

RACIAL DIFFERENCES IN MORTALITY FROM OBESITY-RELATED CHRONIC DISEASES IN US WOMEN DIAGNOSED WITH BREAST CANCER

Objective: Previous studies have focused on racial differences in cancer-specific mortality among US women diagnosed with breast cancer. In view of rising prevalence rates of obesity and persistent racial differences in obesity in the United States, this study considered risk of death from obesity-related causes.

Methods: For 233,329 women diagnosed with invasive breast cancer in 9 SEER areas in 1975–1995, all with at least 5 years of potential follow-up after diagnosis, Cox proportional hazards regression was used to analyze relative risks (RRs) of death (underlying cause) from 4 obesity-related chronic diseases (diabetes mellitus, hypertension, coronary heart disease or CHD, and cerebrovascular disease) for “White,” “African-American,” and “Asian-American” patients.

Results: RRs were statistically significantly higher for African Americans vs Whites for the 4 obesity-related causes, and for diabetes in Asian Americans vs Whites.

Conclusions: Interventions must be designed to address these racial disparities among women diagnosed with breast cancer. (*Ethn Dis.* 2004;14:463–468)

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INTRODUCTION

An estimated 203,500 invasive breast cancers were diagnosed in US women in 2002.¹ The primary-care needs of the large number of breast cancer survivors include weight loss and “careful management of other existing conditions that may affect mortality from either breast cancer or other causes,” such as diabetes mellitus, hypertension, and hyperlipidemia.² For breast cancer patients identified through population-based cancer registries, survival rates improved over time, but racial differences in risk of death from breast cancer persisted, while deaths attributed to causes other than cancer and to unknown cause were excluded.³ In a meta-analysis of studies of patients diagnosed with various cancers (including breast) at comparable stages and who were receiving comparable treatment, exclusion of non-cancer causes of death reduced Black-White differences in survival rates; however, the need to address racial disparities in co-morbid conditions among cancer patients was also recognized.⁴ Co-morbidity at diagnosis is associated with higher risk of death from breast cancer, and from causes other than breast cancer.⁵

For this report, risk of death from obesity-related chronic diseases was examined by race and time period of diagnosis in a large sample of US women diagnosed with invasive breast cancer. Obesity-related diseases are important because of the rising prevalence rates of obesity in the US population, including all racial-ethnic groups, and due to the persistently high prevalence of obesity in African-American women, shown by

measured weight/height⁶ and by self-reported weight/height.⁷

METHOD

The database^{1,8} involved the 9 geographic areas (Atlanta, Ga; Connecticut; Detroit, Mich; Hawaii; Iowa; New Mexico; San Francisco-Oakland, Calif; Seattle, Wash; and Utah) covered since 1975 by the US National Cancer Institute’s Surveillance, Epidemiology and End Results (SEER) Program of high-quality population-based cancer registries. Due to the absence of high-quality cancer registries in some states, SEER data are often used to estimate cancer trends in the entire United States. The database included follow up until date of death, date of last contact if not known to have died, or Dec. 31, 2000. Years of diagnosis were divided into time periods of 1975–1979, 1980–1984, 1985–1989, and 1990–1995, to allow for at least 5 years of potential follow up after diagnosis for all patients. For analyses of 10-year follow up, years of diagnosis 1975–1979, 1980–1984, and 1985–1990 were used.

The 4 obesity-related non-cancer causes of death (underlying cause, coded to ICD 8, 9, or 10) selected were diabetes mellitus (ICD codes 250 or F10–14), hypertension (codes 400–405 or I10–15), coronary (ischemic) heart disease (CHD) (codes 410–414 or I20–25), and cerebrovascular disease (codes 430–438 or I60–69). The estimated attributable risk for obesity is higher for type 2 diabetes (20%–90%) than for the other diseases.^{9,10} Body mass index (BMI) is associated with risk of hyper-

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tension, CHD, and diabetes in both Blacks and Whites,¹¹ and intentional weight loss reduces the risk for at least some of these diseases in both racial groups.¹² Cardiovascular diseases account for a third of the Black-White disparity in premature mortality, or potential years of life lost, due more to hypertension than CHD, but diabetes mellitus is also important.¹³

International Classification of Diseases for Oncology, Version 2 (ICD-O-2) site codes C50.0–50.9 for invasive breast cancer were used, after excluding lymphomas, as in SEER reports.^{1,8} All 237,170 women in the 9 SEER areas diagnosed with invasive breast cancer as their only or first primary cancer in 1975–1995 were originally selected. Included were 208,176 with race coded as “White,” and 17,682 coded as “Black” (African American). “Japanese” (3,527), “Chinese” (2073), and “Filipino” (1,871) were combined, as in a previous study,³ as “Asian American.” Excluded were 1,168 patients of unknown race, and small numbers of patients coded as: “Hawaiian” (1,371); “American Indian/Aleutian/Eskimo” (615); or other specific groups with <200 patients. Analyses using the SEER “Spanish surname or origin” variable are not tabulated because studies have demonstrated substantial misclassification of Hispanics (especially women) in cancer registries,

compared to self-reported Hispanic ethnicity.¹⁴ Only 6,633 patients were coded as “Spanish surname/origin” Whites, and their exclusion from all Whites had little effect on the results (data not shown). Methods used by hospitals to obtain information on race-ethnicity are undocumented.¹⁴ Repeatability of hospital coding may be highest for African Americans, but apparently only small samples of Asian-American patients have been studied.¹⁵

Cox proportional hazards regression was used to obtain relative risks (RRs), or hazard ratios for death, from the selected causes for independent variables (age, race, and time period of diagnosis). The younger mean age at diagnosis for the non-White groups (ie, 57.0 years for African Americans, and 57.1 years for Asian Americans) compared to Whites (61.9 years) affects mortality analyses, but age at diagnosis was included as a continuous variable, while other variables were categorical.

SEER historical stage at diagnosis (ie, local, regional, distant, or unknown)^{1,8} was included in all models of risk of death from breast cancer. Stage was also included in some models for the 4 chronic diseases, because use of certain adjuvant cancer therapies has been associated with adverse cardiovascular effects.² While adjuvant treatment is under-reported in SEER registries, and chemotherapy is not included in the public-use file,⁸ treatment differs by stage, and stage differs by race. Roughly parallel lines for the racial groups, used as strata in stratified models, in log-minus-log (LML) survival plots¹⁶ supported the assumption of proportionality of hazards for race. Survival times were censored at either 5 or 10 years to provide equal duration of follow-up among groups. Confidence intervals (95% CIs) on RRs were based on the normal distribution.¹⁶

RESULTS

Using Whites as the reference category in the proportional hazards mod-

els, adjusted RRs were statistically significantly elevated for African Americans, but not Asian Americans, for all causes, for each of the 4 chronic diseases (diabetes, hypertension, cerebrovascular disease, and CHD), unknown cause, and breast cancer (with stage included in the model) (Table 1). Relative risks (RRs) were statistically significantly reduced for Asian Americans vs Whites for CHD and for breast cancer, but not for hypertension (1.44, not statistically significant). For 10-year follow up, findings were similar except that the RR for diabetes in Asian Americans vs Whites was statistically significantly elevated (Table 1). For death from any of the 4 chronic diseases, racial differences were consistent within each age group: <50 years, 50–59 years, 60–69 years, and 70–79 years. For those aged 80+ years, the risk of death was found to be slightly lower in African Americans than Whites.

In analyses controlling for stage at diagnosis, data for 10-year potential follow up are shown because of larger numbers of deaths than at 5-year follow up. Relative risks (RRs) for death from any of the 4 chronic diseases for African Americans vs Whites, and Asians vs Whites (Table 2), were similar to those shown in Table 1. The RRs adjusted for stage were much lower for death from the 4 chronic diseases than for death from breast cancer (Table 2). Adjusted RRs declined after years of diagnosis 1975–1979, but the racial differences in RRs for death from any of the 4 chronic diseases were evident in a similar model (not shown) limited to diagnoses in 1985–1990. The RRs were 1.31 (95% CI=1.18–1.46) for African Americans vs Whites, and 0.83 (95% CI=0.68–1.01) for Asian Americans vs Whites.

DISCUSSION

Study limitations include the use of SEER data as representative of the entire United States, in the absence of data on

Table 1. Relative risks (RRs) for death from all causes, four chronic diseases, breast cancer, and unknown cause by racial group: Cox proportional hazards regression models

Cause of Death	5-Year Follow-up (Diagnosed 1975–1995)								
	White* (N=208,176)			African American (N=17,682)			Asian American (N=7,471)		
	No.†	RR	No.	RR	95% CI	No.†	RR	95% CI	
All causes	57,506	1.00	6,958	1.81	1.77–1.86	1,379	0.75	0.71–0.79	
Four chronic	8,620	1.00	685	1.55	1.43–1.68	140	0.78	0.62–0.92	
Diabetes	535	1.00	82	2.67	2.10–3.35	16	1.09	0.92–1.27	
Hypertension	396	1.00	75	3.48	2.71–4.47	13	1.44	0.82–2.50	
CHD	5,513	1.00	382	1.36	1.23–1.51	70	0.63	0.49–0.79	
Cerebrovascular	2,176	1.00	148	1.35	1.14–1.59	41	0.93	0.68–1.27	
Breast cancer	34,926	1.00	4,876	1.58	1.53–1.63	926	0.83	0.77–0.85	
Unknown cause	1,525	1.00	203	1.93	1.66–2.23	66	1.28	1.00–1.63	

Cause of Death	10-Year Follow-up (Diagnosed 1975–1990)								
	White* (N=149,032)			African American (N=12,007)			Asian American (N=4,778)		
	No.†	RR	No.	RR	95% CI	No.†	RR	95% CI	
All causes	70,060	1.00	6,844	1.61	1.56–1.65	1,536	0.74	0.7–0.78	
Four chronic	11,502	1.00	798	1.45	1.35–1.56	174	0.76	0.66–0.89	
Diabetes	659	1.00	82	2.36	1.88–2.97	27	1.64	1.11–2.40	
Hypertension	506	1.00	92	3.72	2.98–4.66	13	1.21	0.70–2.10	
CHD	7,418	1.00	445	1.26	1.15–1.39	88	0.61	0.49–0.75	
Cerebrovascular	2,919	1.00	179	1.30	1.12–1.51	46	0.82	0.61–1.09	
Breast cancer	39,192	1.00	4,421	1.43	1.38–1.47	984	0.81	0.76–0.86	
Unknown causes	2,226	1.00	228	1.67	1.45–1.91	77	1.10	0.88–1.38	

Note: Age (continuous variable) and time period of diagnosis were also included in all the models; the models for breast cancer also included stage at diagnosis. White was the reference category for the race variable.

CHD=coronary heart disease; CI=confidence interval.

* Reference category in regression model.

† Number of deaths (total or by underlying cause).

survival of cancer patients throughout the country. Comparisons of cancer mortality rates and trends in SEER areas with the entire United States have shown only small differences, however.¹⁷ Using census data, the SEER population (in 198 counties) is more affluent and more urban than the non-SEER population, but the proportion of the population that is White differs little from all other counties (78.1% vs 80.5%),¹⁸ and SEER registries were selected (in part) to obtain substantial numbers of minority cancer patients.¹⁹

Other limitations include the inability to control for socioeconomic status (SES), because cancer registries have been unable to obtain SES indicators from individual patients. Also, county of residence was the only variable available⁸ for use as an ecologic indicator of SES. In addition, numbers of deaths

from unknown cause were substantial and RRs differed by race (Table 1), and resulting biases in cause-of-death analyses by race are unknown. There are uncertainties in the accuracy of SEER data on race (especially “Asian” groups), the racial groups are heterogeneous, and data using “Spanish surname or origin” were not tabulated. An expert panel of the North American Association of Central Cancer Registries has recommended new guidelines for “indirect” identification of Hispanic persons.²⁰ However, the required data on maiden name, birthplace, and marital status are frequently missing from central cancer registries.²¹

Mortality from breast cancer was not the focus of this study, but breast cancer was the leading underlying cause of death for both 5-year and 10-year follow up (Table 1). The racial differences

in RRs for death from breast cancer (Table 1) are close to those previously reported using SEER data.³ When both treatment and stage are similar, or closely controlled in analyses, however, residual Black-White differences in risk of death from breast cancer may be small, and control for SES is often not included.^{4,22}

The substantial numbers of deaths from the 4 obesity-related non-cancer causes (Table 1) are consistent with evidence from studies of smaller samples of breast cancer patients.^{5,23} Among 1,800 post-menopausal patients diagnosed in 1992 at age 55+ years from 6 SEER registries, 51.3% of the 263 deaths in the 30-month follow up were from breast cancer (underlying cause), and 17.1% from heart disease.³ In the present study, which included all ages at diagnosis, the 4 chronic diseases ac-

Table 2. Relative risks (RRs) for death within 10 years after diagnosis of breast cancer, including stage at diagnosis of breast cancer: Cox proportional hazards regression models

Predictor	Underlying Cause of Death			
	Breast Cancer		Any of Four Chronic Diseases*	
	RR	95% CI	RR	95% CI
Year of diagnosis				
1975–1979	1.00	Referent	1.00	Referent
1980–1984	0.93	0.91–0.95	0.80	0.76–0.83
1985–1990	0.76	0.74–0.78	0.66	0.63–0.68
Stage				
Local	1.00	Referent	1.00	Referent
Regional	3.42	3.34–3.50	1.17	1.12–1.21
Distant	17.64	17.13–18.16	1.59	1.45–1.74
Unknown	4.50	4.31–4.70	1.32	1.22–1.42
Race				
White	1.00	Referent	1.00	Referent
African American	1.43	1.38–1.47	1.42	1.32–1.53
Asian American	0.81	0.76–0.86	0.77	0.66–0.89

Note: Age at diagnosis (as a continuous variable) was also included in both models.
 CI=confidence interval.
 * See Table 1 and text.

counted for 9,445 deaths at 5-year follow up, and 12,474 at 10-year follow up (Table 2), or about 15% of all deaths. For 10-year follow up of patients diagnosed at age 60+ years, the figure was 22.4% (11,723/52,309). The temporal decline in RRs for any of the 4 obesity-related chronic diseases, relative to the earliest period of diagnosis (1975–1979) (Table 2), is consistent with the temporal declines in hypertension, cerebrovascular disease and CHD in US women in all race and sex groups.⁹ Most of the decline in CHD mortality since 1980 may reflect improved medical care of CHD patients.^{9,24}

It might be hypothesized that medical follow up of patients during the first few years after the diagnosis of breast cancer could result in smaller racial differences in risk of death from non-cancer chronic diseases than those found in the general US population. However, racial differences in RRs were apparent both at 5 and 10 years of potential follow up (Table 1). Noteworthy in this regard are the higher RRs for Black,

compared to White, breast cancer patients for diabetes, hypertension, CHD and cerebrovascular disease, vs the higher RRs for death from diabetes, but not CHD or cerebrovascular disease, in Asian American vs White patients, using 10-year follow up (Table 1). These latter findings among breast cancer patients are similar to those for the general US population,⁹ showing that age-adjusted mortality rates for diseases of the heart in 1999 were 35% higher for African-American females compared to Whites, and 56% lower for Asian Americans/Pacific Islanders than for Whites, whereas 1999 mortality rates for diabetes were higher for both Blacks and Asian/Pacific Islanders than for Whites.²⁵ Asian Americans, or specific subgroups (especially Japanese Americans), have higher prevalence rates of type 2 diabetes mellitus than Whites, and an increased prevalence of nephropathy,²⁶ despite exhibiting lower BMI; one possible explanation involves central adiposity.²⁷ Rising breast cancer incidence rates in the Asian-American female population covered by the Los Angeles County CA

SEER registry, mainly for Japanese Americans,²⁸ suggest that diabetes control in Asian-American breast cancer patients will increase in importance.

Chemotherapy and radiotherapy for breast cancer have been associated with a slightly elevated risk of death from heart diseases,³ although a recent cohort study found no evidence for excess morbidity and mortality from CHD after 10 years of follow up among women treated with radiotherapy to the left breast.²⁹ The impact of cancer treatment on racial differences in cardiovascular disease mortality among breast cancer patients is unlikely. While routinely reported SEER data on adjuvant therapy are incomplete, other evidence suggests that use of adjuvant treatments for breast cancer tends to be less frequent in minority groups than in Whites.^{30,31} Also, while later stage at diagnosis is associated with receipt of chemotherapy,³⁰ the results of Cox proportional hazards models for risk of death from the 4 chronic diseases were similar, whether stage was excluded (Table 1) or included (Table 2). A recent study found lower risk of hospitalization for acute myocardial infarction among elderly survivors of early-stage postmenopausal breast cancer, compared to other Medicare beneficiaries, possibly due to the effects of treatment of some breast cancer patients with the selective estrogen receptor modulator tamoxifen.³²

The much smaller adjusted RRs for later vs earlier stage at diagnosis for death from any of the 4 chronic diseases than for death from breast cancer (Table 2) suggest limited inaccuracies in distinguishing breast cancer from other chronic diseases as the underlying cause of death.³³ The weak association between stage at diagnosis and risk of death from chronic diseases (Table 2) also could reflect uncontrolled effects of SES, as well as a possible impact of the poorer health status of late-stage breast cancer patients on mortality from non-cancer causes of death.⁵

The higher prevalence of obesity in

The higher prevalence of obesity in African-American women, compared to Whites,^{6,7} is undoubtedly only one factor explaining the racial differences in risk of death from the chronic diseases examined.

African-American women, compared to Whites,^{6,7} is undoubtedly only one factor explaining the racial differences in risk of death from the chronic diseases examined. Among elderly US breast cancer patients in SEER areas, Medicare data have shown statistically significantly lower odds ratios for African-American vs White women for receipt of two or more preventive services, including blood lipid testing.³⁴ Similar studies are needed, and should include younger patients and other specific preventive health services in various racial-ethnic groups. Tailored interventions have been advocated to improve quality of management of chronic conditions, with a national goal of reducing or eliminating racial-ethnic disparities in rates of cardiovascular disease and diabetes.³⁵ This goal should include addressing racial disparities in deaths from chronic diseases among breast cancer patients. Weight gain may occur after chemotherapy for breast cancer.³⁶ Clinical trials on reducing weight,³⁶ along with changing diet and exercise patterns should be designed for breast cancer patients^{37,38} in order to establish interventions for further reducing risks of death from chronic diseases, and addressing racial disparities in these risks. Analyses of racial-ethnic disparities will be enhanced by data on survival for Los Angeles County, and San Jose-Monterey, Calif, beginning with diagnoses in 1992, and for addi-

tional registries including the rest of California, which were added to the SEER Program in 2002.¹

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