Contemporary Risk Profile of Prostate Cancer in the United States

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National-level data that characterize contemporary prostate cancer patients are limited. We used 2004–2005 data from the Surveillance, Epidemiology, and End Results Program to generate a contemporary profile of prostate cancer patients (N = 82 541) and compared patient characteristics of this 2004–2005 population with those of patients diagnosed in 1998–1989 and 1996–1997. Among newly diagnosed patients in 2004–2005, the majority (94%) had localized (ie, stage T1 or T2) prostate cancer and a median serum prostate-specific antigen (PSA) level of 6.7 ng/mL. Between 1988–1989 and 2004–2005, the average age at prostate cancer diagnosis decreased from 72.2 to 67.2 years, and the incidence rate of T3 or T4 cancer decreased from 52.7 per 100 000 to 7.9 per 100 000 among whites and from 90.9 per 100 000 to 13.3 per 100 000 among blacks. In 2004–2005, compared with whites, blacks were more likely to be diagnosed at a younger age (mean age: 64.7 vs 67.5 years, difference = 2.7 years, 95% confidence interval [CI] = 2.5 to 2.9 years, *P* < .001) and to have a higher PSA level at diagnosis (median PSA level: 7.4 vs 6.6 ng/mL, difference = 0.8 ng/mL, 95% CI = 0.6 to 1.0 ng/mL, *P* < .001). In conclusion, more men were diagnosed with prostate cancer at a younger age and earlier stage in 2004–2005 than in earlier years. The racial disparity in cancer stage at diagnosis has decreased statistically significantly over time.

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The incidence of prostate cancer has increased substantially since the introduction of prostate-specific antigen (PSA) testing in the late 1980s (1). It has been predicted that the increasing number of prostate cancer cases that are diagnosed earlier in the course of disease as a result of PSA testing may change the risk profile of patients with prostate cancer. Previous studies have documented the changing risk profile of prostate cancer in the United States (2–5); however, most of those studies were conducted in a selected population or had limited data on important prognostic factors. Population-based studies of prostate cancer patients that are representative of the US population are lacking. We undertook a nationwide study of newly diagnosed prostate cancer across the United States using 2004–2005 data from the Surveillance, Epidemiology, and End Results (SEER) Program. Following its expansion in 2001, SEER now collects cancer incidence data from registries that cover approximately 26% of the US population and has 98% completeness in case ascertainment (6,7). Individual PSA values and Gleason scores at diagnosis were first available in the SEER public dataset starting in 2004.The PSA value recorded in SEER is the highest PSA laboratory value before the diagnostic biopsy or treatment. We used SEER data to provide a contemporary risk profile of prostate cancer in the United States. There were 98 486 newly diagnosed prostate cancer cases in 2004–2005 in the SEER database. Subjects who were aged 24 years or younger at diagnosis or for whom age at diagnosis was missing (n = 67), whose race was listed as other than black or white (n = 8432), or who had missing PSA values, Gleason score, or clinical stage (n = 7446) were excluded from these analyses. After these exclusions, 82 541 cases were eligible for this study and they were stratified by the patient's age at diagnosis (25–54, 55–64, 65–74, ≥75 years), self-reported race in the medical record (black, white), and cancer features (PSA level, Gleason score, and cancer stage). The cutpoints for age at diagnosis were chosen because 65 years is the starting age of enrollment of Medicare. We categorized the patients' ages into 10-year groups for ease of presentation. Patients were categorized into three risk groups on the basis of the American Joint Committee on Cancer clinical stage (8,9), PSA level, and Gleason score, as was done in previous studies (10,11): low risk (stage T2a or lower, a PSA level ≤10 ng/mL, and a Gleason score of 6 or lower), intermediate risk (stage T2b or a PSA level from 10.1 to 20 ng/mL or a Gleason score of 7), and high risk (stage T2c or higher or a PSA level >20 ng/mL or a Gleason score of 8 or higher). We compared the proportions of prostate cancer patients stratified by age at diagnosis, PSA level, Gleason score, and cancer stage between whites and blacks. We also examined temporal trends in age at prostate cancer diagnosis, cancer grade, and tumor stage from 1988 to 2004 using data from the SEER 9 registries, which include Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco–Oakland, Seattle–Puget Sound, and Utah. We restricted our trend analysis to the area covered by SEER 9 to ensure that patients were from the same catchment area so that these trends would be comparable over time. Furthermore, we compared the characteristics of men in the

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2004–2005 SEER database with those of men enrolled in the Scandinavian Prostate Cancer Group 4 (SPCG-4) (12) to provide insight about the generalizability of the result of this trial in the US population. The independence of distributions in these factors between blacks and whites was tested using χ^2 tests. Secular trends in the proportions for blacks and whites were evaluated separately by using the asymptotic Kruskal–Wallis test (13). Trends in mean age at diagnosis were tested by one-way analysis of variance using linear contrast. The PSA distribution for patients in the 2004–2005 SEER database and for patients in SPCG-4 was tested by an ordered χ^2 test. All statistical tests were two-sided and were performed by using SAS version 9.0 (SAS Institute, Cary, NC). This study was approved by the institutional review board of University of Medicine and Dentistry of New Jersey.

We first examined descriptive and tumor characteristics of this cohort of 82 541 patients who were diagnosed with prostate cancer during 2004–2005 (Table 1). Among all patients, the mean age at diagnosis was 67.1 years (67.5 years in whites and 64.7 years in blacks, difference = 2.7 years, 95% confidence interval [CI] = 2.5 to 2.9 years, $P < .001$). Among all patients, 41% were aged 64 years or younger at diagnosis (39% of whites and 50% of blacks) and 24% were aged 75 years or older (25% of whites and 16% of blacks). Among all patients, 94% were diagnosed with localized (ie, stage T1 or T2) prostate cancer (94% of whites and 93% of blacks). Almost half of the patients (47% of whites and 44% of blacks) had a biopsy Gleason score of 6 or lower. Thirty-six percent of patients had a biopsy Gleason score of 7 (36% of whites and 38% of blacks), 25% had primary pattern 3 and secondary pattern

Table 1. Clinical characteristics of prostate cancer patients, Surveillance, Epidemiology, and End Results (2004–2005)*

Characteristic	All patients, N = 82 541	White, n = 71 346	Black, n = 11 195	P†
Age at diagnosis, y				
Mean (SD)	67.1 (9.75)	67.5 (9.72)	64.7 (9.68)	
25–54, %	10	9	15	<.001
55–64, %	31	30	35	
65–74, %	36	36	34	
≥75, %	24	25	16	
PSA level, ng/mL				
Median (range)	6.7 (0.1–99.0)	6.6 (0.1–99.0)	7.4 (0.1–99.0)	
≤2.5, %	6	6	5	<.001
2.6–4, %	7	7	6	
4.1–6.9, %	35	35	31	
7–10, %	17	17	16	
10.1–20, %	14	14	16	
>20, %	12	12	17	
Unknown, %	10	10	10	
Gleason score, %				
2–6‡	46	47	44	<.001
7	36	36	38	
3+4§	25	25	26	
4+3‖	10	10	10	
8–10	15	15	16	
Unknown	2	2	3	
Tumor stage, %				
T1¶	51	50	53	<.001
T2#	43	44	40	
T3**	3	3	2	
T4**	1	1	1	
Unknown	2	2	3	

* For some categories, the percentages do not total 100 because of rounding. PSA = prostate-specific antigen.

† χ^2 test (two-sided) was used to test independence of distributions between blacks and whites.

‡ Gleason score 2–4 accounted for 2% of Gleason score 2–6.

§ Primary pattern 3, secondary pattern 3.

‖ Primary pattern 4, secondary pattern 3.

¶ T1c accounted for 95% of T1.

T2a accounted for 12% of T2.

** 30% of T3 and T4 cancers were classified as distant cancers.

CONTEXT AND CAVEATS

Prior knowledge

The increasing number of prostate cancer cases that are diagnosed earlier in the course of disease as a result of prostate-specific antigen testing may change the risk profile of patients with prostate cancer. However, population-based studies of contemporary prostate cancer patients that are representative of the US population are lacking.

Study design

Surveillance, Epidemiology, and End Results Program data for 2004–2005 were used to generate a contemporary profile of prostate cancer patients and to compare the characteristics of the 2004–2005 patient population with those of patients diagnosed in 1988–1989 and 1996–1997 and with those of participants in a randomized trial of radical prostatectomy vs watchful waiting that showed better survival for patients aged 65 years or younger in the radical prostatectomy group.

Contribution

Patients diagnosed in 2004–2005 were younger and had earlier stage cancers than patients diagnosed in earlier years. The incidence of stage T3 or T4 cancer at diagnosis has decreased in both blacks and whites and the racial disparity in cancer stage at diagnosis has decreased over time. Compared with patients in the trial, patients in the Surveillance, Epidemiology, and End Results population had a lower prostate-specific antigen level and earlier cancer stage at diagnosis.

Implications

It remains to be determined whether more patients being diagnosed at earlier stages ultimately results in a decreased mortality and whether the narrowing of the racial disparity in the presentation of advanced prostate cancer is ultimately accompanied by similar trend in mortality.

Limitations

Changes in prostate-specific antigen level at diagnosis of prostate cancer patients over time could not be directly compared. A more refined classification of Gleason scores before 2004 was not possible.

From the Editors

4, and 10% had primary pattern 4 and secondary pattern 3 (14,15). The median serum PSA level at diagnosis was 6.7 ng/mL (6.6 ng/mL in whites and 7.4 ng/mL in blacks, difference = 0.8 ng/mL, 95% CI = 0.63 to 0.97 ng/mL, $P < .001$). Approximately 13% of patients had a PSA level of 4 ng/mL or less. Among these patients, 46% had PSA level of 2.5 ng/mL or less.

Overall, older age at diagnosis was associated with a higher PSA level (Supplementary Figure 1, available online) and with a higher biopsy Gleason score (Supplementary Figure 2, available online) in both blacks and whites. Within each age stratum, blacks had a higher median PSA level and a slightly higher proportion of biopsy Gleason score of 7 or higher compared with whites. We examined the distribution of risk groups by race and age at diagnosis (Figure 1). The proportion of patients who exhibited intermediate- or high-risk disease at diagnosis increased with increasing age at diagnosis in blacks and in whites. In each age-at-diagnosis stratum, blacks were more likely than whites to have intermediate- or high-risk cancers.

We examined temporal trends in age at prostate cancer diagnosis, cancer grade, and tumor stage from 1988 to 2005 in SEER 9 area (Supplementary Table 1, available online). The average age of patients at diagnosis decreased from 72.2 years in 1988–1989 to 69.2 years in 1996–1997 to 67.2 years in 2004–2005. In general, the incidence of stage T3 or T4 prostate cancer among newly diagnosed patients decreased from 55.5 per 100 000 in 1988–1989 to 44.6 per 100 000 in 1996–1997 to 8.4 per 100 000 in 2004–2005. The incidence of a biopsy Gleason score of 8–10 among newly diagnosed patients also decreased from 47.5 per 100 000 in 1988–1989 to 38.3 per 100 000 in 2004–2005. During the same period, we observed a marked decrease in the incidence of a biopsy Gleason score of 2–4 and a large increase in the incidence of a biopsy Gleason score of 5–7 among newly diagnosed patients. The extremely low incidence (2.3 per 100 000) of patients with a biopsy Gleason score of 2–4 in 2004–2005 may reflect changes in clinical grading over time. For example, several studies (16,17) have shown that pathologists have lowered the threshold of Gleason grading and have assigned patients to higher grade over time.

Previous studies have documented that blacks were more likely than whites to be diagnosed at a more advanced stage of prostate cancer (18–20). However, we found that this racial difference has narrowed considerably from 1988 to 2005. The incidence of stage T3 or T4 prostate cancer among newly diagnosed black patients decreased from 90.9 per 100 000 in 1988–1989 to 13.3 per 100 000 in 2004–2005, whereas the incidence in newly diagnosed white patients over the same time period decreased from 52.7 per 100 000 to 7.9 per 100 000 (Supplementary Table 1, available online). In 1988–1989, the absolute difference in the incidence of T3 or T4 prostate cancer between blacks and whites was 38.2 per 100 000, and this disparity dropped to 5.4 per 100 000 by 2004–2005. Although blacks had slightly higher Gleason scores and PSA levels than whites in 2004–2005 (Supplementary Figures 1 and 2, available online), the difference between blacks and whites in stage at diagnosis that was recorded in the SEER database during 2004–2005 was smaller than that reported during 1996–1997 or earlier (18). This lower race–stage disparity may be due, in part, to the recommendation from the American Cancer Society and the American Urological Association (21,22) of prostate cancer screening for men younger than 50 years who have a family history of prostate cancer or are black, but further studies are needed to confirm this hypothesis. In recent years, young black men have undergone PSA testing at a higher rate compared with similarly aged white men, reflecting the increased awareness by health-care providers that blacks are at a higher risk of developing prostate cancer than whites (23,24). Although the median PSA level and the Gleason score increased with increasing age in both black and white patients (Supplementary Figures 1 and 2, available online), at all age ranges, more blacks than whites were categorized into the high-risk group (Figure 1). Indeed, results of two gene association studies suggest that specific alleles at chromosome 8q24 that are associated with an increased risk of developing prostate cancer and having high-grade disease are especially common in blacks (25,26). This genetic finding highlights the need for additional studies to elucidate genetic risk factors for prostate cancer and to translate these findings into clinical practice.

Results of SPCG-4 (12)—a randomized trial of radical prostatectomy vs watchful waiting that showed better survival for patients aged 65 years or younger in the radical prostatectomy group—are often cited in support of early screening and treatment. To assess whether prostate cancer patients in the United States might be expected to achieve a similar benefit from radical prostatectomy as reported in the SPCG-4 trial, we compared the baseline characteristics of men in the 2004–2005 SEER database with those of men enrolled in SPCG-4 (n = 695). We restricted the comparison to the US patients who met the eligibility criteria for inclusion in SPCG-4 (ie, those with localized disease and who were younger than 75 years at diagnosis;

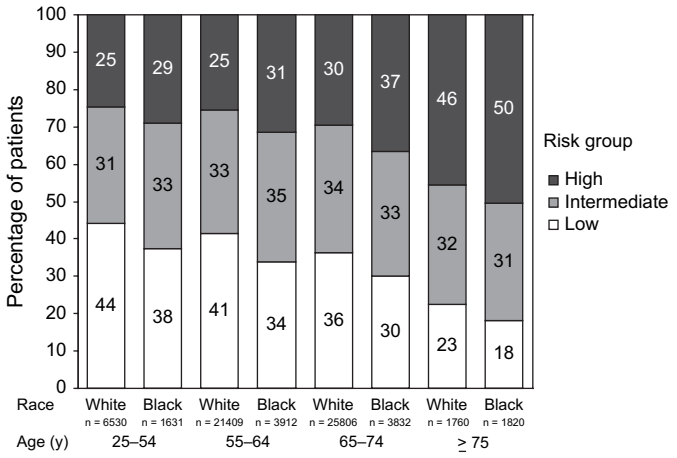

Figure 1. Patient risk stratification by age at diagnosis and race. Patients were categorized into three risk groups on the basis of clinical stage, prostate-specific antigen (PSA) level, and Gleason score as previously described (10). Low risk = stage T2a or lower, PSA level ≤10 ng/mL, and a Gleason score ≤ 6; intermediate risk = stage T2b or Gleason score 7 or a PSA level >10 and ≤20 ng/mL; and high risk = stage T2c or higher or PSA level >20 ng/mL or Gleason score ≥8. All categories do not total 100% because of rounding.

n = 66 001). Patients in the 2004–2005 SEER database were slightly younger at diagnosis than men enrolled in SPCG-4 (63.2 vs 64.7 years) and had a much higher percentage of PSA screen-detected cancer (defined in SPCG-4 as T1c) (53.3% vs 11.7%). Almost half of the SPCG-4 patients had a PSA level greater than 10 ng/mL, whereas 53% of the SEER population had a PSA level less than 7 ng/mL (Supplementary Figure 3, available online). On the basis of the results of this randomized trial, which showed better survival for patients aged 65 years or younger in the radical prostatectomy group, physicians may feel compelled to treat patients who are younger than 65 years with definitive therapy. However, the risk profiles for SPCG-4 trial patients and contemporary patients in the United States differ substantially. For example, patients in the United States are more likely to be diagnosed through screening and to have low-risk disease. Thus, the survival advantage observed in the SPCG-4 trial for patients who were randomly assigned to radical prostatectomy might not be reproducible in this largely low-risk group of patients.

This study has some limitations due to the nature of the data. Before 2004, SEER coded PSA information into positive, negative, or borderline. Therefore, we could not compare the changes in PSA level at diagnosis of prostate cancer patients over time. In addition, Gleason scores were grouped as 2–4, 5–7, and 8–10 before 2004, which prevented us from doing a more refined classification of Gleason scores before 2004.

In conclusion, our study showed statistically significant changes in the risk profile of prostate cancer patients over time. Patients who were diagnosed in 2004–2005 were younger and had earlier stage cancers than patients diagnosed in earlier years (Table 1). Importantly, the incidence of stage T3 or T4 cancer at diagnosis has decreased statistically significantly in both blacks and whites and the racial disparity has decreased over time (Supplementary Table 1, available online). Finally, compared with patients in the SPCG-4 trial, patients in the SEER population had a much lower PSA level and earlier cancer stage at diagnosis. It will be important to examine whether more patients being diagnosed at earlier stages ultimately results in a decreased mortality from this highly prevalent malignancy and whether the narrowing of the racial disparity in the presentation of advanced prostate cancer is ultimately accompanied by similar trend in mortality.

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