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Clinical Features of Familial or Hereditary Prostate Cancer in Korean Men: A Pilot Study

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Purpose: There are few data regarding the epidemiology of hereditary or familial prostate cancer (PCa) in East Asians, especially in Korean men. Therefore, we evaluated the incidence of familial and hereditary PCa and the relation between socioeconomic status and the incidence of nonsporadic prostate cancer (NSPC).

Materials and Methods: We collected data from all patients who were treated for PCa at our center between November 2009 and January 2010. All patients were either newly diagnosed or had been diagnosed with PCa and seen as outpatients during the study period.

Results: In a sample of 218 patients with PCa; 25 (11.5%) were NSPC patients, and 193 (88.6%) were sporadic PCa sporadic prostate cancer (SPC) patients. Overall, 11.5% of the patients had a positive family history. There was one hereditary PCa family (three patients, 1.4%) and 11 familial PCa families (22 patients, 10.1%). Patients were divided into three different age groups. Of these, 18 (9.3%) SPC patients and 6 (24%) NSPC patients were diagnosed with the disease at the age of 55 years or younger (p=0.02). Prostate-specific antigen (PSA) levels in the NSPC group were significantly higher than in the SPC group (7.2±3.2 versus 6.3±4.9 ng/ml, p=0.042). SPC patients had larger waist circumferences than did NSPC patients (p=0.041). There were no significant differences between the SPC and NSPC groups in terms of socioeconomic status, Gleason score, pathological stage, or pathologic Gleason grade.

Conclusions: East Asian NSPC patients are diagnosed at earlier ages than are SPC patients, even though the incidence of NSPC in the East Asian population is lower than in Western men.

Key Words: *Epidemiology; Prostatic neoplasms; Siblings*

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INTRODUCTION

In recent years, prostate cancer (PCa) has become the most common malignancy among men in most Western countries. Due to the aging of the population, the absolute number of new PCa diagnoses is expected to increase up to 64% by the year 2020 [1]. Epidemiological and linkage studies have revealed a significant hereditary component to PCa [2,3]. Approximately 10% to 20% of patients with PCa have a positive family history, which increases the lifetime risk of the disease 2- to 11-fold [2,4]. The risk is highest for relatives of patients diagnosed before the age of 60 and for those with more than one affected relative. Hereditary PCa is typically diagnosed 6 to 7 years earlier than is the sporadic form [5]. These findings suggest a potential genetic etiology for the familial aggregation of PCa.

Unfortunately, there are no data regarding either the epidemiology or genetics of hereditary or familial PCa in East Asians, especially in Korean men. Most studies have been confined to subjects of European descent, and little is known about the familial aggregation of PCa in populations with a low incidence of disease. Therefore, we evaluated the incidences of familial and hereditary PCa among Korean outpatients with previously or newly diagnosed

PCa. We also evaluated the relation between socio-economic status and the incidence of nonsporadic prostate cancer (NSPC).

MATERIALS AND METHODS

We collected data from all patients who were treated for PCa at our center between November 2009 and January 2010. These patients were either newly diagnosed or were known to have PCa and were seen as outpatients during the study period. In-person interviews were conducted by trained male interviewers using standardized question-naires. We observed 229 PCa patients during the study period. Eleven patients who did not know their genea-logical data and were unable to answer related questions were excluded. We enrolled 218 patients in our study: 25 patients (11.4%) with NSPC and 193 patients (88.6%) with sporadic prostate cancer (SPC). Among the NSPC patients, 19 were diagnosed and treated at our hospital.

The family medical information collected included pedi-gree, cancer history, medical history, and social and demo-graphic factors. Clinical information was obtained from 193 SPC and 19 NSPC patients, including Gleason score, 2005 TNM stage, serum prostate-specific antigen (PSA) level at diagnosis, primary treatment, and disease pro-gression.

Systematic genealogical analyses of probands were per-formed by questionnaire to classify the patients into three epidemiologic categories of PCa according to Carter's cri-teria [6]: SPC; familial prostate cancer (FPC), which was PCa with an unpredictable clustering in families; and he-reditary prostate cancer (HPC), which was PCa with a strong clustering pattern and early onset of PCa. FPC and HPC were defined as NSPC. All patients were also strati-fied in three categories according to age at onset of PCa: 55 years or less, 56 to 65 years, and 65 years or older.

Descriptive statistics were used for frequency estimates with exact 95% confidence intervals (CIs). Differences in PSA, clinical stage, and Gleason scores between the NSPC and SPC groups according to age were compared by using the Wilcoxon test. Fisher's exact test or Pearson's chi-square test were used to compare categorical variables.

RESULTS

In our sample of 218 patients with PCa, 1 sample was from an HPC family (three patients in a family, 1.4%) and 11 were from FPC families (2 patients in each family, total of 22 patients, 10.1%) according to Carter's criteria. Eight SPC patients (9.3%) and six NSPC patients (24%) were di-agnosed at 55 years or younger (p=0.02). In our study sam-ple, the youngest NSPC patient was 46 years old and the youngest SPC patient was 51 years old. Of 18 patients who were newly diagnosed with PCa during the study period, 4 patients were diagnosed with NSPC and 14 patients were diagnosed with SPC.

The characteristics shared between the SPC and NSPC

TABLE 1. Clinical and pathological characteristics of SPC and NSPC patients

	SPC	NSPC	p-value
No. of patients	193	19	
BMI	24.8±4.5	23.2±3.1	0.082[a]
Waist circumference (cm)	87.9±6.9	82.8±8.1	0.041[a]
Age at diagnosis (yr)			
Median	68	66	
Mean±SD	69.1±3.4	64.6±4.8	0.035[a]
Follow-up duration from diagnosis (yr)			
Median	2.8	1.7	
Mean±SD	1.4±0.5	1.9±0.7	0.116[a]
PSA	7.2±3.2	6.3±4.9	0.042[a]
Biospy Gleason scores (n)			0.986[b]
6 or less	82 (42.5)	8 (42.1)	
7	69 (35.8)	7 (36.8)	
8 or above	42 (21.8)	4 (21.1)	
Pathologic stage			0.135[b]
T2N0M0	146 (75.6)	16 (84.1)	
T3N0M0	45 (23.3)	2 (10.5)	
Greater than T4N0M0	2 (1.0)	1 (5.2)	
Primary treatment			0.678[b]
Surgery	149 (77.2)	13 (68.4)	
Hormonal treatment	32 (16.6)	5 (26.3)	
Other treatment	12 (6.2)	1 (5.3)	

Data in parentheses are percentages. SPC: sporadic prostate can-cer, NSPC: non-sporadic prostate cancer, PSA: prostate-specific antigen, [a]: Wilcoxon test, [b]: chi-square with Fisher's exact test

groups are given in Table 1. The mean age at diagnosis was 68.0 years for all patients. The mean age at diagnosis of NSPC patients (64.6±4.8 years) was significantly earlier (p=0.035) than that of SPC patients (69.1±3.4 years). SPC patients had larger waist circumferences than did NSPC patients (p=0.041). Whereas biopsy Gleason scores were not significantly different between the two groups, PSA levels in the NSPC group were significantly higher than in the SPC group (7.2±.3.2 vs. 6.3±4.9 ng/ml, p=0.042). Among the patients who underwent surgery (149 SPC and 13 NSPC patients) as the primary treatment, there were no significant differences in pathological stage or Gleason grade between the two groups.

Table 2 shows the socioeconomic status of the SPC and NSPC patients. There was no significant difference be-tween the NSPC and SPC patients in the duration of smoking. There were no associations between marital sta-tus, monthly income, education level, smoking, alcohol in-take, or occupational physical activity and risk of NSPC at diagnosis.

DISCUSSION

A positive family history is one of the strongest epidemio-logic risk factors for PCa [7,8]. In general, familial cancer accounts for 15% to 20% of all PCa, and hereditary cancer for 5% to 10% [5]. In our Korean sample, the incidence of

TABLE 2. Socioeconomic status of SPC and NSPC patients

	SPC	NSPC	p-value
	181	17	
Marital status			0.336[a]
Married/living together	137 (75.6)	12 (70.6)	
Divorced, separated, or widowed	42 (23.2)	4 (23.5)	
Single	2 (1.1)	1 (5.9)	
Monthly income, US $ (₩)			0.773[a]
<1,500 (1,650,000)	135 (74.6)	12 (70.6)	
>1,500 (1,650,000)	46 (25.4)	5 (29.4)	
Education level			0.661[a]
<High school	29 (16.0)	3 (17.6)	
High school graduate	77 (42.6)	9 (53.0)	
>High school	75 (41.4)	5 (29.4)	
Smoking at diagnosis			0.558[a]
Yes	139 (76.8)	12 (70.6)	
No	42 (23.2)	5 (29.4)	
Alcohol intake at diagnosis			0.454[a]
>30 g/d	83 (45.9)	6 (35.3)	
<30 g/d	98 (54.1)	11 (64.7)	
Mean (SEM) duration of smoking, pack years	27 (1.6)	18 (2.5)	0.072[a]
Occupational physical activity at diagnosis			0.118[a]
Very active	63 (34.8)	10 (58.8)	
Moderately active	92 (50.8)	5 (29.4)	
Inactive	26 (14.4)	2 (11.8)	

Data in parentheses are percentages except for smoking. SPC: sporadic prostate cancer, NSPC: non-sporadic prostate cancer, [a]: chi-square with Fisher's exact test

FPC was 10.1% and that of HPC was 1.4%, which is relatively low compared with the incidences of FPC and HPC in Western men. However, we were unable to distinguish whether this low familial incidence of NSPC in Korea was "real" or was simply an artifact of "unknown" deaths of the first generation in the pre-PSA era (PSA-unavailable era). The incidence of PCa has rapidly increased over the past 10 years in East Asia, including Korea. PCa is currently the fifth most common cancer in Korean men and resulted in 1,168 deaths in 2007 [9]. The results of our pilot study suggest that future studies to elucidate the epidemiology of NSPC in Korea are warranted.

In the present study, we found no significant differences in tumor stage or Gleason grade between SPC and NSPC patients. However, we did not calculate the survival rates of SPC and NSPC patients. Many recent studies have suggested that there are no differences in the aggressiveness of PCa between SPC and FPC [10-12]. Kupelian et al reported that there were no associations between the presence of a family history of PCa and any demographic, clinical, or treatment factors, except age [10]. Lee et al performed a retrospective analysis of 557 men with localized PCa who were treated by radical prostatectomy and showed that the NSPC patients were younger at the time

of surgery than were the SPC patients [11]. Roemeling et al analyzed the characteristics of NSPC by use of the screening arm of the Rotterdam section of the European Randomized Study of Screening for Prostate Cancer and reported that the cancer detection rate in 1,364 men with a positive family history was 7.7% (106 cancers in 1,364 screened men with a positive family history) in the prevalence screen, whereas the positive predictive value of biopsies was 32.2% (154 cancers in 532 biopsies) [12]. In 12,803 sporadic cases, the detection rate was 4.7% and the positive predictive value was 23.6% (p=0.0001 and 0.003, RR 1.63). However, there were no clinicopathological differences between the groups. In the present study, patients with a positive family history presented at a younger age (69.1 vs. 64.6 years) despite similar socioeconomic status between the SPC and NSPC patients. Our results were similar to those of previous studies. In a younger subgroup of patients, positive family history is more likely to be indicative of genetic predisposition, as suggested by the results of studies showing that loci of PCa susceptibility genes, such as PCa and HPC, are associated with earlier age at the time of diagnosis [13-15]. Another plausible hypothesis is that our patients were screened at earlier ages because men with positive family histories are known to be at a higher risk of developing PCa. Thus, men with close relatives affected by PCa may participate in screening more often or earlier.

Interestingly, we observed that body mass index (BMI) was lower in the NSPC patients than in the SPC patients, although this difference was not significant. However, the waist circumference of the NSPC patients was significantly lower than that of the SPC patients. Even though the role of obesity as a risk factor for PCa remains unclear, body size is one of several factors hypothesized to be related to PCa [16,17]. In addition, the role of obesity across different populations has been suggested by several epidemiologic and anthropometric studies [17,18]. However, there are few reports regarding whether BMI or waist circumference influences the incidence of PCa in East Asian men, who are relatively slim according to Western criteria. Our results suggest that factors other than body mass might contribute to the occurrence and progression of NSPC. Moreover, a recent study showed that visceral adipose tissue is strongly associated with adverse pathologic features in patients with localized PCa, including higher Gleason score and PCa risk groups [19]. Concerning this result, we believe that abdominal circumference might be a more important factor associated with PCa aggressiveness than generalized adiposity deposition as measured by BMI.

Valeri et al reported that the proportion of relatives with PSA greater than 4 ng/ml and PCa detection was not significantly different according to familial status (sporadic or nonsporadic) [20]. However, our results differed. This may be because the study subjects had different ethnicity and eating habits. However, we believe that further studies are needed.

There are several limitations to our study. First, this was

a cross-sectional pilot study, and we did not collect data regarding differences in long-term survival between SPC and NSPC patients. Second, our sample of NSPC patients was small, which imposed limitations on statistical power. Our results suggest that larger population-based studies are warranted. In addition, to improve the identification of HPC and to clarify its clinical importance, it is necessary to study its genetic characteristics in depth. These include performing linkage studies to better define high-penetrance PCa susceptibility genes, large association studies to clarify the role of low-penetrance polymorphic alleles, and gene expression profile analyses to compare HPC forms with SPC forms.

CONCLUSIONS

In this pilot study, we confirmed that in Korea, NSPC patients are diagnosed at an earlier age than are SPC patients, even though the incidence of NSPC is lower than in Western men. Our analyses of the relations between family history and socioeconomic status, preoperative PSA, biopsy Gleason score, pathological stage, and pathologic Gleason grade did not reveal any significant differences between SPC and NSPC patients. Our results suggest that studies with a long-term follow-up and large samples of East Asian male NSPC patients are warranted.

Conflicts of Interest
The authors have nothing to disclose.

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