DETECTION RATE OF PROSTATE CANCER ON BIOPSY ACCORDING TO SERUM PROSTATE-SPECIFIC ANTIGEN IN KOREAN MEN: A MULTICENTER STUDY

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ABSTRACT

OBJECTIVES. To evaluate the detection rate of prostate cancer on biopsy according to the serum prostate-specific antigen (PSA) level in Korean men and compare the detection rate with those of Japanese and American men in other studies.

METHODS. We retrospectively analyzed 2422 Korean men who had undergone prostate biopsy at 12 medical centers from 1993 to 2002. In the case of a PSA level greater than 4.0 ng/mL or abnormal digital rectal examination findings, prostate biopsy was performed.

RESULTS. Of the 2422 men, 962 (39.7%) were diagnosed with prostate cancer. With PSA levels between 4.0 and 10.0 ng/mL, the detection rate of prostate cancer was 15.9%. This rate was similar to that of Japanese men (15.8%), but lower than that of American men (25%). In the cases with a PSA level greater than 10.0 ng/mL, the detection rate for Korean and Japanese men was 59.5%, and was also lower than the 67% rate for American men. When serum PSA levels were divided into five subgroups (less than 4.0, 4.0 to 10.0, 10.0 to 20.0, 20.0 to 100.0, and greater than 100.0 ng/mL), the detection rate of prostate cancer was 12.4%, 15.9%, 34.1%, 66.2%, and 93.8%, respectively.

CONCLUSIONS. In Korean men, the detection rate of prostate cancer on biopsy according to serum PSA level appears to be comparable to that for Japanese men and lower than that for American men.


The introduction of prostate-specific antigen (PSA) in 1986 has resulted in a dramatic worldwide increase in the reported incidence of prostate cancer. In particular, PSA determination has resulted in the earlier diagnosis of nonpalpable, clinically localized (Stage T1c) disease.1–4

After Myrtle and Ivor5 established a reference range of 0 to 4 ng/mL to define the normal serum PSA level, Catalona et al.6 confirmed the PSA cutoff of 4 ng/mL as a threshold for performing prostate biopsies. Since this observation, subranges of serum PSA levels have been used to help counsel men with regard to the detection rate of cancer on biopsy. This is the basic information used by patients and clinicians to determine the necessity of prostate biopsy. In the United States, where the incidence of prostate cancer is quite high, such studies of a large number of patients have already been reported.2,6 However, the incidence of prostate cancer varies widely according to country and race. The incidence of prostate cancer in white American men is 101 in 100,000, but in Japanese men who are similar in race to Korean men, it has been reported to be only 9 in 100,000.7

This study was a multicenter study that evaluated the detection rate of prostate cancer at biopsy in Korean men according to the serum PSA level.
We compared our results with those of studies of Japanese and American men.

MATERIAL AND METHODS

PATIENTS

This study was performed on 2467 men who underwent prostate biopsy at 12 hospitals from 1993 to 2002. Of the results, 42 men who had findings that were not informative or inadequate for interpretation and 3 men diagnosed with mucinous carcinoma of unknown primary origin were excluded, leaving a total of 2422 biopsy results. These results were analyzed retrospectively. Biopsy was performed for clinically suspicious prostate cancer, a serum PSA level that was greater than 4.0 ng/mL, or abnormal digital rectal examination (DRE) findings. The number of asymptomatic patients screened for prostate cancer was 339 (14.0%), and the number of symptomatic patients was 2083 (86.0%).

BIOPSY METHOD

The serum PSA levels were measured using three different assays: Abbott AxSYM, Abbott Architect i2000 (Abbott Laboratories, Abbott Park, Ill), or Elecsys 2010 (Roche Diagnostics, Mannheim, Germany). Patients were placed in the lateral supine position, and transrectal ultrasound-guided needle biopsy was performed. A spring-fired biopsy instrument attached to an 18-gauge needle was used. Transverse and longitudinal section images were obtained. The prostate volume was calculated by applying the prolate ellipsoid formula (prostate size = 0.5233 × length × width × anteroposterior length). The number of patients who underwent 6, 8, 10, and 12-core biopsy was 1869 (77.2%), 210 (8.6%), 303 (12.5%), and 40 (1.7%), respectively. The mean number of cores was 6.8 (range 6 to 12).

STATISTICAL ANALYSIS

The detection rates of cancer on biopsy according to the subgroups of total PSA were obtained. Statistical analysis was performed by applying the independent t test and Pearson’s chi-square test. P < 0.05 was considered statistically significant. The statistical program, Statistical Package for Social Sciences, version 11.0, for Windows, was used.

RESULTS

The mean age of the study population was 69.7 years (range 38 to 91). Of the 2422 men enrolled in this study, 962 (39.7%) were diagnosed with prostate cancer histologically. Of the 1460 men who were found not to have prostate cancer, the histological diagnosis was normal prostatic tissue in 813 (55.7%) and benign disease, such as benign prostatic hyperplasia or inflammation, in 589 (40.3%). The remaining diagnoses were atypical small acinar proliferation in 26 men (1.8%), prostatic intraepithelial neoplasia (PIN) in 14 (1.0%), and prostatic tuberculosis, transitional cell carcinoma, lymphoma, or sarcoma in 5 men each (0.3%).

The median serum PSA value was 37.7 ng/mL (range 0.4 to 10,900) in the prostate cancer group and 8.3 ng/mL (range 0.1 to 178) in the non-prostate cancer group (P < 0.001). No significant difference in patient age, prostate size, or number of biopsy cores was observed between the two groups (Table I).

When the serum PSA levels were divided into less than 4.0, 4.0 to 10.0, 10 to 20, 20 to 100, and greater than 100.0 ng/mL, the cancer detection rate was 12.4%, 15.9%, 34.1%, 66.2%, and 93.8%, respectively (Table II). No significant difference in the detection rate was found according to the number of biopsy cores in all subgroups.

The detection rate of the asymptomatic patients undergoing screening for prostate cancer and those who presented with symptomatic disease was 19.5% and 43.0%, respectively (P < 0.01). The stratification of clinical T stage is summarized in Table III. The corresponding percentages of poorly differentiated cancer (Gleason score 8 to 10) in each subgroup were 17.0%, 32.6%, 56.7%, and 73.4%, and was significantly greater as the PSA level increased.
The sensitivity, specificity, positive predictive value, and negative predictive value of serum PSA to detect cancer was 97.5%, 11.6%, 42.1%, and 87.6%, respectively, when the cutoff value was 4.0 ng/mL.

**COMMENT**

The incidence of prostate cancer is increasing in Korea. However, compared with Western countries, the incidence has not been as consistent as in Japan. The detection rate of prostate cancer according to serum PSA level is supposed to be different in Korean men, but it is not well known.

In this study, the detection rate of prostate cancer in patients with a PSA value between 4 and 10 ng/mL was 15.9%, similar to the 15.8% rate in Japanese men reported by Egawa et al., but lower than the 25% rate in American men reported by Gretzner and Partin.9 (The selection criteria of prostate biopsy for the three studies were the same.) In the men with a PSA level greater than 10 ng/mL, the detection rate of prostate cancer in Korean and Japanese men was 59.5%, also lower than the 67% in American men. By the detection rate of prostate cancer on biopsy, it can be postulated that Korean and Japanese men are similar ethnically. In another study on Korean men, Kim et al.10 showed that the cancer detection rate for PSA subgroups of 4 or more to less than 10 ng/mL and 10 or more to less than 20 ng/mL was 13.8% and 21.2%, respectively. In the latter group, the detection rate in the study by Kim et al. was significantly lower than that of our study (34.1%; \( P = 0.036 \)). Also, the study population was quite smaller than ours. Therefore, we assume that our data would represent the detection rate of prostate cancer on biopsy according to the serum PSA value in Korean men.

From the mid-1990s to the early 2000s, the diagnosis of prostate cancer by serum PSA determination has been actively performed in Korea, similar to the policies in Western countries. The 2002 survey by the Korean National Cancer Institute stated that the incidence registration rate of prostate cancer was 3.0% of all cancer occurring in men, and was sixth in prevalence. During 1999 to 2001, the incidence of prostate cancer in Korean men was calculated to be 7.12 in 100,000, lower than the 9 in 100,000 for Japanese men and much lower than the 101 in 100,000 for American men. The mortality rate of prostate cancer was 2.4 in 100,000. However, in the same survey, prostate cancer was reported to be the most rapidly increasing cancer (21%) in the past 10 years.

No official guideline is available for prostate cancer screening in Korea because of its low incidence. Therefore, in this study, the screened population was relatively small (14%). The others (86%) were men who visited the urologic department because of voiding symptoms, hematuria, or some other problem. As a result, the proportion of advanced disease seemed very high compared with that in Western countries. Practically, more than 30% of men in our study had a PSA level of more than 20 ng/mL.

The total number of laboratories performing PSA testing was 11, and three different assays were used in this study. Therefore, some variation in the PSA value might have occurred. The coefficient of variation for the Abbott AxSYM, Abbott Architect i2000, and Elecsys 2010 has been reported as 11.24%, 5.36%, and 9.65%, respectively. However, the coefficient of variation of PSA in each laboratory was about 10%, similar to the coefficient of variation for one assay.

The data in this study were analyzed regardless of the DRE findings. As is widely known, the most effective method to increase the detection rate of prostate biopsy is to consider the DRE findings and serum PSA level concomitantly. However, the DRE is a subjective test dependent on the examiner, and, in this study, it was performed by about 200 clinicians who were faculty or residents majoring in urology during the 10-year study period. Nonetheless, in the PSA range of 4 or more to less than 10 ng/mL and 10 or more to less than 20 ng/mL, significant differences in the detection rate were found according to the DRE findings \( P < 0.001 \), Table IV). In our study, all patients with a PSA level less than 4 ng/mL had abnormal DRE findings. Of these 194 men, 24 (12.4%) were diagnosed with prostate cancer. In the study by Egawa et al.,8 the rate was 14.7% and in other studies of Western men, the rate was reported as 10% to 21%.6,13–15 We believed that a study to elucidate the correlation between the detection rate of cancer and DRE findings in subjects with a serum PSA level less than 4 ng/mL was important to establish the criteria for prostate biopsy.

Although atypical small acinar proliferation and PIN may be diagnosed as prostate cancer by repeat

**TABLE IV. Incidence of abnormal DRE findings and cancer detection rate according to DRE**

<table>
<thead>
<tr>
<th>PSA (ng/mL)</th>
<th>Negative DREs</th>
<th>Positive DREs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence (%)</td>
<td>Detection Rate (%)</td>
</tr>
<tr>
<td>4–10*</td>
<td>66.8</td>
<td>11.8</td>
</tr>
<tr>
<td>10–20*</td>
<td>33.0</td>
<td>16.8</td>
</tr>
<tr>
<td>20–100</td>
<td>11.1</td>
<td>64.9</td>
</tr>
<tr>
<td>≥100</td>
<td>5.2</td>
<td>90.1</td>
</tr>
</tbody>
</table>

*Key: DRE = digital rectal examination. \( P < 0.001; \) chi-square test.
biopsy, we classified these in the non-cancer group because our study was only on the findings from the first biopsy. In Western countries, the incidence of high-grade PIN on prostate biopsy specimens has been reported as an average of 6% (range 1.5% to 16.5%). In our study, the rate was 0.58%. We do not know the exact reason. However, we have postulated that the incidence of high-grade PIN would be much lower, associated with the lower incidence of prostate cancer in Korea. The other possible factor is that the uropathologists in Korea could not detect high-grade PIN as well as Western pathologists.

Other shortcomings of this study were that the number of biopsy cores was not standardized, and the biopsies were not performed by one investigator. This is a problem of retrospective, multicenter studies, such as ours. However, the mean number of biopsy cores in our study was 6.8, in accordance with the systematic six-core biopsy. Also, even if the biopsy result may be different, dependent on the investigator, because the prostate biopsy is performed randomly, such an effect may be relatively smaller than that with a targeted biopsy. This must be overcome in a future prospective study.

CONCLUSIONS

In Korean men, the detection rate of prostate cancer on biopsy according to serum PSA level appears to be comparable to that of Japanese men and lower than that of American men.

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REFERENCES