A comparative study of prostate cancer detection and management in China and in France

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Objective: *To compare the detection and management of prostate cancer in one French and six Chinese urological institutions.*

Patients and methods: *All the patients subjected to prostate biopsy for suspected prostate cancer in six Chinese urological institutions and in the department of urology of the Cochin hospital, France, between January 2003 and December 2005 were included. The characteristics of patients and tumors, and the management of prostate cancer were then analyzed.*

Results: *In the Chinese institutions, 95.8% of patients undergoing prostate biopsy presented with urinary disorders. The rate of abnormal digital rectal examination (DRE) ranged from 29.2% to 45.1%. In the French institution, 72.7% of prostate biopsies were performed as a result of prostate cancer screening, and the rate of abnormal DRE was 16.8%. In the Chinese institutions, a total of 979 patients underwent prostate biopsy, with median PSA values varying between 10.2 ng/ml and 33 ng/ml among the institutions. Overall, 408 cases of prostate cancer were diagnosed, with median PSA values varying between 24.3 ng/dl and 174.9 ng/dl and 19.4% of tumors were clinically localized. In the French institution, 565 patients underwent prostate biopsy, with a median PSA value of 7.4 ng/ml and 251 cases of prostate cancer were diagnosed, with a median PSA value of 8.1 ng/ml and 80.9% of tumors were clinically localized. In the Chinese institutions, the majority of patients received surgical or medical castration. The rate of patients subjected to surgical castration varied between 24.2% and 100%. Radical prostatectomy (RP) was performed in only three Chinese hospitals, in which the percentage of patients treated with RP varied between 12.1% and 31.1%. In the French institution, RP was the most common treatment of prostate cancer (43.8% of patients).*

Conclusion: *In China, most patients subjected to prostate biopsy suffer from urinary symptoms and have elevated PSA levels. The lack of mass screening for prostate cancer results in a high rate of advanced tumors with nodal involvement and/or metastases. RP is rarely performed in Chinese hospitals, and castration represents the usual treatment of prostate cancer.*

Key Words: prostate cancer, biopsy, prostate specific antigen, detection, screening

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M. Peyromaure and K. Mao have made an equal contribution to this work.

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Introduction

Prostate cancer is less common in Asia than in Europe or in the United States.[1] Cook et al analyzed the incidence of prostate cancer among Chinese, Japanese and Filipino immigrants to the United States and among their descendants.[2] Among the Asian-Americans, the annual

rate per 100,000 for native Chinese (24.0), Japanese (29.6) and Filipino (56.8) men was approximately half that of United States-born Chinese, Japanese and Filipino men (44.4, 42.2 and 111.3, respectively). Among the United States residents, the annual incidence of prostate cancer for all generations of Asian-Americans was half that of white men born in the United States. It is likely, therefore, that Asian-American men retain some lifestyle and/or genetic factors that reduce their risk of prostate cancer.

Some recent reports indicate that the incidence of prostate cancer is increasing rapidly in China. The increase in prostate cancer incidence may be partly due to lifestyle changes, but also to the recent interest in cancer detection. Because screening for prostate cancer is not performed routinely in China, only few data are available regarding the characteristics and the management of this tumor. In a collaborative study between the Cochin hospital in Paris, France and six Chinese institutions, we reviewed all the prostate biopsies performed in these institutions over a 3 year period. We then compared the characteristics and the treatments of tumors between all the institutions involved.

Patients and methods

All the patients subjected to prostate biopsy for a suspicion of prostate cancer in six Chinese urological institutions and in the department of urology of the Cochin hospital, France between January 2003 and December 2005 were included. The Chinese institutions included five departments of urology of Shanghai hospitals (Shanghai-East, Chang Hai, First People's, Gongli and Bao Steel), and the department of urology of the First hospital affiliated to the Nanchang university, in the province of Jiangxi. All these institutions, except for Gongli hospital, are associated with a medical university.

The departmental head of each Chinese institution collected the patients' medical charts. Only the patients subjected to prostate biopsy for the first time were included. After inclusion, no patients were excluded from analysis. This study did not require institutional review board approval. The age of patients, clinical presentation (PSA screening or symptoms), digital rectal examination (DRE), prostate-specific antigen (PSA) values, Gleason score and clinical stage of tumors, and

TABLE 1. **Clinical presentation, results of clinical examination and PSA values of patients undergoing prostate biopsy in one French and six Chinese institutions**

Institution	N	Median (years)	Clinical presentation*	Suspicion of prostate cancer on DRE*	Median PSA (ng/ml)	Median free/total PSA ratio
Chang Hai	394	70	PSA screening: 13 (3.3) Urinary symptoms: 378 (95.9) Bone pain: 3 (0.8)	Yes: 134 (34) No: 157 (39.9) NA: 103 (26.1)	11.5	0.17
First People	322	74	Urinary symptoms: 304 (94.4) Bone pain: 9 (2.8) Surgery for BPH: 7 (2.2) Abdominal lymph nodes : 2 (0.6)	Yes: 94 (29.2) No: 209 (64.9) NA: 19 (5.9)	15.3	0.16
Nanchang	174	71	Urinary symptoms: 171 (98.3) Abdominal lymph nodes: 3 (1.7)	Yes: 55 (31.6) No: 119 (68.7)	13.6	0.13
Gongli	51	73	Urinary symptoms: 51 (100)	Yes: 23 (45.1) No: 28 (54.9)	33	0.09
Shanghai-East	19	68	Urinary symptoms: 16 (84.2) NA: 3 (15.8)	Yes: 8 (42.1) NA: 11 (57.9)	10.2	0.18
Bao Steel	19	69	Urinary symptoms: 18 (94.7) Abdominal lymph nodes: 1 (5.3)	Yes: 6 (31.6) No: 13 (68.4)	19.5	0.18
Cochin (France)	565	65	PSA screening: 411 (72.7) Urinary symptoms: 160 (28.3) Surgery for HBP: 6 (1.1) NA: 5 (0.9)	Yes: 95 (16.8) No: 426 (75.4) NA: 44 (7.8)	7.4	0.15

*Percentages in parentheses; BPH: benign prostatic hyperplasia; NA: not available; PSA: prostate-specific antigen

treatment of prostate cancer were recorded. The lifestyle characteristics of patients were not recorded.

Screening for prostate cancer is performed in only one Chinese institution (Chang Hai hospital). In the French institution, and in the Chang Hai hospital, a PSA determination and a DRE is recommended annually after the age of 50, and prostate biopsy is performed when PSA is higher than 4 ng/ml. We did not record the methods used for PSA determinations. Therefore, PSA tests might have varied significantly between all the institutions. In opposite, the technique of prostate biopsies was similar in all the institutions. Transrectal ultrasound-guided biopsies were performed in an outpatient basis, and the number of biopsy cores varied between 10 and 12.

After the medical charts had been collected, we compared the indications for prostate biopsy and the characteristics of the patients and of the tumors detected in each institution. The clinical stage of tumors was determined using the 2002 TNM classification. To compare the PSA values between patients with cancer and those without cancer, we performed the Student t-test using Statistical Analysis System, version 8.2 (SAS Institute Inc., Cary, NC, USA). Statistical significance was set at p value < 0.05.

Results

The clinical presentation, the results of DRE and the PSA values of patients undergoing prostate biopsy in each institution are listed in Table 1. In the Chang Hai hospital, where a screening for prostate cancer is recommended, 3.3% of the patients underwent prostate biopsy because of a PSA elevation detected by screening. In contrast, in the French institution, 72.7% of patients underwent prostate biopsy as a result of prostate cancer screening. In all the Chinese institutions, the majority of patients presented with urinary symptoms. Overall, 95.8% of patients from the Chinese institutions presented with urinary symptoms that led to the suspicion of prostate cancer.

In the Chinese institutions, the rate of abnormal DRE ranged from 29.2% to 45.1%, whereas it was 16.8% in the French institution. Moreover, the median PSA values

TABLE 2. **Comparison of patients with and without cancer on prostate biopsy**

Institution	N*	Median age (years)	Patients with abnormal DRE (%)	PSA values (ng/ml) Mean/median	Free/total PSA ratio Mean/median
Chang Hai					
Positive biopsies	119 (30.2)	72	84.9	48.9/25	0.18/0.14
Negative biopsies	275 (69.8)	69	12	11.2/8.9	0.19/0.8
First People					
Positive biopsies	164 (50.9)	75	49.4	81/24.3	0.18/0.15
Negative biopsies	158 (49.1)	73	8.2	13.9/13.7	0.23/0.21
Nanchang					
Positive biopsies	80 (46)	72	56.3	130/68	0.15/0.09
Negative biopsies	94 (54)	71	10.6	11.3/7.7	0.17/0.14
Gongli					
Positive biopsies	33 (64.7)	75	66.6	432/53.3	0.14/0.09
Negative biopsies	18 (35.3)	72.5	5.6	20/14	NA
Shanghai-East					
Positive biopsies	8 (42.1)	66	87.5	47/174.9	0.22/0.21
Negative biopsies	11 (57.9)	68	9.1	8.7/9.6	0.22/0.18
Bao Steel					
Positive biopsies	4 (21.1)	66.5	100	50/54	0.21/0.19
Negative biopsies	15 (78.9)	69	13.3	22/15	0.23/0.17
Cochin (France)					
Positive biopsies	251 (44.4)	67	31.5	27.2/8.1	0.15/0.12
Negative biopsies	314 (55.6)	63	5.1	8.5/7.1	0.18/0.16

*Percentages in parentheses; NA: not available

TABLE 3. **Characteristics and treatments of prostate cancer in each institution**

Institution	N	Clinical stage T*	Presence of metastases (N+ and/or M+)*	Gleason score*	Treatment*
Chang Hai	119	T1: 1 (0.8) T2: 63 (52.9) T3: 50 (42) T4: 5 (4.3)	No: 66 (55.4) Yes: 52 (43.7) NA: 1 (0.9)	< 6: 13 (10.9) 6: 29 (24.4) 7: 40 (33.6) > 7: 37 (3.1)	MC: 13 (10.9) SC: 60 (50.4) RP: 37 (31.1) MC + EBR: 7 (5.9) WW: 2 (1.7)
First People	164	T1: 14 (8.6) T2: 54(32.9) T3: 56 (34.1) T4: 19 (11.6) NA: 21 (12.8)	No: 25 (15.3) Yes: 83 (50.6) NA: 56 (34.1)	< 6: 17 (10.4) 6: 25 (15.2) 7: 23 (14) > 7: 11 (6.7) NA: 88 (53.7)	MC: 102(62.2) SC: 60 (36.6) MC + EBR: 1 (0.6) WW: 1 (0.6)
Nanchang	80	T2: 6 (7.5) T3: 30 (37.5) T4: 7 (8.8) NA: 37 (46.2)	No: 11 (13.8) Yes: 24 (30) NA: 45 (56.2)	NA	MC: 3 (3.7) SC: 67 (83.8) NA: 10 (12.5)
Gongli	33	T1: 10 (30.3) T2: 20 (60.6) T3: 3 (9.1)	No: 15 (45.4) Yes: 18 (54.6)	< 6: 8 (24.2) 6: 3 (9.1) 7: 13 (39.4) > 7: 9 (27.3)	SC: 8 (24.2) RP: 4 (12.1) SC + EBR: 18 (54.6) MC + EBR: 1 (3) WW: 2 (6.1)
Shanghai-East	8	T2: 2 (25) T4: 1 (12.5) NA: 5 (62.5)	Yes: 1 (12.5) NA: 7 (87.5)	< 6: 1 (12.5) 6: 1 (12.5) NA: 6 (75)	SC: 3 (37.5) RP: 1 (12.5) NA: 4 (50)
Bao Steel	4	T1: 3 (75) T2: 1 (0.25)	No: 1 (25) NA: 3 (75)	NA	SC: 4 (100)
Cochin (France)	251	T1: 128 (60) T2: 77 (30.7) T3: 37 (14.7) T4: 9 (3.6)	No: 154 (61.4) Yes: 19 (7.6) NA: 78 (31)	< 6: 9 (3.6) 6: 148 (59) 7: 75 (29.9) > 7: 19 (7.5)	MC: 43 (17.2) MC + EBR: 47 (18.7) EBR: 38 (15.1) RP: 110 (43.8) BT: 13 (5.2)

*Percentages in parentheses; NA: not available; MC: medical castration; SC: surgical castration; RP: radical prostatectomy; EBR: external beam radiation; WW: watchful waiting; BT: brachytherapy

were higher in the Chinese institutions: the median PSA value ranged from 10.2 ng/ml to 33 ng/ml, whereas it was 7.4 ng/ml in the French institution.

Table 2 compares the characteristics of patients with and without prostate cancer on biopsy for each institution. The rate of palpable tumors was higher in the Chinese institutions, ranging from 49.4% to 100%, whereas it was 31.5% in the French institution. Similarly, the median PSA values in patients with positive biopsies were higher in the Chinese institutions: the median PSA values varied from 24.3 ng/ml to 174.9 ng/ml, whereas the median value was 8.1 ng/ml in the French institution. In four Chinese institutions (Chang Hai, First People's hospital, Nanchang and Gongli), as well as in the French institution, the median PSA value was significantly higher in patients with positive biopsies than in those with negative biopsies ($p < 0.001$, $p = 0.005$, $p < 0.001$, $p < 0.001$ and $p = 0.024$, respectively). In the First People's hospital and in the French institution, the median free/total PSA ratio was significantly lower in patients with positive biopsies than in those with negative biopsies ($p = 0.005$ and $p = 0.001$, respectively).

Table 3 lists the characteristics and the treatments of tumors in each institution. In the Chinese institutions, the incidence of extracapsular clinical stage varied

markedly among different institutions. The highest reported incidence of clinically extracapsular tumors was in the department of urology of Chang Hai hospital, where 46.3% of tumors were classified as T3/T4. In the Chinese institutions, the incidence of metastatic tumors varied between 12.5% and 54.6%, whereas it was 7.6% in the French institution.

In the Chinese institutions, the most common treatment was androgen deprivation. The percentage of patients treated with medical castration alone varied between 3.7% and 62.2%, and that of patients subjected to surgical castration varied between 24.2% and 100%. Radical prostatectomy was performed in only three Chinese hospitals, in which the percentages of patients treated with radical prostatectomy were 12.1%, 12.5% and 31.1%, respectively. In contrast, in the Cochin hospital, radical prostatectomy was the most common treatment of prostate cancer (43.8% of patients), and hormone therapy alone was relatively unusual (17.2% of patients).

Discussion

The current study compared the results of prostate biopsies in 979 patients from six Chinese institutions and 565 patients from one European institution. It is noteworthy that, in the Chinese institutions, the vast majority of patients presented with urinary symptoms. Only the Chang Hai hospital performed screening for prostate cancer. However, in this hospital only 3.3% of the patients underwent prostate biopsy as a result of prostate cancer screening. In contrast, in the French hospital, 72.7% of patients underwent prostate biopsies due to prostate cancer screening. As the PSA cutoff was the same for both hospitals, more biopsies should have been performed in Chang Hai. It is likely that Chinese patients are often reluctant to undergo prostate biopsy. The influence of culture may partly explain the differences that we observed between both countries.

Our study has shown that the management of prostate cancer differed significantly between Chinese institutions. The number of patients undergoing prostate biopsy during a 3 year period ranged from 19 to 394. In the Shanghai-East and Bao Steel hospitals, only eight and four patients were diagnosed as having prostate cancer, respectively. In each of these institutions, abdominal CT scan and bone scintigraphy were performed in only one patient with prostate cancer. Therefore, only scant data were available regarding the tumor stage. In the Shanghai-East hospital, the Gleason score was not available for 75% of patients. Treatment consisted of surgical castration in 37.5% of patients, but therapeutic data were not available in 50% of cases. In the Bao Steel hospital, the Gleason score was not determined in any patient, and treatment consisted of surgical castration in all cases. These findings suggest that there are wide variations between Chinese institutions regarding the management of prostate cancer. One explanation is that the interest in this tumor has arisen only recently in China.

Surgical or medical castration represents the most common option for patients with prostate cancer in China. In our current study, the percentage of patients treated with medical castration varied between 3.7% and 62.2%, and that of patients subjected to surgical castration varied between 24.2% and 100%. RP was performed in only three hospitals, in which the percentages of patients treated with radical prostatectomy varied between 12.1% and 31.1%. This may be due to the high rate of advanced tumors, and to the lack of experience with that surgical procedure. In contrast, in the Cochin hospital, RP was performed in 43.8% of patients diagnosed with prostate cancer, and hormone therapy was proposed only to 17.2%.

The major limitation of our study is the lack of homogeneity among different Chinese institutions. Five hospitals in Shanghai and one hospital in the Jiangxi province participated in our study. A medical and university collaboration between the Cochin hospital of Paris and these six Chinese institutions has been developed since 2002. This is the reason why only these hospitals were represented. The data regarding the Chinese patients included in our study were heterogeneous. Moreover, the PSA tests varied among hospitals. Our study may not, therefore, be representative of all Chinese institutions. These differences could affect interpretation of the general characteristics of prostate cancer in China. On the other hand, as only few data are available regarding prostate cancer in China, our present study may provide new information regarding the management of this tumor in that country.

Some recent reports have shown an increasing incidence of prostate cancer in Asia.[3,4] Sim and Cheng reviewed the registered cases of prostate cancer in several Asian countries between 1978 and 1997, and found that the incidence of prostate cancer had risen by 5%-118%.[3] In another study, Zhang et al reviewed the cases of urological cancer registered between 1973 and 1999 in Shanghai.[4] These authors found that the incidence of tumors of prostate, bladder and kidney had risen substantially, with annual changes of 6.6%, 1.1% and 5.3%, respectively. The increase in prostate cancer incidence could be due to lifestyle changes, but also to the recent interest in prostate cancer detection.

In China, the high rate of advanced prostate cancer is probably due to the lack of mass screening. Our team has previously analyzed a series of 431 patients treated for prostate cancer in six Chinese institutions.[5] At least 10.2% of patients had metastases to lymph nodes, and 26% had bone metastases at diagnosis. Several studies dealing with prostate cancer screening in China have been published recently. The most important is that of Zhang et al, who analyzed the results of PSA screening in 12027 men over 50 years old from Changchun.[6] In this study, prostate biopsies were performed in 273 patients with a PSA level > 4 ng/ml. Of these men, 69 (25.3%) were found to have prostate cancer. The overall cancer detection rate was 0.57%, and the rate of clinically localized tumors was 57.9%. This study therefore confirmed that mass screening for prostate cancer in China could allow the detection of early stage tumors. In another study, Kuwahara et al compared the results of mass screening for prostate cancer in 3566 Chinese men and 2212 Japanese men older than 55.[7] The PSA positive rates (PSA > 4 ng/ml) and the cancer detection rates in the Chinese and Japanese men were 5.2% and 8.5%, and 0.8% and 2.1%, respectively.

In Western countries, prostate cancer is the most common malignant tumor in men over the age of 50 years, and it represents the second cause of death from cancer after lung cancer. Prostate cancer screening represents, therefore, a priority. Since the PSA era, a migration toward early stage has been observed.[8] In our current study, the characteristics of tumors detected in the Cohin hospital were in accordance with recent European reports.[9] The patients with prostate cancer had a median PSA value of 8.1 ng/ml, and 80.9% of tumors were clinically localized.

The screening for prostate cancer is based on serum PSA determination. In China, screening for prostate cancer would raise the question of which PSA cutoff could allow an optimal detection rate. In a recent study, 1096 healthy Chinese men underwent serum PSA determination.[10] The median serum PSA value was 0.82 ng/ml for men 50-59 years old, 0.93 ng/ml for men 60-69 years old and 1.17 ng/ml for men aged 70 years or over. The median PSA values for Chinese men after the age of 50 were significantly lower than those for other races—even those for other Asian men. To our knowledge, the role of free/total PSA ratio in the Chinese population has not been clarified. In a meta-analysis, Wang et al evaluated the diagnostic performance of PSA tests for the diagnosis of prostate cancer among Chinese.[11] These authors suggested that the use of free/total PSA ratio < 0.15 as threshold had a good accuracy for prostate cancer detection.

In conclusion, the current study confirms that the majority of patients subjected to prostate biopsy in China suffers from urinary symptoms and have elevated PSA levels. The lack of mass screening for prostate cancer results in a high rate of metastatic tumors. In the near future, the increasing interest in PSA screening will probably give rise to a greater proportion of localized tumors, and will improve the outcome of patients. □

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