# Prostate Cancer Predicting Factors

## A Preliminary Report from Tehran

Gholamreza Pourmand,[1] Farzad Allameh,[1] Kazem Mohammad,[2] Sanaz Dehghani,[1] Bita Pourmand,[3] Abdolrasoul Mehrsai,[1] Seyed Hamed Hosseini[1]

[1] Urology Research Center, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran
[2] Epidemiology & Biostatistics Department, Tehran University of Medical Sciences, Tehran, Iran
[3] Research Development Center, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran

Corresponding Author:

Sanaz Dehghani, MD
Urology Research Center, Sina Hospital, Imam Khomeini St., Hassan Abad Square, Tehran, Iran

Tel: +98 21 6634 8560
Fax: +9821 6634 8561
E-mail: sanaz_dehghani2002@yahoo.com

Received August 2011
Accepted January 2012

**Purpose:** To determine the probability of having prostate cancer (PCa) using the combination of serum level of prostate-specific antigen (PSA) and age.

**Materials and Methods:** A total of 160 patients and 190 controls were enrolled in this hospital-based case-control study. Using a logistic regression model and the odds ratio of age and PSA level, the probability of PCa was estimated based on serum level of PSA and age of the participants.

**Results:** The mean age of patients with PCa and benign prostatic hyperplasia (BPH) was 67.75 ± 8.81 and 62.07 ± 8.71 years, respectively ($P < .000$). Using univariate analysis, we found that increase in life decades of the cases almost doubles the risk of having PCa (odds ratio = 1.95; $P = .00$), and the probability of developing cancer may increase by 74% in ketchup consumers. After multiple variable regressions, it was revealed that the odds of developing PCa increase by 90% only for every decade, and other variables did not have any significant association with PCa.

**Conclusion:** In clinical practice, PSA level combined with the age at presentation can be used as predictors of PCa probability and the necessity of biopsy.

**Keywords:** prostatic neoplasms, prostate-specific antigen, epidemiology, sensitivity and specificity, mass screening

## INTRODUCTION

Prostate cancer (PCa) is the third most commonly diagnosed cancer in many countries and the second cause of cancer death among men.[1] In Iran, PCa is reportedly the 3rd most commonly diagnosed visceral cancer, accounting for almost 7.75% of new cancer cases, and is the 7th most common cause of cancer death.[2] The overall detection rate of PCa in Iran is 3.5%.[3,4]

According to the Ministry of Health Cancer Registry report in 2004 and 2005 to 2006, the age-standardized rate of incidence of PCa in Iran are respectively 7.24 and 9.22 men per 100 000.[5,6] This rate is apparently less than the rate reported for Western countries, especially for the US (49.4 per 100 000 and 158.2 per 100 000, respectively), but it is still considerable in comparison to the rate in Eastern Asian countries (1.6 per 100 000).[3]

Among various important determinants of PCa development,[4] serum level of prostate-specific antigen (PSA) and age are considered to be the most important factors. The annual PCa screening is rootinely performed using serum PSA test and digital rectal examination (DRE), which leads to earlier diagnosis and more efficacious treatment of PCa. However, there is uncertainty about the significance of this screening for assessing tumor control and its impact on prostate cancer-specific mortality.[7]

A serum PSA level of 4 ng/mL is usually considered the cutoff threshold, above which further evaluations (prostate biopsy) are required. But recently, there have been many debates about the poor specificity of this test in cases in which PSA levels are below 10 ng/mL and in the range of 4 to 10 ng/mL.

It is evident that in epidemiologic studies, sometimes diagnoses are made higher or lower in frequency compared to the real-life situation in the society. In case of PCa, underdiagnosis of the disease is rather common.[8,9] Accepting a lower threshold for higher detection rate of PCa will result in many unnecessary biopsies and their complications, such as bleeding, hematuria, urinary tract infection, and sepsis.[10]

As Schroder and colleagues have discussed, no single threshold with concomitant high specificity and sensitivity could be identified.[4]

To increase the predictive value for PSA and improve its positive predictive value in screening tests, several methods have evolved recently for earlier detection of PCa and avoiding unnecessary biopsies. Prostate-specific antigen doubling time (PSADT), PSA velocity, percent free PSA, and age-specific ranges are some of them.

Regarding the above-mentioned facts, an individual with an elevated level of PSA may ask his urologist about the probability of having cancer. The primary study objective was to help urologists decide whether or not a patient needs a transrectal ultrasonography (TRUS)-guided biopsy to rule out PCa. In the current study, we provided a model analyzed by the logistic regression to predict the risk of PCa based on age and the serum PSA level in Iranian population.

## MATERIALS AND METHODS

The study population comprised patients referred to our clinic for TRUS-guided biopsy from April 2009 to September 2009. The study protocol was approved by Medical Ethics Committee of Tehran University of Medical Sciences.

Patients with a confirmed diagnosis of cancerous TRUS-guided biopsy served as the case group and individuals with any pathologic diagnosis other than PCa as controls. Accordingly, 160 patients were included in the case group and 190 patients entered the control group. Both groups had same socio-economic status. The same urologist performed 12-core TRUS-guided biopsy for all the patients.

Using an unconditional logistic regression model and the odds ratio (OR) regarding PSA and age, the probability of PCa was estimated based on age at presentation and serum PSA level. The results are presented as mean ± standard deviation. In univariate analysis, OR was calculated for evaluating the strength of association. The appropriate variables were entered in the final logistic regression model using Hosmer-Lemeshow test. The accuracy of the diagnostic tests was studied by receiver operating characteristic (ROC) curve analysis. The significance of all comparative analyses was considered at $P < .05$.

## RESULTS

The mean age of patients with and without PCa was 67.75 ± 8.81 and 62.07 ± 8.71 years, respectively ($P < .00$). Other demographic and clinical characteristics are presented in Ta-

**Table 1.** Basic characteristics of patients in PCa and BPH groups.*

| Variables | PCa | BPH | Odds ratio$_{crude}$ (*P*) |
|---|---|---|---|
| **Age, y** | | | |
| ≤ 50 | 6 (1.6%) | 16 (8.4%) | |
| 50 to 59 | 80 (21.4%) | 70 (36.8%) | 1.95 ( .00) |
| 60 to 69 | 135 (36.1%) | 69 (36.3%) | |
| ≥ 70 | 153 (40.9%) | 35 (18.4%) | |
| **Marriage** | 157 (98.1%) | 188 (98.9%) | 0.56 ( .52) |
| **Family history** | 23(14.4%) | 19 (10%) | 1.51 ( .21) |
| **Vasectomy** | 4 (2.1%) | 1 (0.6%) | 0.29 ( .27) |
| **Smoking** | 27 (16.9%) | 44 (23.2%) | 0.67 ( .15) |
| **Diabetes mellitus** | 12 (7.5%) | 17 (8.9%) | 0.83 ( .63) |
| **Garlic consumption** | | | |
| Never | 35 (21.9%) | 43 (22.6%) | |
| Low | 78 (48.8%) | 94 (49.5%) | 1.05 ( .68) |
| Moderate | 31 (19.4%) | 37 (19.5%) | |
| High | 16 (10%) | 16 (18.4%) | |
| **Ketchup consumption** | | | |
| Low | 36 (22.9%) | 70 (36.8%) | 1.74 ( .00) |
| Moderate | 77 (48.1%) | 90 (47.4%) | |
| High | 72 (29.4%) | 30 (15.8%) | |
| **Red meat consumption** | | | |
| Low | 69 (43.1%) | 59 (31.4%) | 0.75 ( .07) |
| Moderate | 68 (42.5%) | 99 (52.7%) | |
| High | 23 (14.4%) | 30 (16.0%) | |
| **Fatty diet** | | | |
| Low | 123 (76.9%) | 132 (69.8%) | 0.86 ( .40) |
| Moderate | 23 (14.4%) | 43 (22.8%) | |
| High | 14 (8.8%) | 14 (7.4%) | |

*PCa indicates prostate cancer; and BPH, benign prostatic hyperplasia.

ble 1.

The increase in life decades of the cases almost doubled the risk of developing PCa (OR = 1.95; $P < .00$). Furthermore, the probability of developing PCa reached 74% in ketchup consumers (low, moderate, and high). Other variables (except red meat that showed a protective effect against developing PCa; OR = 0.75; $P = .07$) did not have any significant relationship with developing PCa (Table 1).

Age was the only PCa predicting variable that remained unchanged after multivariate logistic regression analysis. We found that the probability of developing PCa increased by 90% for every decade after adjustment ($OR_{adj} = 1.90$; $P < .00$). As it is shown in Table 2, there was a significant difference between free, total, and free/total PSA in both groups. The difference between patients with PCa and BPH is presented in Figures 1 to 3 according to various age groups. In addition, using free/total PSA provided a more precise means of differentiating patients with BPH (Table 3 and Figure 4).

## DISCUSSION

Findings of the present study showed that the probability of developing PCa almost doubles for every life decade. Furthermore, no significant relationship was observed between other risk factors, including ketchup, red meat, garlic, and fatty diet, and developing PCa.

The rate of cancer detection varies in different countries with regard to PSA level. A study on 297 male US residents with either high PSA or abnormal DRE reported the PCa detection rate of 44% following prostate biopsy.[9,11] However, the data are not compatible with the studies performed in similar countries. The study accomplished by Catalona and colleagues reported the cancer detection rate of about 4.6%.[12] With a cutoff level of 2 ng/mL for serum total PSA, the detection rate is 3.8% in Iran.[4] These different results confirm the

**Table 2.** Comparing lab criteria in PCa and BPH groups.*

| | PCa | BPH | Mean difference (95% confidence interval) |
|---|---|---|---|
| Total PSA, ng/mL | 28.04 ± 60.82 | 6.08 ± 5.99 | -21.95 (-28.19 to -15.71) |
| Free PSA, ng/mL | 2.97 ± 9.32 | 1.30 ± 1.59 | -1.67 (-2.77 to -0.57) |
| Total/Free PSA | 11.63 ± 6.40 | 19.60 ± 18.01 | 7.97 (4.52 to 11.42) |
| Prostate volume, mL | 48.84 ± 25.21 | 57.49 ± 35.91 | 8.65 (2.81 to 14.48) |

*PCa indicates prostate cancer; BPH, benign prostatic hyperplasia; and PSA, prostate-specific antigen.

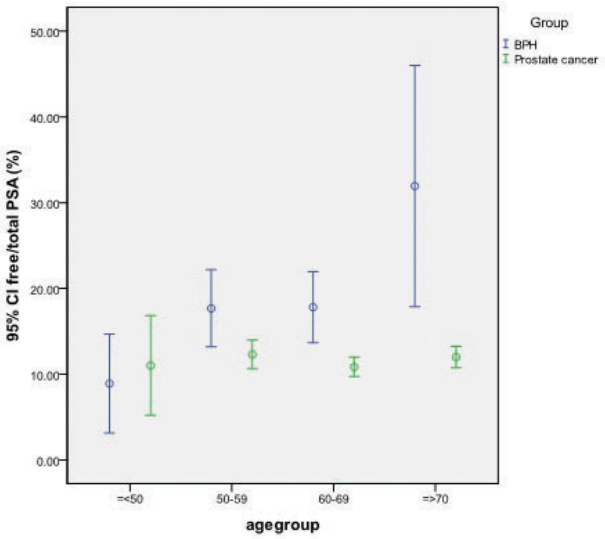


**Figure 1.** Mean (95% confidence interval) serum level of free/total PSA in different age groups of patients with prostate cancer and benign prostatic hyperplasia.

need for regional models to estimate the pretest probability of PSA in different parts of the world.

Prostate Cancer Prediction Trial (PCPT), conducted by National Cancer Institute, was a seven-year study of US men with PSA < 3 ng/mL and normal DRE. Several risk factors, such as race, DRE, family history, annual biopsies, and age, were considered along with PSA level. This study evaluated the risk of cancer detection in US low-risk population.[13] The European Randomized Study of Screening for Prostate Cancer (ERSPC) was also performed to develop a statistical model for PCa prediction in the European population. In this study, the prostate volume was added to assess factors in PCPT study in order to enhance the accuracy of PCa risk assessment model.[8]

In our study, the factors, including ketchup, red meat, garlic, and fatty diet, were also studied. Some studies have shown

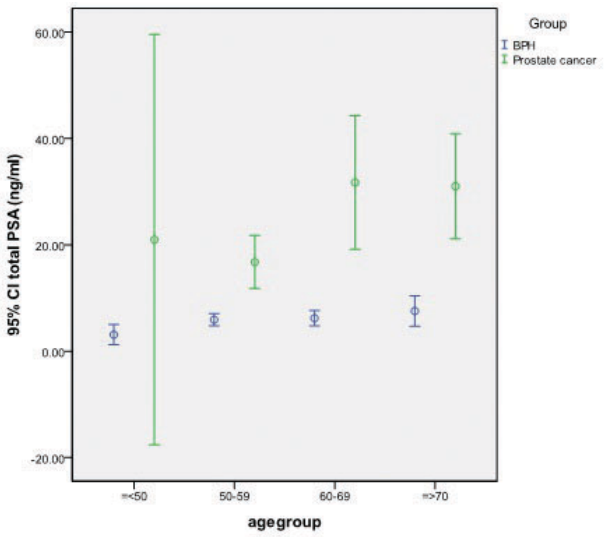


**Figure 2.** Mean (95% confidence interval) of total PSA in different age groups of patients with prostate cancer and benign prostatic hyperplasia.

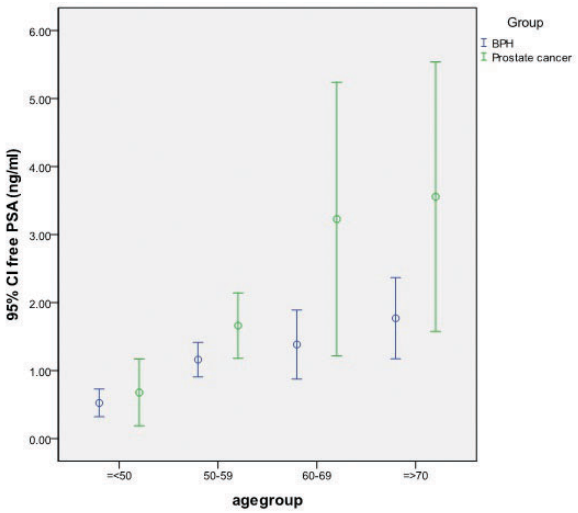


**Figure 3.** Mean (95% confidence interval) serum level of free PSA in different age groups of patients with prostate cancer and benign prostatic hyperplasia.

**Table 3.** lab tests accuracy in diagnosing patients with PCa and BPH. *

| | Area under curve | 95% confidence interval | *P* |
|---|---|---|---|
| Total PSA, ng/mL | 0.798 | 0.757 to 0.839 | .000 |
| Free PSA, ng/mL | 0.623 | 0.570 to 0.675 | .000 |
| Total/Free PSA | 0.817 | 0.776 to 0.858 | .000 |

*PCa indicates prostate cancer; BPH, benign prostatic hyperplasia; and PSA prostate-specific antigen.

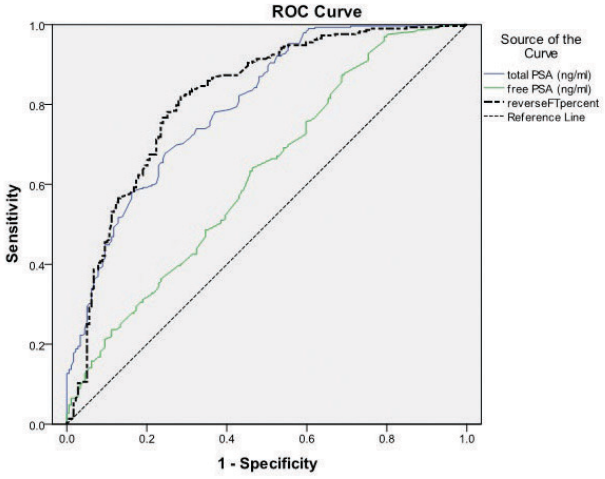


**Figure 4.** Receiver operating characteristic curve, comparing total PSA, free PSA, free/total PSA sensitivity and specificity.

a relationship between the aforementioned risk factors and PCa. However, in the final model of our study, a significant relationship was found between age and PCa.

The predictive value of PSA test increases with age.[14] Studies show that positive predictive value for PSA > 4 ng/mL is about 5.6% and the cancer detection rate by simple PSA test is 4.6%. These odds differ when PSA values are interpreted with regard to the age of patients. The rate of cancer detection in people aged between 40 and 49 years is 1.4% while it is 1.6% in 50 to 59 years. This rate is over 4.9% in 60 to 69 years and reaches 12.9% for men older than 70 years.[15] As a result, age was included in our analytic model as an important determinant for the risk of PCa. Our results cannot be generalized to other counties and populations.

## CONCLUSION

Considering the obtained results, it seems that age of the patients as well as free/total PSA results are the best predicting factors of PCa in hospital-based urology clinic patients.

## ACKNOWLEDGEMENTS

This study was supported by grants from Tehran University of Medical Sciences Research Fund. We would like to thank Ms Heidari for her cooperation and assistance as well as the patients who participated in this study.

## CONFLICT OF INTEREST

None declared.

## REFERENCES

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. CA: a cancer journal for clinicians. 2009;59:225-49.
2. Mousavi SM. Toward prostate cancer early detection in Iran. Asian Pac J Cancer Prev. 2009;10:413-8.
3. Parkin DM, Pisani P, Ferlay J. Global cancer statistics. CA Cancer J Clin. 1999;49:33-64, 1.
4. Schröder FH, Gosselaar C, Roemeling S, Postma R, Roobol MJ, Bangma CH. PSA and the detection of prostate cancer after 2005. Part I. EAU-EBU Update Series. 2006;4:2-12.
5. *Center for Disease Control, Noncommunicable Deputy, Cancer Control Office: Iranian Annual of National Cancer Registration Report 2004*. 2 ed: Iran ministry of health and medical education, Health deputy; 2006.
6. *Center for Disease Control and Prevention, Noncommunicable Deputy Cancer Office. Iranian Annual National Cancer Registration Report 2005 – 2006*: Tehran (Iran): Ministry of Health and Medical Education; 2007.
7. Andriole GL, Crawford ED, Grubb RL, 3rd, et al. Mortality results from a randomized prostate-cancer screening trial. N Engl J Med. 2009;360:1310-9.
8. van den Bergh RC, Roobol MJ, Wolters T, van Leeuwen PJ, Schroder FH. The Prostate Cancer Prevention Trial and European Randomized Study of Screening for Prostate Cancer risk calculators indicating a positive prostate biopsy: a comparison. BJU Int. 2008;102:1068-73.

9. Hernandez DJ, Han M, Humphreys EB, et al. Predicting the outcome of prostate biopsy: comparison of a novel logistic regression-based model, the prostate cancer risk calculator, and prostate-specific antigen level alone. BJU Int. 2009;103:609-14.

10. Rodriguez LV, Terris MK. Risks and complications of transrectal ultrasound guided prostate needle biopsy: a prospective study and review of the literature. J Urol. 1998;160:2115-20.

11. Sadjadi A, Nooraie M, Ghorbani A, et al. The incidence of prostate cancer in Iran: results of a population-based cancer registry. Arch Iran Med. 2007;10:481-5.

12. Catalona WJ, Smith DS, Ratliff TL, Basler JW. Detection of organ-confined prostate cancer is increased through prostate-specific antigen-based screening. JAMA. 1993;270:948-54.

13. Thompson IM, Ankerst DP, Chi C, et al. Assessing prostate cancer risk: results from the Prostate Cancer Prevention Trial. J Natl Cancer Inst. 2006;98:529-34.

14. Moul JW, Sun L, Hotaling JM, et al. Age adjusted prostate specific antigen and prostate specific antigen velocity cut points in prostate cancer screening. J Urol. 2007;177:499-503; discussion -4.

15. Ishidoya S, Ito A, Orikasa K, et al. The outcome of prostate cancer screening in a normal Japanese population with PSA of 2-4 ng/ml and the free/total PSA under 12%. Jpn J Clin Oncol. 2008;38:844-8.