Progression of Prostatic Cancer in Relation to Age in Patients Detected by Mass Screening Program

HIROKI WATANABE, MUNEKADO KOJIMA and SHUICHI NAKAGAWA

Department of Urology, Kyoto Prefectural University of Medicine, Kyoto 602–0841

WATANABE, H., KOJIMA, M. and NAKAGAWA, S. Progression of Prostatic Cancer in Relation to Age in Patients Detected by Mass Screening Program. Tohoku J. Exp. Med., 1998, 184 (1), 61–65 —— With the aim of revealing the natural history of prostatic cancer, the distribution of age was examined in relation to disease progression in patients detected by mass screening programs. Between 1975 and 1996, such programs detected a total number of 132 patients with prostatic cancer. The mean ages of patients with Stage B, Stage C and Stage D disease were 71.2, 73.8 and 75.3 years, respectively. This might suggest that the difference of 3 years in mean age between Stage B and Stage C disease reflects the time interval of the progression of prostatic cancer from the early (Stage B) to the advanced (Stage C) stage. These results coincided well with the natural history of prostatic cancer, which we proposed previously based upon the “size of ranking” analysis of latent prostatic cancer and doubling time obtained from ultrasonic measurement of prostatic volume. An epidemiological study of prostatic cancer detected by mass screening would offer data of value for the elucidation of the natural history of that disease. ——— prostate; neoplasm; natural history; mass screening © 1998 Tohoku University Medical Press

The natural history of prostatic cancer forms the background for both the diagnostic and the therapeutic approaches to the disease. Recently, through the comprehensive analyses of data obtained by mass screening programs for prostatic cancer, we noticed results of interest concerning the progression of the disease in relation to age. The present study describes these results and follows with a discussion on the possible use of this approach for the investigation of the natural history of prostatic cancer.

MATERIALS AND METHODS

Over the years, we have conducted two mass screening programs for prostatic...
cancer. The first program (Program A), based upon transrectal sonography (TRS), was performed between 1975 and 1996 on a total of 18,369 men aged 55 years or more in community based populations in Japan (Watanabe et al. 1977, 1984). This program detected 104 cases of prostatic cancer, which corresponded to 0.6% of examinees (Nakagawa et al. 1997). Their ages ranged from 55 to 89 years, with a mean of 72.2 years.

In 1995, a new mass screening program for prostatic cancer (Program B) was carried out in an urban area of Kyoto in combination with the annual health checkup organized by the government (Nakagawa et al. 1997). This program employed the prostate-specific antigen (PSA) assay of dried blood samples on a filter paper (Watanabe et al. 1995) as a simple screening test, detecting 28 cases (1.2%) of prostatic cancer among 2,387 men over 55 years of age. Their ages ranged from 65 to 87 years, with a mean of 74.9 years. In the total number of 132 cases of prostatic cancer detected by either Program A or Program B, the mean age was 72.8 years (range: 55–89 years). None of these cases had had previous treatment for prostatic cancer.

In both programs, definitive diagnosis of prostatic cancer was confirmed by needle biopsy of the prostate. Clinical stage was determined by digital rectal examination, TRS and imaging modalities such as computed tomography and bone scintigraphy according to the staging system used by the Japanese Urological Association and the Japanese Society of Pathology (1992).

Results

The mean ages of prostatic cancer cases detected by Programs A and B are detailed in Table 1. In both programs, almost half of the cases (47% in Program A and 61% in Program B) belonged to the early stage (Stage B). Interestingly, the mean age increased as the clinical stage advanced. There was a difference of nearly 3 years in mean age (2.9 years in Program A and 3.0 years in Program B) between cases of Stage B and Stage C disease. This was also the case when all 132 cases were analyzed together. The mean age of cases of Stage C disease was 2.6 years older than that of Stage B disease. The difference in mean age between cases of Stage C and Stage D prostatic cancer was not remarkable, being 1.2 years

<table>
<thead>
<tr>
<th>Stage</th>
<th>Program A</th>
<th>Program B</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>70.5±6.3(n = 49)</td>
<td>73.4±7.6(n = 17)</td>
<td>71.2±6.7(n = 66)</td>
</tr>
<tr>
<td>C</td>
<td>73.4±8.6(n = 35)</td>
<td>76.4±4.4(n = 5)</td>
<td>73.8±8.2(n = 40)</td>
</tr>
<tr>
<td>D</td>
<td>74.6±7.1(n = 20)*</td>
<td>77.7±4.8(n = 6)</td>
<td>75.3±6.7(n = 26)*</td>
</tr>
<tr>
<td>Total</td>
<td>72.2±7.4(n = 104)</td>
<td>74.9±6.7(n = 28)</td>
<td>72.8±7.3(n = 132)</td>
</tr>
</tbody>
</table>

*p < 0.05 vs. Stage B
in Program A and 1.3 years in Program B.

**Discussion**

Despite its great importance in the investigation of prostatic cancer, the natural history of the disease still remains unknown. In particular, a better understanding of its natural history would make a great contribution to the development of effective early detection or screening programs for the disease (Watanabe 1987).

The full configuration of the natural history of neoplastic diseases is extremely difficult due to the lack of methodologies for accurately monitoring the growth of neoplasms and the considerable variance in disease progression between individuals. In this situation, however, an epidemiological study on neoplasms detected by mass screening might offer important information for the elucidation of the natural history, because they are screened randomly from community-based populations.

As for cervical cancer, Noda (1979) compared the mean ages of cases of cervical neoplastic lesions at different stages detected by mass screening. For cases with severe dysplasia, carcinoma in situ and microinvasive cancer mean ages were 40.2, 43.8 and 45.7 years, respectively. The mean age of invasive cancer (Stages Ib and II) patients was 48.7 years. The author proposed that cervical neoplastic lesions would progress from severe dysplasia to invasive cancer in a 3 to 4 year period. These results were of particular interest and prompted us to carry out the same kind of epidemiological study on prostatic cancer detected by our mass screening programs.

As early as 1975, we first began mass screening for prostatic cancer using TRS (Watanabe et al. 1977), and to date a great deal of evidence has accumulated in support of the usefulness of such a program (Watanabe 1996). All 132 cases of prostatic cancer used in this study were detected by our mass screening programs. Among them, 104 cases were detected by mass screening program using TRS as a screening test (Program A), and 28 by the program using PSA (Program B). Comparing these two screening programs, there were differences in several points such as time period, location and screening test. Among them, the most remarkable was the difference in the detection rate of prostatic cancer (0.6% in Program A vs. 1.2% in Program B), which could be due to the improved sensitivity of PSA to prostatic cancer (Kojima and Babaian 1995).

Although the reason was unknown, the mean age of cases in Program B was higher than those in Program B (74.9 vs. 72.2 years). More importantly, there was nearly a 3 year interval between early (Stage B) and advanced (Stage C) prostatic cancer in both Program A and Program B. Supposing that these cases were detected completely at random and all the cancer lesions increased on the same time scale, these results could indicate that prostatic cancer progresses from early (Stage B, organ confined) to advanced (Stage C, extraprostatic extension) disease.
over a 3 year period.

Surprisingly enough, this result coincided well with the model of the natural history of prostatic cancer, which was proposed by Watanabe (1989a)(Fig. 1), based principally upon the “size of ranking” analysis of latent cancer in Japanese (Yatani et al. 1986). In constructing the model, it was supposed that all cancer lesions progressed on the same time scale according to Collin’s model (Collins et al. 1956). Additionally, the significant positive relationship between tumor size and disease progression proposed by McNeal et al. (1986) was taken into consideration. In this model, the doubling time of clinically manifest cancer was set at 1 year, based upon the results obtained from the sequential measurement of prostatic volume using TRS (Watanabe et al. 1974), which indicated doubling time to be almost 1 year (Watanabe 1989b). According to this model, a clinically detectable prostatic cancer lesion 1 cm in diameter is likely to progress to an advanced one 2 cm in diameter with extraprostatic extension and/or metastases over 3 year period.

Along with the prevalent use of PSA, screening for prostatic cancer is becoming widespread. Epidemiological studies on prostatic cancer detected in this way as reported here might be promising for the investigation of the natural history. It is hoped that more researchers carry out such studies on different cohorts of subjects.

References

2) Japanese Urological Association and the Japanese Society of Pathology (1992)


