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# Severity of coronary artery disease and prostate-specific antigen relationship in men

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**Abstract. – OBJECTIVE: Prostate-specific antigen (PSA) is a well-known prostate cancer marker. Recent studies have shown that serum PSA levels can fluctuate in response to cardiovascular stress. In this study we aimed to determine if serum PSA levels correlate with the presence and stages of coronary artery disease (CAD) and whether PSA can be used as a marker for the diagnosis and severity of CAD.**

**PATIENTS AND METHODS: This was a retrospective chart review of male patients who underwent coronary angiography for suspected CAD. A total of 100 patients with angiographic data and baseline serum PSA measurements were included. Patients with previous history of coronary angiography, stent implantation, benign prostate hypertrophy, known prostate cancer or prostatitis were excluded.**

**RESULTS: The mean age was 57±10 years. Coronary angiography results were normal in 13%, non-obstructive CAD (non-critical plaque formation) in 16%, one-vessel disease in 21%, two-vessel disease in 30% and multi-vessel disease in 20%. Mean values of total and free serum PSA were 1.4±1.3 ng/mL and 0.4±0.4 ng/mL, respectively. Although there was an increasing trend of PSA with more advanced stages of CAD, no significant relationship was established ($p > 0.05$). Patients with hypertension had significantly elevated total and free serum PSA compared to normotensives. There is no comparison of PSA levels between patients with CAD and without CAD.**

**CONCLUSIONS: Our study suggests that there is no direct relationship between increasing levels of PSA and stage of CAD. Thus, PSA level does not appear to be a suitable marker for diagnosis or severity of CAD.**

*Key Words:*
Prostate-specific antigen, Severity of coronary artery disease, Coronary angiography.

## Introduction

Prostate-specific antigen (PSA) is a serine protease of kallikrein family encoded by hKLK3 gene located on chromosome 19. PSA is expressed at high quantities in the prostate epithelium and secreted in the lumen where it helps to liquefy semen through its protease action[1]. Although initially PSA was thought to be a tissue and male specific marker, later studies have shown that it is up-regulated by steroid hormones to be expressed in non-prostatic tissues, both in males and in females[2].

PSA is also present in the bloodstream of males at low levels (< 4 ng/mL). Serum PSA is mostly bound by protease inhibitors with a small fraction circulating in free form (free serum PSA). In the majority of prostate cancer cases serum PSA is elevated, making it a useful marker for early cancer detection[3]. Some recent studies and case reports suggested that serum PSA can fluctuate in response to acute cardiovascular stress, making it unreliable as a marker following events such as prolonged cardiopulmonary resuscitation, extracorporeal cardiopulmonary bypass, and acute myocardial infarction[4]. Elevation in serum PSA levels was also observed following stent implantation in patients with coronary artery disease (CAD)[5]. Furthermore, CAD itself may also have an association with serum PSA and the presence of benign prostate hypertrophy (BPH), as elderly men with < 1 ng/mL PSA were less likely to have CAD than those with higher serum PSA[6].

In this study we aimed to determine if serum PSA levels correlate with the presence and stages of CAD and whether PSA can be used as a marker for the diagnosis and severity of CAD, using a retrospective chart review of male patients who underwent coronary angiography for suspected CAD.

## Patients and Methods

### Study Design

This was a retrospective chart review of subjects who underwent coronary angiography for suspected coronary artery disease. Subject charts containing coronary angiographic data and baseline laboratory values of total and free serum



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PSA were included. Patients with previous history of coronary angiography, stent implantation, were excluded. All patients examination by a urologist and underwent transrectal ultrasonography to evaluate prostate volume by a single radiologist. Patients who had history of prostate cancer, prostatitis, prostatectomy, benign prostate hypertrophy (BPH) were also excluded.

A total of 100 patients fulfilled the study criteria. Informed consents of all of the patients were obtained. All procedure performed were in accordance with the Declaration of Helsinki.

### Coronary Angiography

Coronary angiography was performed as described before[7]. Basically, conventional Judkins technique was used and each angiogram was interpreted by two cardiologists. A significant obstructive atherosclerotic lesion was defined as 50% or greater lumen narrowing in one or more coronary arteries. The degree of CAD was assessed on a scale of 0 to 5: 0, normal coronary angiogram; 1, non-obstructive CAD; 2, one-vessel disease; 3, two-vessel disease; 4, multiple-vessel disease; 5, main coronary artery stenosis.

### Biochemical Studies

Serum PSA levels were measured in each patients. Serum PSA levels were measured with Architect 16000 Abbott (immunoassay method) (Abbott, Diagnostic, Abbott Park, IL USA). Primary end-point of the study was the relationship between baseline total and free serum PSA levels and the stage of CAD established by coronary angiography.

### Statistics

Statistical analysis of the study was conducted using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Numerical variables were expressed as mean, standard deviation, median, minimum and maximum; categorical variables were expressed as percentage. For total and free serum PSA, between group differences were analyzed by Mann-Whitney U test (if two groups) or Kruskal-Wallis test (if > 2 groups). Spearman correlation analysis was used to determine the correlation between numerical variables. Statistical significance was set at $p \leq 0.05$.

## Results

A total of 100 patients charts fulfilling the study criteria were included in the analysis. Mean age of the patients undergoing coronary angiography was 57±10 years. Medical history of the patients revealed hypercholesterolemia (62%), hypertension (53%), diabetes mellitus (20%), and family history of CAD (7%). Thirty-seven percent of the patients were cigarette smokers. Coronary angiography results were normal in 13%, non-obstructive CAD (non-critical plaque formation) in 16%, one-vessel disease in 21%, two-vessel disease in 30% and multi-vessel disease in 20%. Mean values of total and free serum PSA were 1.4±1.3 ng/mL (median, 0.87; range, 0.13-6.25) and 0.4±0.4 ng/mL (median 0.27; range, 0.05-2.34), respectively. Total PSA was elevated (≥ 4 ng/mL) in 7 patients (7%), while free PSA was elevated (≥ 0.5 ng/mL) in 25 patients (25%). Although there was an increasing trend of total and free serum PSA with more advanced stages of CAD, no significant relationship was established ($p > 0.05$; Table I and Figure 1). However, patients with hypertension were found to have significantly higher total ($p = 0.011$) and free ($p = 0.003$) serum PSA levels compared to normotensives (Table 1). Interestingly, free serum PSA was significantly higher in non-smokers compared to smokers ($p = 0.036$), although total serum PSA was not affected by smoking status ($p > 0.05$, Table I). In Spearman correlation analysis, coronary angiography results were not correlated with either total or free serum PSA levels ($p = 0.362$ and $p = 0.455$, respectively). There is no comparison of PSA levels between patients with CAD and without CAD.

## Discussion

In this study, we investigated the effect of different stages of CAD on PSA levels in a retrospective review of patient charts who underwent coronary angiography for suspected CAD and had baseline PSA values measured before the angiography. We were unable to find a significant correlation between CAD and serum PSA levels in this study.

A number of studies and case reports show an elevation in PSA levels in response to acute cardiovascular stress such as prolonged cardiopulmonary resuscitation[8], extracorporeal cardiopulmonary bypass[9-11], stent implantation[5] and acute myocardial infarction[12-15]. The rise in serum PSA under these conditions could be a reaction of the prostate gland in response to ischemic damage[5,8]. However, in a study of acute myocardial infarction (AMI) patients PSA values were shown to decrease by approximately 20% on day 2 after AMI compared to day 1 and day 3[16]. In addition, in a series of three less severe cases of AMI not involving stenosis of major

**Table I.** Total and free serum PSA with CAD relationship.

| | N | Total serum PSA mean±SD | p | Free serum PSA mean±SD | p |
|---|---|---|---|---|---|
| **Coronary angiography** | | | | | |
| Normal | 13 | 0.94 ± 0.71 | 0.769 | 0.28 ± 0.14 | 0.714 |
| Non-obstructive CAD | 16 | 1.05 ± 0.85 | | 0.31 ± 0.18 | |
| One-vessel CAD | 21 | 1.36 ± 0.99 | | 0.41 ± 0.30 | |
| Two-vessel CAD | 30 | 1.65 ± 0.60 | | 0.43 ± 0.43 | |
| Multi-vessel CAD | 20 | 1.60 ± 1.60 | | 0.55 ± 0.57 | |
| **Hypercholesterolemia** | | | | | |
| No | 38 | 1.28 ± 0.98 | 0.637 | 0.34 ± 0.22 | 0.898 |
| Yes | 62 | 1.46 ± 1.46 | | 0.46 ± 0.46 | |
| **Smoking** | | | | | |
| No | 63 | 1.45 ± 1.13 | 0.138 | 0.43 ± 0.33 | 0.036 |
| Yes | 37 | 1.29 ± 1.55 | | 0.39 ± 0.47 | |
| **Hypertension** | | | | | |
| No | 47 | 1.08 ± 1.05 | 0.011 | 0.33 ± 0.32 | 0.003 |
| Yes | 53 | 1.67 ± 1.43 | | 0.49 ± 0.43 | |
| **Diabetes mellitus** | | | | | |
| No | 80 | 1.28 ± 1.19 | 0.218 | 0.39 ± 0.39 | 0.085 |
| Yes | 20 | 1.84 ± 1.62 | | 0.51 ± 0.38 | |
| **Family history of CAD** | | | | | |
| No | 93 | 1.43 ± 1.33 | 0.341 | 0.42 ± 0.40 | 0.437 |
| Yes | 7 | 0.85 ± 0.53 | | 0.29 ± 0.18 | |

PSA: Prostate-specific antigen; CAD: Coronary artery disease; SD: Standard deviation.

arteries patients were observed to have diminution of PSA as opposed to elevation[17]. It was, therefore, speculated that PSA may somehow be more directly involved with the cardiovascular system[18].

There is only one study suggesting a correlation between CAD and elevated serum PSA. In a retrospective chart review of 702 elderly patients at a urology clinic, Weisman et al[6] showed that benign prostate hypertrophy (BPH), defined as a serum PSA, reading of > 1 ng/mL, correlated with history of coronary artery disease. Specifically, history of CAD was present in 29% of the patients with BPH compared to 9% of patients with no BPH. They hypothesized that CAD and BPH can both be androgen-dependent such that elderly men not having BPH are less likely to have CAD. We asked whether serum PSA might show a correlation with the presence and stages of CAD in our patient cohort so that it can be used as a marker for the diagnosis and severity of CAD. However, our results

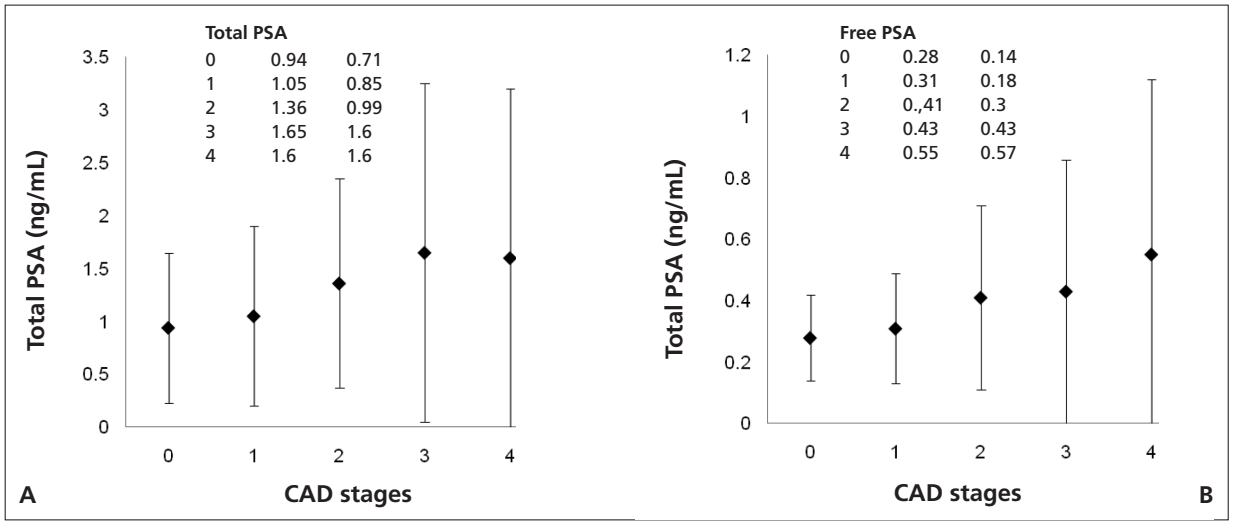


**Figure 1.** Total serum PSA *(A)* and free serum PSA *(B)* values according to the stages of CAD. Data is presented as mean ± standard deviation. CAD stages are: 0, normal; 1, non-obstructive CAD; 2, one-vessel CAD; 3, two-vessel CAD; 4, multi-vessel CAD.

failed to show a significant association between these two parameters. There were several differences between our study and the study of Weisman et al[6]. They included elderly patients of 65-80 years, while our patients were aged 32-83 years, with a median of 57 years. In Weisman et al, history of CAD was defined as any past events of MI, coronary angioplasty, or coronary artery bypass grafting, thus silent cases of CAD, especially those at early stages were missed. Instead, we attempted to investigate the whole spectrum of CAD patients. However, patients with hypertension were found to have significantly higher total and free serum PSA levels compared to normotensives. There are some studies suggesting a correlation between essential hypertension and low-grade inflammatory. Therefore, essential hypertension and arterial stifnes emphasized of showing the increase in blood levels of inflammatory markers[19]. There is only one study suggesting a correlation between essential hypertension and elevated serum PSA[20]. In addition, further studies are needed on this issue.

## Conclusions

While CAD may be less likely in elderly patients with low serum PSA values, our study suggests that there is no direct relationship between increasing levels of PSA and stage of CAD. Thus, PSA level does not appear to be a suitable marker for diagnosis or severity of CAD.

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