Blackwell Publishing

Asian J Androl 2008; 10 (2): 325–331
DOI: 10.1111/j.1745-7262.2008.00345.x

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·*Clinical Experience*·

Individualized prostate biopsy strategy for Chinese patients with different prostate-specific antigen levels

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Abstract

Aim: To evaluate the best individualized prostate biopsy strategies for Chinese patients with suspected prostate cancer. **Methods:** The present study included 221 Chinese patients who underwent transrectal ultrasound guided prostate biopsies for the first time. All patients underwent the same 10-core biopsy protocol. In addition to the Hodge sextant technique, four more biopsies were obtained from the base and middle regions of bilateral peripheral zones. The differences between 10-core and sextant strategies in cancer detection among patients with different prostate specific anitgen (PSA) levels were evaluated. The relationship between PSA level, number of positive biopsy cores and organ-confined cancer rate in prostate cancer patients was also analyzed. **Results:** The overall prostate cancer detection rate was 40.7% in the 221 patients. The 10-core strategy increased cancer detection by 6.67% (6/90) in our patients ($P < 0.05$). The increased cancer detection rates decreased significantly when the patient PSA level increased from 0–20 ng/mL to 20.1–50 ng/mL and > 50 ng/mL ($P < 0.01$). The number of positive biopsy cores in prostate cancer patients increased significantly with increasing patient PSA level ($P < 0.01$). The rate of organ-confined prostate cancer decreased significantly with increasing patient PSA level ($P < 0.01$). **Conclusion:** The extended 10-core strategy is recommended for Chinese patients with PSA ≤ 20 ng/mL and the sextant strategy is recommended for those with PSA > 50 ng/mL. For patients with PSA ranging from 20.1 ng/mL to 50 ng/mL, the 10-core strategy should be applied in patients with life expectancy ≥ 10 years and the sextant strategy should be applied in those with life expectancy < 10 years. *(Asian J Androl 2008 Mar; 10: 325–331)*

Keywords: prostate; prostatic neoplasms; diagnosis; biopsy; Asian continental ancestry group

1 Introduction

Prostate cancer is one of the most common cancers in the world. The estimated number of cases worldwide was 513 000 in the year of 2000 [1]. However, the incidence rate of prostate cancer varies widely among countries and racial groups. The age-standardized incidence rate of prostate cancer was 173.8/100 100 in the USA in 2002 as compared with 7.7/100 000 in the city of Shanghai, China in 2000 [2, 3].

Because of the low incidence rate, extremely limited data regarding the diagnosis and treatment of pros-

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Received 2007-06-11 Accepted 2007-10-02

tate cancer in Chinese patients have been reported in English language articles.

Transrectal ultrasound (TRUS) guided prostate core needle biopsy has become the standard method for diagnosing prostate cancer in developed countries since Hodge *et al.* [4] proposed the systematic sextant biopsy protocol in 1989. Recently, the value of this sextant biopsy strategy was challenged by the extended prostate biopsy strategies, which can increase cancer detection rate by more than 30% [5]. Therefore, an increasing number of medical centers in the developed world have begun to apply extended biopsy strategies [5]. However, the equipment and techniques of TRUS-guided prostate biopsy were introduced into China less than a decade ago and very limited data or experience from Chinese patients in this field have been reported. In the present study, we investigated the efficiency of the TRUS-guided systematic 10-core biopsy strategy for Chinese patients who were suspected of having prostate cancer and who underwent biopsy for the first time. The purpose of the present study is to find out the best prostate biopsy strategy for Chinese patients.

2 Materials and methods

2.1 Patients

Between March 2005 and February 2007, 221 Chinese patients who underwent TRUS-guided prostate biopsies for the first time at our institution were included in this study. Indications for prostate biopsy were abnormal digital rectal examination (DRE) and/or serum prostate specific anitgen (PSA) level greater than 4.0 ng/mL. The DRE and PSA results of each patient were available before biopsy. 500 mg levofloxacin once daily and 400 mg metronidazole twice daily were administered to each patient orally 3 days before biopsy and another 3 days after biopsy. All patients received an enema 2 h before biopsy procedures. For patients who were diagnosed with prostate cancer, further investigations such as abdomen ultrasound, pelvic computed tomography scan and bone scintigraphy were performed to evaluate clinical stages and to determine therapeutic plans. All patients were interviewed through telephone 2 weeks after biopsy about the complications.

2.2 Biopsy technique

All patients were placed in the left lateral decubitus position with knees and hips flexed 90 degrees. All biopsies were performed with a Falcon 2101 EXL type transrectal ultrasound scanner, an 8808 5-10 MHz type probe and a UA 1257 type biopsy adaptor (B-K Medical, Herlev, Denmark). All patients were thoroughly examined by TRUS before biopsy procedures and prostate volumes were calculated by the ellipsoid prostate formula [6]. All lesions detected by TRUS were recorded in detail. An 18-gauge Bard Magnum core biopsy needle mounted on a spring loaded automatic biopsy gun (Bard, Covington, GA, USA) was used to obtain 22 mm long core samples.

All patients underwent the same 10-core biopsy protocol regardless of the ultrasound appearance of the prostate. In addition to the Hodge sextant technique [4], 4 more biopsies were obtained from the lateral peripheral zones by positioning the probe just medial to the lateral edge of the prostate at the base and middle regions bilaterally, as described by Ravery *et al.* [7] and Eskicorapci *et al.* [8].

2.3 Pathological evaluation

All 10 biopsy specimens were labeled according to the site and submitted separately in 10 formalin-filled containers to the Department of Pathology at our institution. The core from each container was embedded in a block individually and at least five sections were obtained from each block. The pathological diagnosis was given to each core and the individual Gleason score was given to each core containing prostate cancer. The atypical cases were further evaluated with immunohistochemical markers, such as AMACR, p63, 34βE12, PSA, PAP and so on. If only biopsies from the four lateral peripheral zones had been positive for cancer, we would have concluded that the conventional sextant protocol missed the diagnosis of prostate cancer.

2.4 Statistical analysis

SPSS 11.0 for Windows (SPSS, Chicago, IL, USA) was used for the statistical evaluation. Differences between the prostate cancer and non-prostate cancer patients were evaluated using the Mann-Whitney *U*-test for continuous variables, the χ^2-test and the Pearson χ^2-test for discontinuous variables. The McNemar test was used to compare the cancer detection rates between the 10-core and the sextant biopsy strategies. The Pearson χ^2-test was used to compare the improvements in cancer detection of the 10-core strategy in patients with different PSA levels. The Kruskal-Wallis *H*-test and the Pearson

χ^2-test were used for comparison of positive biopsy core number and organ-confined prostate cancer rate according to prostate cancer patient PSA level. A probability of less than 5% ($P < 0.05$) was considered statistically significant.

3 Results

The overall prostate cancer detection rate was 40.7% (90/221) in the whole study group. Table 1 shows clinical characteristics of the prostate cancer patients and the non-cancer patients. Median patient age, median PSA level, median PSA density (PSAD), abnormal DRE rate and abnormal TRUS rate were significantly higher in prostate cancer patients. The cancer detection rate increased significantly with increasing serum PSA level. The cancer detection rate also increased significantly with increasing patient age.

Table 2 lists clinical and pathological characteristics of our 90 prostate cancer patients. Of our prostate cancer patients, 76.7% (69/90) had lymph node or distant metastases at the time of diagnosis. Only 16.7% (15/90) of patients who had clinical stages ≤ T3N0M0 were treated by radical prostatectomy or radical radiotherapy. In this study, only 21.1% (19/90) prostate cancer patients had biopsy Gleason scores of less than 7 and there was no clinically insignificant cancer.

Table 3 shows that as compared with the sextant strategy, the 10-core strategy increased the cancer detection rate by 6.67% (6/90) in the whole group of patients. The improvement in cancer detection of the 10-core strategy decreased significantly with increasing patient serum PSA level. In patients whose PSA levels were greater than 50 ng/mL, the sextant biopsy strategy could detect the same number of cancers as the 10-core strategy did.

The median number of positive biopsy cores in prostate cancer patients increased significantly from 2 cores to 5 and 10 cores when the patient PSA level increased

Table 1. Patient characteristics according to biopsy outcome. *Mann-Whitney *U*-test. †χ^2-test. ‡Pearson χ^2-test . cc, cubic centimeter; PSA, prostate specific antigen.

	Positive biospy	Negative biopsy	*P* value	Overall
Number of patients (%)	90 (40.7)	131 (59.3)		221
Median age (range)	72 (48–91)	67 (44–85)	0.002*	69 (44–91)
Age range (%)				
< 60 years	18 (32.1)	38 (67.9)	0.013‡	56
61–70 years	21 (30.4)	48 (69.6)		69
71–80 years	40 (53.3)	35 (46.7)		75
> 80 years	11 (52.4)	10 (47.6)		21
Median PSA (ng/mL) (range)	74.2 (2.8–6006.2)	7.7 (0.8–77.3)	< 0.001*	13.5 (0.8–6006.2)
PSA range (ng/mL) (%)				
0–4	1 (3.7)	26 (96.3)	< 0.001‡	27
4.1–10	5 (6.9)	67 (93.1)		72
10.1–20	8 (22.2)	28 (77.8)		36
20.1–50	16 (69.6)	7 (30.4)		23
50.1–100	26 (89.7)	3 (10.3)		29
>100	34 (100)	0 (0)		34
Median prostate volume (mL) (range)	37.5 (20.5–111.0)	36.8 (16.5–131.5)	0.560*	37.1 (16.5–131.5)
PSA density	1.85 (0.23–142.33)	0.17 (0.06–1.62)	< 0.001*	0.33 (0.06–142.33)
Digital rectal examination (%)				
Abnormal	74 (57.8)	54 (42.2)	< 0.001†	128
Normal	16 (17.2)	77 (82.8)		93
Transrectal ultrasound (%)				
Abnormal	82 (53.6)	71 (46.4)	< 0.001†	153
Normal	8 (11.4)	62 (88.6)		70

from 0–20 ng/mL to 20.1–50 ng/mL and > 50 ng/mL (Table 4). However, the proportion of organ-confined prostate cancer decreased significantly from 64.3% to 12.5% and 0% when the prostate cancer patient's PSA level increased from 0–20 ng/mL to 20.1–50 ng/mL and > 50 ng/mL, respectively (Table 4).

Table 2. Clinical and pathological characteristics of prostate cancer patients.

	Number of patients (%)
Biopsy Gleason score	
2–4	2 (2.2)
5–6	17 (18.9)
7	37 (41.1)
8–10	34 (37.8)
Positive biopsy cores	
1	4 (4.4)
2–4	17 (18.9)
5–9	30 (33.3)
10	39 (43.3)
Mean	7.4
Median	9
Clinical stage	
T1cN0M0	4 (4.4)
T2N0M0	7 (7.8)
T3N0M0	4 (4.4)
T4N0M0	6 (6.7)
TxN1M0	4 (4.4)
TxNxM1	65 (72.2)
Treatment	
Radical prostatectomy	11 (12.2)
Radical radiotherapy	4 (4.4)
Hormonal therapy	69 (76.7)
Hormonal therapy + radiotherapy	6 (6.7)
Overall	90

There were only two (0.9%) major complications requiring hospitalization in our group: one delayed severe rectal bleeding and one confirmed systemic infection. The two patients recovered shortly after appropriate therapies. Other minor complications included hematuria in 55.2% (122/221), short-term rectal bleeding in 24.9% (55/221), urinary tract infection in 4.1% (9/221) and voiding difficulties in 1.8% (4/221) of patients. Patients with minor complications were treated as outpatients and recovered quickly.

4 Discussion

Although the TRUS-guided prostate biopsy is the gold standard for diagnosing prostate cancer, the best strategy for biopsy remains controversial [9]. An increasing number of studies from developed countries indicate that the traditional sextant biopsy strategy is insufficient for diagnosing prostate cancer as compared with the extended biopsy strategies, which detect probably 30% more cancers without increasing the number of clinically insignificant cancers [5, 8–10]. TRUS-guided prostate biopsy has not been wildly applied in China and other developing countries. Because of the different incidence rates of prostate cancer, different economic conditions and different cultural backgrounds, the experiences from the developed world in this field might not be terribly useful for Chinese patients and other developing countries.

Table 3. Comparison of cancer detection rate between sextant and 10-core biopsy strategy according to different patient characteristic. †χ^2-test; ‡Pearson χ^2-test; *McNemar's test. DRE, digital rectal examination.

	Cancer detection rates (%)		Improvement in cancer detection (%)	*P*-value
	Sextant	10-core		
PSA range (ng/mL)				
0–10	3/99 (3.0)	6/99 (6.1)	3/6 (50.0)	< 0.001‡
10.1–20	6/36 (16.7)	8/36 (22.2)	2/8 (25.0)	
20.1–50	15/23 (65.2)	16/23 (69.6)	1/16 (6.25)	
50.1–100	26/29 (89.7)	26/29 (89.7)	0 (0)	
> 100	34/34 (100)	34/34 (100)	0 (0)	
DRE result				
Normal	14/93 (15.1)	16/93 (17.2)	2/16 (12.5)	0.288†
Abnormal	70/128 (54.7)	74/128 (57.8)	4/74 (5.4)	
Overall	84/221 (38.5)	90/221 (40.7)	6/90 (6.67)	0.031*

Table 4. Comparison of positive biopsy core number and organ-confined prostate cancer rate according to prostate cancer patient PSA level. *Kruskal-Wallis *H*-test. ‡Pearson χ^2-test. †Organ-confined PCa = clinical stage T1-2N0M0 prostate cancer. PSA, prostate specific antigen.

Prostate cancer patient PSA level (ng/mL)	Positive biopsy core number of 10-core strategy				Organ-confined prostate cancer rate† (%)	*P*-value
	Range	Median	Mean	*P*-value		
0–20	1–6	2	2.8	< 0.001*	9/14 (64.3)	< 0.001‡
20.1–50	2–10	5	5.9		2/16 (12.5)	
> 50	4–10	10	8.7		0/60 (0)	
Overall	1–10	9	7.4		11/90 (12.2)	

Table 5. Individualized prostate biopsy strategy for Chinese patients with different PSA levels. PSA, prostate specific antigen.

PSA level (ng/mL)	Recommended biopsy strategy	Reason
0–20	10-core	1. To increase cancer detection by 35.7% over the sextant strategy. 2. 64.3% these PCa patients have organ-confined cancers and need the 10-core strategy to provide more information for guiding treatment.
20.1–50	10-core (patient life expectancy ≥ 10 years) Sextant (patient life expectancy < 10 years)	1. The 10-core strategy only increases cancer detection by 6.25% over the sextant strategy and only 12.5% these PCa patient have organ-confined cancers. 2. The 10-core strategy should be applied in those who can be treated with radical prostatectomy (young and in good health).
> 50	Sextant	1. To detect the same proportion of cancer cases as the extended 10-core strategy. 2. None of these PCa patients have organ-confined cancer and do not need the 10-core strategy to provide more information for guiding treatment. 3. To decrease the rate of some complications. 4. To decrease the pain and discomfort during biopsy. 5. To decrease the expense of tissue sampling.

As one of the largest cancer centers in China, our center is outfitted with TRUS equipment and we have performed TRUS-guided extended 10-core biopsy in 221 patients over the past 2 years. The overall cancer detection rate was 40.7% in our patients. This rate is higher than the data from some contemporary developed-world studies [5, 7–10]. The median patient age, median PSA level, median PSAD, abnormal DRE rate and abnormal TRUS rate were significantly higher in our cancer patients than in non-cancer patients, consistent with previous developed-world studies [7, 8, 10]. In our series, there were 63 (28.5%) patients whose PSA levels were greater than 50 ng/mL before biopsy and 95.2% (60/63) of these patients were diagnosed with prostate cancer. In developed-world studies, there are very few patients with PSA levels > 50 ng/mL before biopsy and some studies even only include patients with PSA levels of less than 10 ng/mL or 20 ng/mL [5]. This major difference explains the higher cancer detection rate in our Chinese patients whose prostate cancer incidence rate was extremely low. For the same reason, in our 90 cancer patients there were only 15 (16.7%) patients with clinical stages ≤ T3N0M0 and 69 (76.7%) of patients had regional lymph nodes or distant metastases at the time of diagnosis. In contrast, because of PSA screening programs, most prostate cancer patients in developed countries are diagnosed at early stages with low PSA levels [11]. In the USA, an estimated 91% of the new cases of prostate cancer are expected to be diagnosed at local or regional stages [2, 11]. In patients with PSA levels of 4–10 ng/mL, the cancer detection rate was only 6.9% in the present study, which is much lower than the

25%–35% cancer detection rate in previous developed-world studies [5, 7–10]. Another study also found cancer detection rates of Chinese patients with different PSA levels to be much lower than those in men from developed countries with the same PSA levels [12]. This phenomenon might be a result of different genetic factors, environmental conditions and lifestyles between men in China and men in developed countries [13].

In the whole group of our patients, the prostate cancer detection rates of the 10-core strategy and the sextant strategy were 40.7% and 38.5%, respectively. The 10-core strategy could only be detected in 6.67% (6/90) more cancers, which was markedly less than in some pervious developed-world studies [5, 7–10]. After classifying our patients according to different serum PSA levels, we found that the extended 10-core biopsy strategy increased cancer detection by 35.7% (5/14) over the sextant strategy in Chinese patients with PSA ≤ 20ng/mL. However, the improvement in cancer detection decreased to 6.25% (1/16) and 0% when patient PSA levels increased to 20.1–50 ng/mL and > 50 ng/mL (Table 3). Published developed-world studies investigating the diagnostic value of the extended prostate biopsy strategies seldom consider the effect of patient PSA level on cancer detection improvement [5, 7–10]. A recently published review article comparing cancer detection rates of different extended prostate biopsy strategies concludes that strategies with 12 cores detect 31% more cancers than the sextant strategy [5]. Nevertheless, some studies investigated by this review only included patients with PSA < 10 ng/mL, others only included patients with PSA < 20 ng/mL, and others included patients with the highest PSA level of 37.4–240 ng/mL [5]. Therefore, the relation between the patient PSA level and the cancer detection improvement of the extended biopsy strategies was not considered by the authors of the review. Because the proportion of patients with PSA > 20 ng/mL was very low in those developed-world studies, the overall cancer detection improvements of the extended strategies were still very high. However, this proportion in our Chinese patients was up to 38.9% (86/221) and it made the overall cancer detection improvement drop to 6.67%. Further investigations showed that the number of positive biopsy cores increased significantly with increasing PSA levels in cancer patients (Table 4). All of our Chinese prostate cancer patients with PSA levels > 50 ng/mL had at least four positive cores. In these patients, cancer tissues had invaded at least half of the prostate glands. This detailed data could explain why the sextant and the extended 10-core biopsy strategies detected the same proportion of cancer cases from our Chinese patients with their PSA > 50 ng/mL.

The aforementioned differences between our Chinese and developed-world patients at the time of biopsy must be considered in our clinical practice. For patients with high PSA and metastatic diseases, the prostate core needle biopsy can only establish the pathological diagnosis of prostate cancer. However, for patients with low PSA levels and localized diseases, the biopsy should not only establish the diagnosis but also provide more vital information for guiding treatment [14]. Previous studies demonstrate that compared with the sextant strategy, the extended strategies could increase the cancer detection rate and predict the Gleason score, the extraprostatic extension and the total tumor volume more accurately in organ-confined prostate cancer patients [15–17]. These advantages of the extended strategies are particularly important for those who can be treated with radical prostatectomy. For example, the cancer involvement of base biopsies might influence bladder neck sparing radical prostatectomy and extensive cancer in one lobe, which correlates with ipsilateral extraprostatic extension, and might influence nerve sparing radical prostatectomy [14]. According to our data, the proportion of organ-confined prostate cancer decreased significantly with increasing patient PSA levels (Table 4). Therefore, it is of no use to provide such information for cancer patients with PSA levles > 50 ng/mL.

As compared with the sextant strategy, the extended biopsy strategies increase the rate of some complications, the duration of pain and discomfort during biopsy procedures and the expense of tissue sampling and pathological diagnosis. Previous studies demonstrate that there is no statistically significantly difference between the rate of major complications of the extended strategies with 10–12 cores and that of the sextant strategy; however, the rate of minor complications, such as bleeding, was higher in the extended strategies [5, 18–20]. Our data also show that hematuria and rectal bleeding rates were not very low, although they were not higher than those in previous developed world studies [18–20]. Compared with the extended 10-core strategy, the sextant strategy reduces 40% of the expense of tissue sampling and pathological diagnosis. Because china is still a developing country, reducing costs is an important issue in our medical practice. By using the sextant strategy in Chinese

patients, we can obtain the aforementioned advantages without decreasing the cancer detection rate.

Table 5 shows the individualized prostate biopsy strategies we recommended for our Chinese patients who undergoing their first prostate biopsy. Because of the reasons listed in Table 5, the extended 10-core biopsy strategy is strongly recommended for Chinese patient with PSA levels ≤ 20 ng/mL and the conventional sextant strategy is strongly recommended for those with PSA levels > 50 ng/mL. For Chinese patient with PSA levels ranging from 20.1 ng/mL to 50 ng/mL, the extended 10-core strategy only increased cancer detection by 6.25% over the sextant strategy and only 12.5% or these prostate cancer patients had organ-confined cancers. Therefore, it is not necessary to use the extended 10-core strategy for every patient. We recommend that the 10-core strategy should be applied in patients with life expectancy longer than 10 years and the sextant strategy should be applied in those with life expectancy less than 10 years.

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Edited by Dr Gail S. Prins