

# Evaluation of prostate cancer prevalence in Iranian male population with increased PSA level, a one center experience

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**Purpose:** This study was conducted to evaluate the incidence of prostate cancer (PCa) in Iranian male patients with increased prostate-specific antigen (PSA), and normal or abnormal digital rectal examination (DRE) that underwent prostate biopsy.

**Materials and methods:** From March 2006 to April 2009, a total of 346 consecutive males suspected of having PCa due to increased PSA levels underwent transrectal ultrasonography (TRUS)-guided sextant biopsy of the prostate. The total PSA (tPSA), demographic data, incidence of PCa, benign prostate hyperplasia (BPH), and prostatitis were assessed.

**Results:** The patients were divided into two groups according to their PSA values (group A serum tPSA level, 4–10 ng/mL; group B serum tPSA level, 10.1–20.0 ng/mL). Of the 346 biopsied cases, 193 cases (56%) had PCa, 80 cases (23%) had BPH, and 73 cases (21%) had prostatitis. The mean PSA and the age of the carcinoma group were significantly higher than those of the benign group ( $P < 0.01$ ). The biopsy results were grouped as PCa, BPH, and prostatitis. Incidence of PCa for group A and group B cases were 115 cases (51%), and 78 cases (65%), respectively. In the case of PCa, BPH, and prostatitis, the mean PSAs were 10.02 ng/mL, 8.76 ng/mL, and 8.41 ng/mL, respectively ( $P < 0.40$ ).

**Conclusion:** TRUS-guided prostate biopsy and interpretation by a skilled team is highly recommended for early detection of PCa or its ruling-out. It seems that a PSA cutoff value of 4 ng/mL may be applied to the Iranian population. Although the chance of PCa is high in the PSA levels of 4–10 ng/mL, the combination of some data, like age and prostate volume, can decrease the rate of unnecessary prostate biopsies. We recommend prostate biopsy when PSA and/or DRE is elevated in symptomatic patients with obstructive and/or irritative lower urinary tract symptoms (LUTS) such as dysuria, frequency, or nocturia. Due to the very high incidence of PCa in the patients with PSA greater than 10 ng/mL, TRUS-guided biopsy is indicated, whatever the findings on DRE and/or LUTS, since the PCa detection rate is high.

**Keywords:** prostate-specific antigen, benign prostate hyperplasia, BPH, prostate biopsy, prostate carcinoma, PCa, digital rectal examination, DRE, lower urinary tract symptoms, LUTS

## Introduction

Prostate cancer (PCa) is one of the most common cancers in the male population and is the second leading cause of cancer death for men in the USA.<sup>1</sup> It is a major cause of morbidity and mortality in Iran,<sup>2</sup> yet there are few studies determining the relation between prostate-specific antigen (PSA) levels and the risk of PCa. The mortality of PCa on the basis of geographic area differs. In the Scandinavian area and southern Europe its prevalence is high, and in eastern Asia its prevalence is the least. Its prevalence is directly related to age. PSA and digital rectal examination (DRE) are

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good screening tools of PCa. In this retrospective study, we evaluated PCa prevalence in Iranian male patients that were referred to our center for transrectal prostate biopsy due to increased PSA level.

Unfortunately, in Iran, most PCa is already associated with nonorgan-confined disease or bone metastasis at detection. Therefore, focusing research on methods of its early detection has developed.<sup>2</sup>

PSA is secreted by the epithelial cells lining the acini and the ducts of the prostate gland in both normal and malignant conditions.<sup>3,4</sup> The serum levels of PSA are elevated in PCa and benign prostate hyperplasia (BPH).<sup>3,5,6</sup> Prostate biopsy has been usually performed in clinical practice in cases with increased PSA levels. Although a serum PSA level of 4.0 ng/mL is used as a cutoff point for PCa screening, it is relatively difficult to differentiate prostate adenocarcinoma from benign prostatic hyperplasia (BPH) in patients with gray-zone PSA levels (4–10 ng/mL).<sup>8–11</sup>

PCa early detection guidelines are mainly based on data from the USA and Europe and may not be relevant to other geographic areas or ethnic groups.<sup>12</sup>

This study was designed to evaluate the significance of total PSA (tPSA) in the PSA of 4–10 ng/mL and its comparison with PSA levels of 10–20 ng/mL for discrimination between benign and malignant prostate disease in Iranian men.

## Materials and methods

This is a retrospective study in which Iranian males with increased PSA levels (4 ng/dL) that referred to transrectal ultrasound (TRUS) prostate biopsy were evaluated. In this study, a total of 346 males with increased PSA values with or without positive DRE (4–20 ng/mL) were evaluated in the 3 consecutive years from March 2006 to April 2009. The mean age of these patients was 65.81 years, ranging from 45 to 87 years, with standard deviation (SD) of 8.50. Of these, 39 (11.3%) were <55 years old, 68 (19.7%) were between 56 and 60 years old, 136 (39.3%) were between 61 and 70 years old, 52 (15%) were between 71 and 75 years old, and 51 (14.7%) were >76 years old (Table 1). This study was

**Table 1** Age distribution of eligible cases

Age, years	n (%)
<55	39 (11.3%)
56–60	68 (19.7%)
61–70	136 (39.3%)
71–75	52 (15%)
>76	51 (14.7%)

performed in Bistoon Uroradiology Private Clinic, Tehran, Iran. Prior to DRE, tPSA were measured for all of these patients. None of them had current urinary tract infections, clinical prostatitis, and history of prior prostate surgery (transurethral resection of the prostate or open prostatectomy). A sextant biopsy was performed from the apex and base of the right and left parasagittal planes of the prostate with 10 core biopsies. If hypoechoic areas were noted on TRUS, a specimen was taken from each of these areas.

Demographic data including age, PSA level, prostate volume, and pathology result were evaluated. PSA was measured by using the Tandem-R assay. Prostate volume was calculated by using the following formula:

$$\Pi/6 \times L \times W \times H, \quad (1)$$

where L = length, W = width, and H = height. The patients were divided into two groups: group A, with PSA level between 4 and 10 ng/dL; and group B, with PSA level between 10 and 20 ng/dL. On the basis of prostate weight, the mean, median, SD, and variance was 56.48 cm<sup>3</sup>, 49 cm<sup>3</sup>, 27.34, and 747.94, respectively.

The total number in group A was 226 (65.3%), and group B was 120 (34.7%) (Tables 2 and 3). One experienced pathologist performed the histopathological examinations. Atypical small acinar proliferation and prostate intraepithelial neoplasia were excluded from the study. Demographic and clinical characteristics of patients with and without prostate adenocarcinoma were compared with the use of statistical *t*-test.

This study was conducted in accordance with the Declaration of Helsinki. The local medical ethical committee approved the study.

TRUS-guided, systematic, sextant, six-core biopsies with two additional biopsies from transition zone were done using a biopsy gun (Promag 1, MD Tech, Gainesville, FL) with an 18-gauge biopsy needle (2.2 Biopsy Needle, MD Tech).<sup>13</sup> The histological criteria for PCa used were those of the World Health Organization.<sup>13,14</sup> Cancers were graded according to the Gleason grading system.<sup>15</sup>

**Table 2** Characteristics of group A and group B

Characteristic	Group A	Group B
PSA, ng/mL	4–10	10–20
Mean age, years	64.38	68.5
Number of cases (%)	226 (65.3%)	120 (34.7%)

**Abbreviation:** PSA, prostate-specific antigen.

**Table 3** Histopathology of biopsied cases

Group	Mean age (SD)	N	n (%)		
			PCa	BPH	Prostatitis
Group A	64.4 (8.13)	226	115 (51%)	59 (26%)	52 (23%)
Group B	68.5 (8.5)	120	78 (65%)	21 (17.5%)	21 (17.5%)

**Abbreviations:** BPH, benign prostate hyperplasia; PCa, prostate cancer; SD, standard deviation.

## Statistical analysis

The statistical analysis of the collected data were performed using SPSS Statistics, version 16.0 (SPSS Inc, Chicago, IL) software.<sup>16</sup> The values of continuous variables were demonstrated as mean  $\pm$  standard deviation. Comparisons of variables (age, prostate volume, PSA, and pathologic diagnosis) were done with the *t*-test. *P*-values less than 0.05 were considered significant.

## Results

The overall final pathologic diagnosis was prostate adenocarcinoma in 193 cases (56%), BPH in 80 cases (23%), and prostatitis – subacute or chronic – in 73 cases (21%). The group specific pathologic diagnosis was as follows: for group A, prostate adenocarcinoma in 115 cases (51%), BPH in 59 cases (26%), and prostatitis – subacute or chronic – in 52 cases (23%) (Table 3); for group B, prostate adenocarcinoma in 78 cases (65%), BPH in 21 cases (17.5%), and prostatitis – subacute or chronic – in 21 cases (17.5%) (Table 3).

The mean (and SD) for age of group A and group B were, 64.38 years (8.134) and 68.5 years (8.56), respectively (Table 3).

The mean (and SD) prostate volume for group A and group B were 55 cm<sup>3</sup> (23.963) and 59.5 cm<sup>3</sup> (32.702), respectively. The mean prostate volume for PCa cases was 46.09 cm<sup>3</sup>. The mean prostate volume for prostatitis cases was 64.67 cm<sup>3</sup>, with SD of 26.304. The mean prostate volume for BPH cases was 74.06 cm<sup>3</sup>, with SD of 33.51 (Table 4).

**Table 4** The relations between the pathologic diagnoses, age, PSA, and prostate volume

	Mean age (SD) <sup>a</sup>	Mean PSA (SD) <sup>b</sup>	Prostate volume <sup>c</sup>
PCa	67.6 (8.9)	10.02 (4.37)	46 cm <sup>3</sup>
BPH	64.5 (7.5)	8.4 (3.56)	74 cm <sup>3</sup>
Prostatitis	62.3 (6.8)	8.7 (3.72)	64.67 cm <sup>3</sup>

**Notes:** <sup>a</sup>*P* = 0.01; <sup>b</sup>*P* = 0.4; <sup>c</sup>*P* = 0.01.

**Abbreviations:** BPH, benign prostate hyperplasia; PCa, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation.

The mean PSA level for PCa was 10.02 ng/dL, with SD of 4.37. The mean PSA level for prostatitis was 8.76 ng/dL, with SD of 3.72. The mean PSA level for BPH was 8.41 ng/dL, with SD of 3.56.

The mean (and SD) age for PCa, prostatitis, and BPH were 67.63 years (8.98), 62.34 years (6.83), and 64.58 years (7.52), respectively (Table 4).

The mean Gleason score for group A was 6.5 and for group B was 6.7 (*P*  $\leq$  0.05).

The statistical relation between the PSA level and PCa was significant (*P* < 0.40).

ANOVA test was used for the determination of the relation between the age and PCa; and it was significant (*P* < 0.01). With this test, the relation between PCa and BPH was significant (*P* < 0.01). The relation between age and PSA was significant (*P* > 0.01). Based on our study, the positive predictive value for PCa in group A was 51% and for group B, 65%.

Age was correlated positively with tPSA in both the PCa group and the BPH group in all tPSA ranges (0.001). This means that in our cases, the proportion of males with PSA levels above the cutoff value increased with age.

The mean PSA value (range, SD) in all men with PCa was 10 ng/mL (4–20 ng/mL, 4.37), in those with BPH was 8.4 ng/mL (4–20 ng/mL, 3.56), and in those with prostatitis was 8.7 ng/mL (4–20, 3.72) ng/mL (*P* < 0.001) (Table 4).

## Discussion

The incidence of PCa in Iran is significantly less than those in developed countries, and similar to eastern Mediterranean regions.<sup>17</sup> PCa is the most frequently reported malignancy in Iranian males after stomach cancer.<sup>18,19</sup> Among genitourinary cancers, it is the second most common cancer after bladder cancer, with an incidence of 33.4%.<sup>20</sup> The lowest recorded PCa rate is 0.4 per 100 000 in Ardabil, northwest Iran.<sup>13,21</sup> Iranian men are ethnically and racially different from most of Asian men,<sup>22</sup> so the biochemical parameters of PCa should be different. In a study by Khezri et al,<sup>23</sup> in a large Iranian healthy male population, the serum PSA concentration correlated directly with the subject's age and prostatic volume. Based on this study, the age-related PSA cutoff point was 2.61 ng/mL for 50–59 years, 3.59 ng/mL for 60–69 years, and 4.83 ng/mL for 70–79 years. The serum PSA levels and prostate volume are age- and race-dependent. For this reason, we chose the cutoff point of 4 ng/mL for prostate biopsy. In another study by Mehrabi et al, the PSA cutoff level in the males older than 69 years is 4.4 ng/mL.<sup>24</sup>

In our study, of 346 patients with serum PSA levels between 4 and 20 ng/mL, only 56% had pathologically diagnosed PCa, which is much lower than values used in Western countries. This can be explained by a widely different geographical prevalence of PCa.<sup>25</sup> Amirrasouli et al<sup>25</sup> evaluated 332 Iranian men with serum tPSA levels of 4–20 ng/mL. After TRUS prostate biopsy, they detected PCa in 15% of their patients. Incidence of PCa for serum tPSA level 10 ng/mL and serum tPSA level of 10.1–20.0 ng/mL was 6.7% and 39.5%, respectively. Catalona et al,<sup>26</sup> found positive findings on prostate biopsy in less than 50% of the patients with PSA of 4–10 ng/mL.

Several studies showed an advantage of using PSAD compared with tPSA alone.<sup>11,12,27–30</sup> Lam et al<sup>31</sup> recommended a PSAD cutoff of 0.15 ng/mL for detection of PCa, which spared half of the patients from undergoing unnecessary biopsies. In spite of its value, we did not consider the role of PSAD in this study.

Although several studies showed that PSA screening had a beneficial effect, the results of the selected studies were inconsistent, and mass screening is not warranted.<sup>32,33</sup> Both PSA and DRE were not recommended for population-based screening programs, but they could be conducted individually.<sup>32</sup>

Hua et al<sup>34</sup> studied the prostate biopsy results in 295 Chinese cases with PSA levels  $\geq 4$  ng/mL; the positive detection rate of PCa was 19.7%. In our Iranian cases, the positive detection rate was 56%.

We observed, like Gohji et al,<sup>35</sup> in the patients with PCa, the prostate volume was smaller, and the age was higher than in the patients with BPH or prostatitis.

In the Safarinejad study,<sup>13</sup> the detection rate of PCa in Iranian males using PSA alone was reported at 3.5%, which reflects an increase in its incidence. In addition, Safarinejad detected 17.5% PCa in cases with PSA 4–10 ng/mL, and 47.6% in cases with PSA 10–20 ng/mL.

## Conclusion

Comparing our study results with others, we found that PSA alone can be used efficiently as a first and/or repeat test for PCa screening of Iranian males. In addition, we found that the chance of PCa increases with increasing age, lesser weight of prostate, and increased tPSA. There was no difference in the Gleason score in our two groups of different PSA levels (4–10 and 10–20 ng/mL).

## Disclosure

The authors report no conflicts of interest in this work.

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