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·Original Article·

Mass screening of prostate cancer in a Chinese population: the relationship between pathological features of prostate cancer and serum prostate specific antigen

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Abstract

Aim: To investigate the pathological features of the prostate biopsy through mass screening for prostate cancer in a Chinese cohort and their association with serum prostate specific antigen (PSA). **Methods:** A total of 12 027 Chinese men in Changchun were screened for prostate cancer by means of the serum total prostate specific antigen (tPSA) test (by Elisa assay). Transrectal ultrasound-guided systematic six-sextant biopsies were performed on those whose serum tPSA value was >4.0 ng/mL and those who had obstructive symptoms (despite their tPSA value) and were subject to subsequent pathological analysis with the aid of the statistic software SPSS 10.0 (SPSS. Inc., Chicago. USA). **Results:** Of the 12 027 cases, 158 (including 137 patients whose serum tPSA values were >4.0 ng/mL and 21 patients [serum tPSA <4. 0 ng/mL] who had obstructive symptoms) undertook prostate biopsy. Of the 158 biopsies, 41 cases of prostatic carcinoma were found (25.9 %, 41/158). The moderately differentiated carcinoma and poorly differentiated carcinoma accounted for 61 % and 34 %, respectively. A significant linear positive correlation between the serum tPSA and the Gleason scores in the 41 cases of prostatic carcinoma ($r = 0.312$, $P < 0.01$) was established. A significant linear positive correlation between the serum tPSA value of the 41 prostatic carcinoma and the positive counts of carcinoma in sextant biopsies was established ($r = 0.406$, $P < 0.01$), indicating a significant linear relationship between serum tPSA and the size of tumor. **Conclusion:** This study was the first to conduct mass screening for prostate cancer by testing for serum tPSA values and the first to investigate the pathological features of prostate cancer in a cohort of Chinese men. Our results reveal that the moderately differentiated carcinoma is the most common type of prostate cancer. This study also has shown that the serum tPSA value in prostate cancer is associated with the Gleason score and the size of tumor. *(Asian J Androl 2005 Jun; 7: 159–163)*

Keywords: prostate cancer; mass screening; prostate specific antigen; pathomorphology

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1 Introduction

Traditionally, it has been thought that the incidence of prostate cancer in China and Japan is low; however, in these countries, the incidental discovery of prostate

carcinoma in autopsies is not uncommon.

Because of the lack of specific clinical symptoms found at the early stages of prostate cancer, in more than half of the cases in China, the disease is not detected until it has reached stage D with metastases. Therefore, mass screening using serum total prostate specific antigen (tPSA) has been adopted as the paramount approach for early detection of prostatic carcinoma. It is recommended that the positive serum tPSA candidates, whose serum tPSA value is > 4.0 ng/mL, should be subject to transrectal ultrasound-guided six-sextant prostate needle-biopsy [1]. Pathological studies on mass screening for prostate cancer demonstrated that in Japan the occurrence of well differentiated and poorly differentiated carcinomas is high [2]; whereas in the USA, moderately differentiated carcinomas are predominant [2, 3]. However, the pathological features of mass screening for prostate cancer in China have not yet been investigated.

The purpose of the present study was to investigate the pathological features of the 158 prostate biopsies through mass screening for prostate cancer in the Chinese population of Changchun and their association with serum PSA.

2 Materials and methods

2.1 Serum tPSA assay

From July 1999 to April 2002, a total of 19 808 Chinese men in Changchun who were > 50 years old were invited for screening. A total of 12 027 men agreed to participate with a refuge rate of 38.28 %. The serum tPSA level was determined using the Elisa assay kit (CanAGDiagnostics, Gothenburg, Sweden).

2.2 Biopsy and immunohistochemistry

Transrectal ultrasound-guided systematic six-sextant biopsies were performed on those whose serum tPSA value were >4.0 ng/mL and those who had obstructive symptoms despite their tPSA value. All specimens were routinely fixed in 10 % neutral buffered formalin and embedded in paraffin. Sections cut into 4 μm were deparaffinized in xylene, rehydrated in graded alcohols and stained with hematoxylin and eosin. Immunohistochemical staining of 16 cases of a typical small acinar proliferation was performed with the avidin-biotin-peroxidase complex method using the monoclonal antibodies against PSA and keratin34βE12 (Dakopatts, Hamburg, Germany).

2.3 Patho-morphological analysis

The Gleason grading system was used for grading prostatic adenocarcinomas; the latter were divided into five grades and nine scores (2–10) [4]. The prostatic adenocarcinomas were divided into three groups: 1) well-differentiated (Gleason scores in the range of 2–4), 2) moderately-differentiated (Gleason scores in the range of 5–7), and 3) poorly-differentiated (Gleason scores in the range of 8–10).

2.4 Prostate intraepithelial neoplasia

Prostate intraepithelial neoplasia (PIN) was divided into low-grade and high-grade. The high-grade PIN is characterized by the proliferation of highly atypical cells having more uniformly enlarged nuclei than low-grade PIN. Prominent nucleoli are present in many of the cells.

2.5 Statistical analysis

An analysis of frequencies, explore, crosstab and correlation was performed using SPSS software 10.0 (SPSS, Chicago, USA). The Correlation analysis was performed with the Pearson and Spearman method.

3 Results

In this study, 12 027 cases of mass screening for prostate cancer (by serum tPSA tests) were performed: 11 214 men whose serum tPSA values were < 4.0 ng/mL accounted for 93.2 % of the total and 813 men whose serum tPSA were > 4.0 ng/mL accounted for 6.8 %. One hundred and fifty-eight patients were subject to prostate biopsies according to the serum tPSA value and clinical manifestation. Of the 158 cases, 137 had a high serum tPSA level >4.0 ng/mL. Of the 137 patients, the serum tPSA value in 82 was 4–10 ng/mL, in 31 cases 10–20 ng/mL and in 24 cases > 20.0 ng/mL. Of the 12 027 men screened, there were 202 candidates who presented because of obstructive outlet symptoms and 21 patients (whose serum tPSA value was later found to be < 4.0 ng/mL) who were biopsied because they had an abnormal digital rectal examination.

There were 96 cases of benign prostate hyperplasia (BPH) (60.8 %, 96/158), 41 cases of prostate carcinoma (Pca) (25.9 %, 41/158), seven cases of PIN (4.4 %), six cases of atypical glands (3.8 %), two cases of suspicious cancer (Sca) (1.3 %) and six cases of granulomatous prostatitis (3.8 %). The diagnosis of atypical glands

and suspicious cancer was made according to the immunochemical staining.

The age and serum tPSA levels of the 12 027 participants and the 158 men who underwent biopsies are shown in Table 1. The detection rate of prostate cancer (Pca) in the different age ranges of the screening cohort of 12027 Chinese men is shown in Table 2. The two tables show that a significant linear positive correlation exists between the serum tPSA and ages ($r = 0.458$, $P < 0.01$) and between the detection rate of Pca and age ($r = 0.205$, $P < 0.05$).

In this study, Gleason grade 1 carcinoma was not observed. Gleason grade 2 carcinoma was seen in nine biopsy sections of the 158 cases. Gleason grade 3 carcinoma was seen in 30 sections, Gleason grade 4 carcinoma in 25 sections and Gleason grade 5 carcinoma in eight sections. The results from this study show that the distribution of patients was 4.9 %, 17.1 %, 22.0 %, 22.0 %, 17.1 %, 17.1 % and 0 % in Gleason scores 4, 5, 6, 7, 8, 9 and 10, respectively.

Special types of prostatic carcinoma were diagnosed, including one case of ductal carcinoma (endometrioid carcinoma) and three cases of signet ring cell carcinoma. Perineural infiltration and adenocarcinoma with glomeruliod structure were seen in three sections and one section, respectively.

There were five cases of low-grade PIN in the 158 prostate biopsies and two cases of high-grade PIN presented in the biopsies.

There were 16 cases that were diagnosed as atypical small acinar proliferations of uncertain significance (ASAPUS) in 158 biopsies [5]. It has been recognized that immunohistochemical staining against 34βE12 has been a useful approach to the discrimination between benign and malignant glands. In this study, the immunohistochemical staining result revealed eight cases of small acinar carcinoma due to the absence of the basal cell layer, two cases of suspicious cancer due to the disruption of the basal cell layers and six cases of atypical glands with normal basal cell layer.

As Figure 1 shows, the incidence of poorly-differentiated adenocarcinoma, and moderately-differentiated adenocarcinoma, was markedly higher than that of well-differentiated prostatic adenocarcinoma.

A correlation analysis between the serum tPSA and Gleason scores and positive counts of carcinoma in the

Table 1. Characteristics of age and serum tPSA in 12 027 men who underwent screening and 158 men who were subjected to biopsy. [c]$P < 0.01$ *vs.* prostate cancer (Pca).BPH: benign prostate hyperplasia; PIN: prostate intraepithelial neoplasia.

	Age(years)	tPSA(ng/mL)
12 027 men in mass screening	63.1 ± 9.2	1.8 ± 4.4
158 men who underwent biopsy	68.5 ± 7.8	13.5 ± 18.8
Pca ($n = 41$)	71.1 ± 7.6	29.3 ± 30.6
BPH ($n = 96$)	67.6 ± 7.1	7.1 ± 4.8[c]
PIN ($n = 7$)	70.7 ± 7.8	10.4 ± 3.3[c]
Granulomatous prostatitis ($n = 6$)	60.6 ± 9.0	10.5 ± 9.3[c]

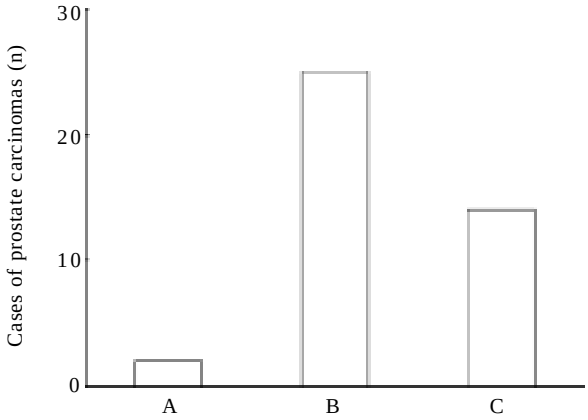

Figure 1. Incidence of the three types of differentiated prostatic adenocarcinomas in 41 cases. A: well-differentiated, B: moderately-differentiated, C: poorly-differentiated.

Table 2. Detection rate of prostate cancer(Pca) in different age groups in 12 027 Chinese men. [a]$R = 0.458$, $P < 0.01$ *vs.* ages; [b]$r = 0.205$, $P < 0.05$ *vs.* ages.

Age range (years)	tPSA (ng/mL)[a]	Biopsy (*n*)	Pca (*n*)	Detection rate of Pca (%)[b]
50–89 ($n = 12027$)	1.8 ± 4.4	58	41	25.9 (41/158)
50–59 ($n = 3958$)	1.1 ± 2.2	20	2	10.0 (2/20)
60–69 ($n = 4842$)	1.6 ± 4.1	60	13	21.7 (13/60)
70–79 ($n = 2932$)	2.4 ± 5.1	66	20	30.3 (20/66)
>80 ($n = 195$)	3.9 ± 8.8	12	6	50 (6/12)

41 cases of prostatic adenocarcinoma is shown in Figures 2 and 3. As Figure 2 shows, a significant linear positive correlation exists between the serum tPSA and the Gleason scores ($r = 0.312$, $P < 0.01$) and a significant linear positive correlation also exists between the serum tPSA value of the 41 cases of prostatic adenocarcinoma and the positive counts of carcinoma in sextant biopsies ($r = 0.406$, $P < 0.01$; Figure 3).

4 Discussion

The present study is the first in China to conduct a mass screening of more than 10 000 men for prostate cancer by testing the serum tPSA value of participants. The detection rate of prostate cancer is influenced by the number of biopsy cores available for study; as compared with the standard sextant biopsy method, increasing core numbers to 12–14 can enhance the detection rate significantly. Currently, however, sextant biopsy is still the standard biopsy technique for mass screening for prostate cancer. In the present study, 158 suspicious cases that had undergone transrectal ultrasound-guided systematic six-sextant biopsy were subject to pathological examination and patho-morphological analysis.

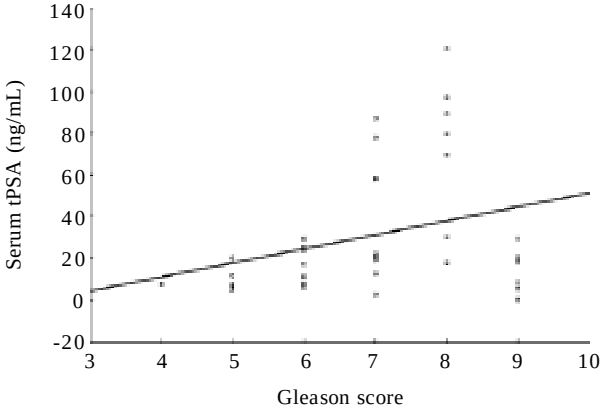

Figure 2. Correlation between serum tPSA levels and Gleason grading in 41 patients with prostatic carcinomas.

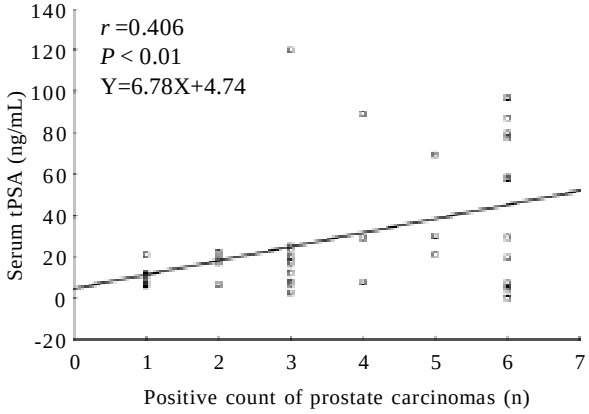

Figure 3. Correlation between Serum tPSA values and positive counts of sextant biopsies in 41 patients with prostatic carcinomas.

This study showed that the tPSA value was increased with age ($r = 0.458$, $P < 0.01$), and also showed that the detection rate of prostate cancer was increased with age ($r = 0.205$, $P < 0.05$). In addition, the serum tPSA value in cases of Pca was higher than that in BPH, PIN and prostatitis. Although our results showed that the mean age of Pca patients was older than that of BPH, PIN and prostatitis patients, this difference was not significant. We believe that this may attribute to the small numbers of biopsies.

In this study, 41 cases of prostatic adenocarcinoma were found in 158 prostatic biopsies. Our results have demonstrated that the moderately differentiated carcinoma is the most common type of prostate cancer accounting for 61.4 %, although the poorly differentiated carcinoma is also frequently found. This is somehow similar to the pathological features of prostate cancer in the American population characterized by the high incidence of moderately differentiated carcinoma [3]. However, Harada *et al.* reported that in Japan the occurrence of well-differentiated (Gleason 2–4 score) and poorly differentiated (Gleason 9–10 score) carcinoma are high [2]. Furthermore, in a cohort of Jamaican men, 60 % of Pca had a Gleason score of 8–10, which indicates that the poorly differentiated carcinoma is the most common type of prostate cancer [6].

The serum tPSA concentration is extremely important in detecting early prostate cancer. Catalona *et al.*[7] reported that the incidence of prostate cancer was 2.2 % in men whose tPSA level was greater than 4.0 ng/mL. The positive predictive value for a tPSA level between 4.1 ng/mL and 10.0 ng/mL was 22.4 %–26.5 % and for a tPSA level above 10.0 ng/mL was 50 %–67 % [7]. In this study, 41 prostatic carcinomas were found and account for 25.9 % of the biopsies. Two cases out of 21 (9.5 %) with a serum tPSA value <4.0 ng/mL had carcinoma detected and in the 81 biopsies where the serum tPSA value was at the range from 4.1 ng/mL to 10.0 ng/mL, 12 cases of prostatic carcinoma were diag-

nosed accounting for 14.8 % (12/81). In the 31 biopsies with a serum tPSA value of 10.1 ng/mL to 20.0 ng/mL, eight prostatic carcinomas were identified accounting for 29.0 % (8/31). Of the 24 biopsies with serum tPSA values above 20 ng/mL, 19 prostatic carcinoma were diagnosed, accounting for 79.0 % (19/24). Our results also reveal that detecting the rate of prostate cancer in biopsy increases with the elevation of serum tPSA levels ($r = 0.428$, $P < 0.001$). This is consistent with the findings of Catalona *et al.* [7].

Emerging evidence has demonstrated that the serum tPSA level is relevant to the Gleason's grading in prostate cancer. In the present study, a linear positive correlation between serum tPSA value and histological grading could be seen. Several studies have shown a direct relationship between serum tPSA levels and estimated prostatic volume [8], while the results from this study have shown that there is a significant linear positive correlation between the serum tPSA value and the positive counts of carcinoma in the sextant prostatic biopsies, thereby indicating an association between the positive counts of carcinoma and the volume of tumors.

In conclusion, this study was the first to conduct mass screening for prostate cancer and to investigate the pathological features of prostate cancer in a cohort of Chinese men. Our results reveal that the moderately differentiated carcinoma is the most common type of prostate cancer. This study also has shown that serum tPSA value is associated with the pathological grading.

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