body Mass Index; Prostate-specific antigen

## Introduction

Radical prostatectomy (RP) remains the gold standard for the treatment of localized prostate cancer in patients with a life expectancy of more than 10 years [1,2]. It is well-known that indicators such as biopsy and prostatectomy Gleason score , pathological stage, preoperative PSA level and surgical margin positivity (SMP) can be utilized in predicting PSA recurrence in cases who underwent radical prostatectomy with the diagnosis of organ-confined prostate cancer [3,4]. Given that prostate adenocarcinoma is a testosterone-dependent tumor, there is a limited number of studies investigating how PSA recurrence is influenced by testosterone levels and obesity that affects hormone levels.

In this study, we investigated the role that body mass index (BMI) as well as preoperative serum total testosterone levels play in the course of the disease in patients who underwent RP with the diagnosis of clinically localized prostate cancer and were followed up.

### Materials and Methods

Fourty eight patients who underwent RP with the diagnosis of prostate confined cancer in single center between 2005 and 2006 were enrolled in this study. The data recorded included the patient's preoperative total testosterone levels and BMI as well as age, serum free and total PSA levels, Gleason score on biopsy, the presence of perineural invasion (PNI), post RP prostate volume and SMP. A positive surgical margin is defined as the presence of tumor at the inked surface of the resected specimen. A positive surgical margin can be resulted from an insicion of a tumor with extraprostatic extension or iatrogenic incision of an organ-confined cancer [5,6].

Testosterone levels were taken as the mean value of two measurements performed before operation and chemiluminescence was used as the method of choice. All operations were performed in a retropubic manner as described by Walsh [7]. After operation, the patients were followed up initially at month 3, then at six months intervals in the second year and subsequently on a yearly basis. Patient follow up was performed using measurements of serum PSA levels and digital rectal examination. The diagnosis of biochemical recurrence was established in patients with a PSA level of 0.2 ng/dl or greater in two subsequent measurements. Time to recurrence was recorded in months. The above mentioned parameters that are likely to influence recurrence were investigated in patients with PSA recurrence.

Data analysis was performed using SPSS statistical software version 15. The T-test, Mann-Whitney U test, Chi square test, Anova and Roc analysis were the methods of choice.

## Results

The 48 patients included in this study had a mean age of 62.6 (51-

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73), a mean PSA level of 8.2 (2.1-19.3), a mean BMI of 26.4 (20.2-33.2) and a mean testosterone level of 4.1 nmol/ml (2.02-6.1). None of the patients received adjuvant therapy in the postoperative early period. Table 1 summarizes the characteristics of the patients.

The mean follow up time of patients was 56.6 (48-70) months. All patients were kept under follow-up and none of the patients were excluded from the study. Biochemical recurrence was detected in a total of 12 patients (25%) who had a mean PSA level of 0.7 (0.2-1.3). Recurrence occurred on postoperative month 17 in average. The analyses performed revealed that serum total testosterone levels (p<0.001), BMI (p=0.04), SMP (p<0.001), biopsy and RP sample Gleason score (p=0.036 and p<0.001), pathological T stage (p<0.001) and preoperative PSA levels (p=0.02) were the independent variables affecting PSA recurrence (Table 2).

Seven of 10 patients with positive surgical margin had biochemical recurrence whereas 3 patients have not had PSA progression. Regarding the parameters that are likely to affect SMP, there were no findings other than gleason scores (p<0.001). However, when these parameters were investigated based on BMI classification, positive surgical margins were observed in 5 of 8 patients (30-39.9 kg/m<sup>2</sup>) diagnosed as obese (p<0.001). No significant findings were noted in terms of the relationship between total testosterone levels and BMI (p=0.09) whereas there was a significant inverse proportion between patients with extraprostatic extension and testosterone levels (p=0.05).

Roc analysis of total testosterone level detected as an independent predictor by multivariate analysis revealed that a testosterone level of less than 2.81 ng/ml was significant for the prediction of PSA recurrence (p=0.047).

Patient Characteristics	No.of patients		
Total patients	48		
Median age	62.6 (51-73)		
PSA level	8.2 (2.1-19.3)		
Biopsy Gleason score	6.2 (6-7)		
Prostatectomy Gleason score	6.4 (6-8)		
Biopsy PNI	14 (% 29.1)		
Prostate volume(cc)	41.4 (28-76)		
BMI	26.4 (20.2-33.2)		
Serum testosterone level Stage (p)	4.1 (2.02-6.1)		
pT2	37 (% 77.1)		
pT3	11 (% 32.9)		
PSM	10 (% 20.8)		
Biochemical failure	12 (% 25)		

PNI: Perineural invasion, PSM: Positive surgery margin

i abie	1: Patient	Characteristics.

Parameters	Value(no)	PSA relapse(%)	Р	
PSA	8.2	12 (25.0)	0.02	
Biopsy PNI	14	4 (28.5)	0.11	
Prostatectomy gleason sum	6.4	12 (25.0)	<0.001	
Prostate volume	41.4	12 ( 25.0)	0.24	
PSM	10	7 (70.0)	<0.001	
ECE	8	2 (25.0)	0.07	
BMI	26.4	12 (25.0)	0.04	
Testosterone level	4.1	12 (25.0)	<0.001	

ECE: Extracapsular extansion

 Table 2.
 The relationship between the investigated parameters and PSA recurrence.

Parameters	Normal (18.5-24.9)	Over weight (25.0-29.9)	Obese (30.0-39.9)	Р
No.of patients	13	27	8	
Pre RP PSA	6.4	10.3	14.03	<0.001
Serum testosterone	5.9	5.8	4.9	0.091
Gleason score	7.02	6.91	7.64	0.19
ECE	1 (% 7.7)	1 (%3.7)	0	0.64
PSM	2 (%15.4)	3 (%11.1)	5(%62.5)	<0.001
PSA relapse	1 (%7.7)	7 (%25.9)	4 (%50)	<0.001

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Table 3: The relationship between the investigated parameters and BMI grouping.

Finally, the operated patients were classified according to BMI international classification and the presence of a relationship with the investigated parameters was investigated. Accordingly, as BMI increased there was a significant relationship between PSA recurrence and preoperative PSA levels and surgical margin positivity (Table 3).

## Discussion

In this study, we found that preoperative testosterone levels of less than 2.8 ng/dl was an important risk factor for biochemical disease recurrence in patients undergoing RP. A review of literature also revealed an inversely proportional relationship between testosterone levels and the aggressivity of the disease, in parallel with this finding [8-11]. Sufficient data to elucidate the mechanism of this relationship can not be obtained from the literature. However, it is a known fact that low testosterone levels indicate that the disease will follow an aggressive course. The most satisfactory explanation in the literaure is that decreased testosterone level is not a cause but a result of the aggressivity of the disease. Miller et al. [12] advocate that inhibin-alpha produced intensely by PC cells affect hypothalamo-pituitary axis, thus reducing testosterone levels. Similarly, Risbridger et al. [13] examined 174 patients and obtained the same result. The rapid increase in post RP testosterone levels and the decrease in inhibin-alpha was one of the reasons why the author advocated the hypothesis related to inhibinalpha. However, studies by Marks et al. [14] and Freedland et al. [15] demonstrated no relationship between testosterone levels and the course of the disease.

One of the results of this study is the positive relationhip between obesity and PSA recurrence. The positive relationship between obesity and the likelihood of developing prostate cancer has been confirmed by a number of studies carried out with large sample size [16,17]. However, the relationship between obesity and post RP recurrence has not been completely elucidated. Even though obesity was identified as a risk factor for PSA recurrence in a study of 3162 patients by Amling et al. [18] the fact that most patients with recurrence were African-American led to questioning of the reliability of the results of the mentioned study. A study by Freedland et al. [19] reported obesity as a risk factor for PSA recurrence. Freedland [19] suggested that increased aromatase activity in adipose tissue may lead to more aggressive tumor development due to increased testosterone-to-estrogen conversion and decreased testosterone levels. Additionally, mitogenic agents that increase with obesity such as serum leptin, insulin, insulin-like growth factor 1 affect the course of the disease.

In addition, SMP in patients with a BMI of 30 or over is also noteworthy. It is well known that surgery is much more difficult and less comfortable with obese patients than that with other patients. Under these circumstances, we believe that high SMP rate is one of the causes of early PSA recurrence in obese patients. Citation: Sımsır A, Cal C, Mammadov R, Cureklıbatır I, Gunaydın G (2011) Could Serum Testosteron Level and Body Mass Index Predict Psa Relaps in Prostate Cancer Patients undergoing Radical Surgery? J Cancer Sci Ther S1. doi:10.4172/1948-5956.S1-007

Conclusion

In this study, we concluded that, besides proven risk factors for PSA recurrence (preop, PSA level, gleason score, SMP and stage), preoperative low testosterone levels and high BMI can also be predictive in patients undergoing RP. However, further well-designed, multi-center studies including patients from different ethnic groups are warranted for these two parameters mentioned to be included in nomograms.

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