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BLACK-WHITE DIFFERENCES IN TUMOR GRADE (AGGRESSIVENESS) AT DIAGNOSIS OF PROSTATE CANCER, 1992–1998

Objectives: To compare recent temporal trends in the proportion of high-grade (less differentiated, or more “aggressive”) prostate cancers for Blacks (African Americans) and Whites. Reports of Black-White differences have generated speculation that genetic factors could be involved.

Methods: The study included all 126,889 non-Hispanic White and 20,247 Black patients with prostate cancer diagnosed in 1992–1998 and reported to the US National Cancer Institute’s Surveillance, Epidemiology and End Results (SEER) Program of population-based cancer registries.

Results: Overall and stage-specific Black-White differences in proportion of high-grade cancers were not large and declined over time (especially among elderly patients). By 1998, the adjusted odds ratio for high (vs other known) grade was not statistically significant for Black vs White elderly patients when age and stage at diagnosis were included in a multiple logistic regression model.

Conclusions: These data provide little justification for speculation about a genetic basis for a higher proportion of aggressive prostate cancer among Black patients. Trends in Black-White differences in the frequency of high-grade cancer suggest Black-White differences in trends in prostate cancer screening rates (especially in the elderly), which require further investigation. (*Ethn Dis.* 2002;12:536–541)

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INTRODUCTION

Reports of a disproportionate number of prostate cancers of high histologic grade (ie, poorly differentiated or undifferentiated) among Blacks compared to Whites have led to suggestions of the disease being more “aggressive” or “virulent” among Blacks, and speculations about genetic explanations,^{1–3} with potential implications for prognosis and therapy for patients diagnosed with prostate cancer.¹ However, racial differences in screening rates and other non-biological mechanisms also have been discussed as possible explanations.^{4,5} According to data from the high-quality population-based cancer registries included in the National Cancer Institute’s SEER (Surveillance, Epidemiology and End Results) Program on prostate cancers diagnosed from 1973–1995, Blacks had only a slightly higher proportion of high-grade and unknown grade tumors compared to Whites; however, data were shown in graphs, without actual percentages.⁶ The present study considers recent trends in the Black-White differences in proportion of high-grade prostate cancer at diagnosis, using data from the SEER Program.

METHODS

Since 1992 (year of diagnosis), when data from the Los Angeles area were first included, SEER has covered about 14% of the US population, and data are believed to be generally representative of the entire United States (in the absence of a national system of cancer registration).⁷ A SEER public-use data file⁸ was

used to identify all patients with prostate cancer diagnosed from 1992–1998, while living in a SEER area. For the time period under study, the SEER Program study population included the metropolitan areas of Atlanta, Ga, Detroit, Mich, San Jose-Monterey, Calif, San Francisco-Oakland, Calif, and Seattle, Wash, along with the states of Connecticut, Hawaii, Iowa, New Mexico, and Utah. Codes for both the “race” and Hispanic ethnicity SEER items, as reported to the registries mainly from (hospital) medical records,⁹ were used to define non-Hispanic White (hereafter, referred to as “White”) and Black categories. SEER efforts in linking surnames to the 1980 Census list of Spanish surnames⁹ improve overall ascertainment of patients who would report themselves as Hispanic.¹⁰ After excluding cases ascertained from death certificate only or autopsy, the study included 147,136 (126,889 White and 20,247 Black) patients.

Analyses included stage at diagnosis, since grade is strongly associated with stage.¹¹ SEER “historical” (also called “summary”) stage is coded as local, regional, distant or unknown; for prostate cancer, local and regional stages are combined,⁹ because stage may be defined only clinically (for patients without surgery), and upstaging (from local to regional) often occurs due to surgery.¹² Grade is coded in SEER as low (well differentiated, Gleason score 2–4), intermediate (moderately differentiated, Gleason score 5–7), and high (poorly differentiated, Gleason score 8–10, or “anaplastic” or “undifferentiated”). Socioeconomic status (SES) was not assessed because the SEER public-use database includes only county of residence

Table 1. Proportion of incident prostate cancers diagnosed as high-grade, for Blacks and non-Hispanic Whites in the Surveillance, Epidemiology and End Results (SEER) Program, by year of diagnosis (1992–1998)

Race-Ethnicity*	Year of Diagnosis							P†
	1992	1993	1994	1995	1996	1997	1998	
All Stages Total No.								
Black	2,969	3,202	2,944	2,751	2,744	2,821	2,816	—
White	23,347	20,141	17,228	16,369	16,492	17,111	16,201	—
% High Grade								
Black	24.7	24.1	23.1	23.3	21.8	20.6	20.8	<.001
White	20.6	19.9	19.4	19.6	19.3	19.1	19.6	<.005
P value‡	<.001	<.001	<.001	<.001	.003	.044	.147	
Local or Regional Stage Total No.								
Black	2,094	2,317	2,183	2,215	2,273	2,406	2,457	—
White	18,470	16,011	14,182	13,823	14,212	15,034	14,597	—
% High Grade								
Black	21.9	20.9	21.9	20.9	19.2	18.4	19.1	<.01
White	19.3	18.5	18.2	18.3	18.2	17.8	18.2	<.005
P value‡	.005	.005	<.001	.003	.261	.531	.149	
Distant Stage Total No.								
Black	380	313	259	242	190	221	180	—
White	1,490	1,206	990	922	851	749	724	—
% High Grade								
Black	45.3	47.0	44.0	50.8	54.2	47.5	41.1	>.250
White	43.5	45.4	42.6	45.3	43.9	45.1	48.2	>.900
P value‡	.573	.675	.740	.147	.013	.583	.105	

* White denotes non-Hispanic White (see text).

† P value from chi-square test for linear trend in proportion from 1992 to 1998, within each racial-ethnic group.

‡ P value from chi-square test for association between race-ethnicity and high-grade cancer within stage/year of diagnosis category.

for each patient (at the time of diagnosis),⁹ whereas smaller geopolitical units are needed to obtain ecologic or proxy estimates of the SES of individuals;¹³ in addition, one SEER area (Los Angeles) includes only a single county.

Time trends in proportion of high-grade cancers (among all cancers, including those of unknown grade) were examined by age at diagnosis (<65 and 65+ years) relevant to Medicare insurance coverage. Statistical methods included chi-square tests for 2-by-2 tables and for linear trends in proportions¹⁴; a P value (alpha level) of <.05 was used for “statistical significance.” Multiple logistic regression analysis¹⁵ was used to examine the independent association between race-ethnicity and high (vs low- intermediate) grade, controlling for stage, age and marital status; 95% confidence limits for adjusted odds ratios were based on

the normal approximation and P values were from the Wald statistic.¹⁵

Age-standardized incidence rates (using the direct method with the age distribution of the total 1970 US population as the standard) for high-grade cancers were obtained with a computer program (SEER*Stat 4.0).⁸

RESULTS

For all stages combined, the Black-White difference in proportion of high-grade cancers reached statistical significance for each year from 1992–1997 but not in 1998. While the test for linear trend (1992–1998) in proportions of high-grade cancers was statistically significant for both Blacks and Whites (Table 1), the magnitude of the decline was greater for Blacks (from 24.7% in 1992 to 20.8% in 1998, a 15.8% re-

duction) than for Whites (from 20.6% in 1992 to 19.6% in 1998, a 4.9% reduction). This change, and also that in proportion of distant stage cancers (ie, 380/2969 or 14.2% for Blacks vs 1490/23,347 or 6.8% for Whites in 1992, to 180/2816 or 6.4% for Blacks vs 724/16,201 or 4.5% for Whites in 1998, see Table 1), reflected a greater decline in the denominator (total number of cancers) in Whites compared to Blacks. The latter difference was due to increasing numbers of locoregional stage cancers in Blacks and decreases in Whites. In contrast, the number of distant-stage cancers declined for both racial-ethnic groups (Table 1).

The age-standardized incidence rate for locoregional cancer declined for Whites but not for Blacks (Table 2). The Black-White differences in proportion of high-grade cancers within loco-

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Table 2. Age-standardized incidence rates (per 100,000 per year, 1992–1998) for locoregional stage prostate cancer among Black and non-Hispanic White males in SEER areas, for all grades and high-grade cancers alone

Year of Diagnosis	All Grades		High-Grade Only	
	Black	White	Black	White
1992	179.0	151.4	39.3	29.2
1993	193.2	131.1	40.7	24.1
1994	177.8	116.5	38.8	21.1
1995	176.8	113.6	37.5	20.3
1996	178.4	116.2	34.4	20.7
1997	183.5	122.1	33.8	21.4
1998	182.7	117.0	35.2	20.8

regional stage declined from 1992 to 1998, and the difference was statistically significant ($P < .05$) in each year from 1992–1995 but not from 1996–1998 (Table 1). However, the Black-White difference in the age-standardized incidence rate of high-grade cancers persisted within locoregional stage (Table 2).

Within distant stage, with a high proportion of high-grade cancers (relative to locoregional stage),¹¹ the Black-White differences in proportion of high-

grade cancers were statistically significant only in 1996; trend tests were not statistically significant (Table 1). Within distant stage, the proportion of high-grade cancers in 1998 was actually higher for Whites than Blacks. However, while unknown grade was uncommon within locoregional stage (4% in Whites and 5%–7% in Blacks; data not shown) it was more common among distant stage cancers and increased among Blacks from 1997 to 1998. Combining high- with unknown-grade cancers in 1998, the difference in proportion of high-grade cancers within distant stage between Blacks (72.8%) and Whites (75.4%) was small. Ungraded cases probably tend to be high grade, in view of the lower survival rates among these cases compared to graded cases.¹¹

In the age category of <65 years at diagnosis, while the proportion of high-grade cancers declined over time, the Black-White differences persisted (Table 3). In the 65+ years of age category, however, the proportion of high-grade cancers declined in Blacks but not Whites, and by 1997 and 1998, the Black-White differences were no longer statistically significant.

Age at diagnosis tended to be earlier for Blacks (mean age of 67.7, median age of 68.0 years) compared to Whites (mean age of 69.9, median age of 70.0 years) ($P < .001$, t test for difference in means). Multiple logistic regression models, with high (vs low or intermediate) grade as the dependent variable, included age at diagnosis (divided by 5) for all cancers of known grade diagnosed in 1998 (the latest year). Distant stage was strongly associated with high-grade cancer. The adjusted odds ratio for race-ethnicity was statistically significant among patients <65 years old but not among patients age 65+ years, independent of age and stage (Table 4).

DISCUSSION

Using data from population-based cancer registries, this study found a small Black-White difference in the proportion of high-grade cancers (Table 1), as found in a previous SEER-wide study.⁶ In addition, a decline occurred from 1992 to 1998 in the magnitude of the racial differences (Table 1), with a greater decline among elderly than non-

Table 3. Proportion of incident prostate cancers diagnosed as high-grade, among Blacks and non-Hispanic White patients in SEER Program, by year of diagnosis (1992–1998) within age at diagnosis (<65 and 65+ years)

Race-Ethnicity*	Year of Diagnosis							P†
	1992	1993	1994	1995	1996	1997	1998	
Age <65 Total No.								
White	4,717	4,580	4,413	4,423	4,926	5,229	5,086	—
Black	828	998	1,017	1,053	1,074	1,101	1,185	—
% High Grade								
White	19.1	19.2	17.7	16.2	16.1	15.9	15.4	<.001
Black	22.5	24.0	21.5	22.1	19.7	18.8	18.5	<.005
P value‡	.028	<.001	.005	<.001	.005	.019	.010	
Age 65+ Total No.								
White	18,630	15,561	12,815	11,946	11,566	11,882	11,115	—
Black	2,141	2,204	1,927	1,698	1,670	1,720	1,631	—
% High Grade								
White	20.9	20.1	20.0	20.8	20.7	20.4	21.5	>.250
Black	25.6	24.2	23.9	24.1	23.1	21.9	22.5	<.025
P value‡	<.001	<.001	<.001	.002	.026	.177	.400	

* White denotes non-Hispanic White (see text).

† P value from chi-square test for linear trend in proportion from 1992 to 1998, within each racial-ethnic group.

‡ P value from chi-square test for association between race-ethnicity and high-grade cancer within age/year of diagnosis category.

Table 4. Multiple logistic regression models for high grade (vs other known grade) among Black and non-Hispanic White patients diagnosed with prostate cancer in 1998, SEER Program

Covariate	Total N	% High Grade	Adjusted Odds Ratio (and 95% CI)	P Value*
Model 1: Age <65 Years				
Age (years/5)	6,039	16.6	1.03 (0.96, 1.10)	.459
Race-ethnicity				
White†	4,915	15.9	1.00 (reference)	—
Black	1,124	19.5	1.21 (1.02–1.44)‡	.029
Stage				
Local-regional	5,737	15.1	1.00 (reference)	—
Distant	150	65.3	10.25 (7.25, 14.48)‡	<.001
Unknown	152	22.4	1.59 (1.07, 2.37)‡	.021
Marital status				
Not married	1,287	18.8	1.00 (reference)	—
Married	4,430	15.8	0.91 (0.77, 1.08)	.580
Unknown	322	18.0	0.93 (0.67, 1.30)	.297
Model 2: Age 65+ Years				
Age (years/5)	11,754	23.5	1.20 (1.16, 1.25)‡	<.001
Race-ethnicity				
White	10,290	23.3	1.00 (reference)	—
Black	1,464	25.1	1.07 (0.94–1.23)	.296
Stage				
Local-regional	10,666	21.2	1.00 (reference)	—
Distant	500	65.0	6.30 (5.20, 7.63)‡	<.001
Unknown	588	29.8	1.47 (1.22, 1.78)‡	<.001
Marital status				
Not married	2,554	26.6	1.00 (reference)	—
Married	8,341	22.8	0.90 (0.81, 1.00)	.057
Unknown	859	21.5	0.76 (0.62, 0.92)‡	.005

CI=confidence interval.

* P values are from the Wald statistic.

† White denotes non-Hispanic White (see text).

‡ CI (95%) does not include 1.00.

elderly patients (Table 3). Larger Black-White differences in grade, and within stage of each grade, found in other studies¹⁻³ may reflect sampling variability (ie, small samples of Black patients) and/or selection bias in these non-population based studies. Differences in the years of diagnosis among studies also must be considered, in view of the temporal trends reported here.

While the source of information on race-ethnicity (ie, patient self-report or other) was not described in one report (from a clinical trial),¹ some misclassification of race-ethnicity occurs in SEER and incidence rates are undoubtedly affected by discrepancies between sources of information on race-ethnicity for rate numerators (medical records) vs

denominators (self-reports from censuses).⁹ However, “non-Hispanic White” patients in this study were defined as in other SEER reports.^{2,6,7,9,12} In addition, analyses in this study were conducted for all Whites (N=137,644), instead of non-Hispanic Whites, and results were very similar to those shown; eg, the proportions of high-grade cancers among all Whites was 20.6% (of 24,842) in 1992, and 19.7% (of 17,811) in 1998, similar to the proportions in Table 1.

Differences may exist among studies in grading and/or in coding of tumors.¹¹ One study (from a clinical trial)¹ was able to perform central pathologic review of biopsy specimens for (Gleason) grading; such central review is not feasible for large population-based regis-

tries. SEER re-abstracting and recoding audits have examined stage and extent of disease,¹⁶ and the accuracy of coding the tumor grade for prostate cancers has been studied by the SEER Program; in a re-abstractation audit of a sample of prostate cancers diagnosed in 1998, the error rate for grade was only 5%, and <1% were changed from unknown to known grade.¹⁷

The small and declining Black-White differences in the proportion of high-grade tumors (Table 1), and the larger decline in elderly patients (Table 3), provide little basis for speculation about “intrinsic” Black-White differences in disease aggressiveness or potential implications for treatment.¹⁻³ By 1998 (year of diagnosis), the Black-White differences in proportion of cancers diagnosed at high grade was not statistically significant for all ages combined (Table 1), or for elderly patients (Table 3), even when age and stage differences between Black and White patients were taken into account (for known grade) (Table 4). While temporal changes in type of surgical treatment can affect trends by tumor grade, because removal of larger amounts of tissue may result in assigning a higher grade,¹² Black-White differences in type of surgery (ie, none or biopsy only, transurethral resection, and prostatectomy) were small by 1998. The addition of type of surgery to the models had little effect on the adjusted odds ratio for race-ethnicity (data not shown).

The temporal decline in the Black-White differences in proportions of high-grade cancers in this study (Table 1), at least among elderly patients (Table 3), could reflect a decline in the Black-White differences in prostate-cancer screening rates. For pretreatment PSA level (an indicator of tumor-cell burden at diagnosis), a statistically significant decline from 1988–1995 among Black but not White prostate cancer patients in Chicago suggested that the higher tumor burdens of Black vs White patients were being ameliorated by greater increases in PSA testing among Blacks compared to

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Whites.¹⁸ There are limited survey data on self-reported PSA testing among Blacks vs Whites.^{19,20} Medicare records demonstrated a larger increase in use of PSA tests among Black compared to White beneficiaries after 1987,²¹ although the rate of PSA testing and prostate biopsy combined was still lower in elderly Blacks compared to elderly Whites in 1997. These rates are difficult to measure accurately, however, because Medicare does not reimburse providers for PSA screening tests.²² Further studies of PSA screening rates are needed for Black and White populations, especially by age group (<65 years and 65+ years).

While this study focused on the proportions of high-grade cancers at diagnosis, screening tends to increase the detection of cancer at an early stage, so that Black-White differences in trends in screening rates also could explain the continuing rise in numbers of locoregional cancers among Blacks (Table 1) and the lack of decline in the incidence rate for locoregional stage cancers among Blacks but not Whites in SEER areas (Table 2). The later peak in the incidence rate for locoregional cancers in Blacks compared to Whites (Table 2) could indicate later dissemination of PSA screening among Blacks. Most prostate cancers are diagnosed at the locoregional stage (Table 1), and a later peak in the total incidence rate for Blacks compared to Whites has been reported for SEER areas.^{6,7,12}

Although recent trends in prostate cancer incidence rates for Blacks and Whites may have been strongly affected by trends in screening, the historically higher incidence rates in Blacks compared to Whites in SEER areas (since 1973)^{6,7} are unexplained.²³ The roles of obesity, diabetes and insulin resistance,²⁴ as well as infectious agents,²⁵ need further study. With declining Black-White differences in distributions of stage and grade (as shown in this study), along with small Black-White differences in stage-specific survival rates,⁷ differences in incidence rates are important in re-

lation to the persistent US Black-White disparity in the age-standardized mortality rate of prostate cancer.²⁶

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