Breast Cancer Incidence in Young Women by Estrogen Receptor Status and Race

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Abstract: A population-based study was utilized to calculate breast cancer incidence rates in White and Black women, ages 30 to 54, according to tumor estrogen receptor status. Both racial groups had higher incidence curves for estrogen receptor negative breast cancer between ages 30 and 49. There was an excess of receptor negative cancer in young Black women, an observation that may help explain the racial disparity in breast cancer survival. (*Am J Public Health* 1989; 79:71–73.)

Introduction

Clinical studies suggest that estrogen receptor analysis should be performed on all primary breast cancers because results provide valuable therapeutic and prognostic information.[1] The presence (estrogen receptor positive) or absence (estrogen receptor negative) of specific estrogen binding protein in breast cancer is related to the biologic characteristics of the tumor. Receptor negativity is associated with larger tumor size and more rapidly proliferating tumor tissue.[2,3] Estrogen receptor status also varies according to some breast cancer risk factors, notably age, menstrual status, and race.[4–11] Despite evidence that receptor results are correlated with prognostic and risk variables, we are aware of only one study that has examined the incidence of breast cancer stratified by receptor results and that study was limited to a predominantly Caucasian population.[12] The present report provides incidence rates of estrogen receptor positive and estrogen receptor negative breast cancer separately for White and Black women based on data collected by a population-based cancer registry.

Methods

Data from the Georgia Center for Cancer Statistics, an affiliate of the Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute, were used to estimate breast cancer incidence rates according to estrogen receptor status. All cases of newly diagnosed, pathologically confirmed breast cancer among women 30–54 years of age were identified during the period of December 1980 through December 1982. Estrogen receptor assay results, abstracted from medical records, were available on 82.4 per cent of the 637 breast cancer cases ascertained during the two-year period (Table 1). Overall, two-thirds of the tumor specimens were assayed at the same laboratory, and 98.6 per cent of the samples were assayed by the standard multipoint titration method using dextran-coated charcoal.[7]

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TABLE 1—Number of Incident Breast Cancer Cases Diagnosed by Age and Estrogen Receptor Status, Atlanta, Georgia, 1980–82

Age (years)	Total No. Cases	Estrogen Receptor Status			
		Positive	Negative	Borderline	Unknown
30–34	55	15	33	2	5
35–39	114	36	57	1	20
40–44	133	45	62	5	21
45–49	174	58	69	6	41
50–54	161	77	54	5	25
Total	637	231	275	19	112

There were 231 estrogen receptor positive, 275 estrogen receptor negative, and 19 estrogen receptor borderline (i.e., equivocal results) breast cancers. (Estrogen receptor borderline tumors behave clinically like receptor negative tumors[1,2]; these 19 cases were therefore combined with the estrogen receptor negative group.) Women of other races (n = 3) and those with unknown receptor values (n = 112) were excluded from the calculation of incidence rates. The percentage of women with unknown receptor values did not differ by race: Whites, 17.9 per cent; Blacks, 16.9 per cent. Within each race, the percentage of unknown receptor values was greatest for women ages 45–49 years: Whites, 22.5 percent; Blacks, 28.6 per cent; the racial distribution of cases with unknown receptor results (Whites, 78.6 per cent; Blacks, 21.4 per cent) was similar to that of cases included in the analysis (Whites, 77.6 per cent; Blacks, 22.4 per cent). Population estimates for age and race were obtained from the US Census, and are specific for the five metropolitan counties served by the Atlanta cancer registry.[13]

Results

The overall breast cancer incidence rates increased with age. Rates of estrogen receptor negativity were higher than rates of estrogen receptor positivity in each five-year age group up to the ages of 50–54 years, where the curves crossed, a pattern generally consistent for Whites (Figure 1) and Blacks (Figure 2). However, the differential between curves for Black women was substantially wider than that for Whites, and Black women ages 30–44 years had higher incidence rates of estrogen receptor negative breast cancer than Whites.

Incidence rate ratios were calculated by age and receptor status (Table 2). Although most of the 95 per cent confidence intervals (CI) include unity, Whites generally have higher receptor positive cancer rates than Blacks among the age groups 35–54 years; Black women ages 30–44 had an excess of estrogen receptor negative cancer.

Logistic regression[14] was used to evaluate the potential confounding effects of stage of disease and laboratory variability on differences in receptor status between Whites and Blacks. The overall age-adjusted risk estimate for an estrogen receptor negative (as opposed to an estrogen receptor positive) tumor in Blacks compared to Whites was 1.9 (95 per cent

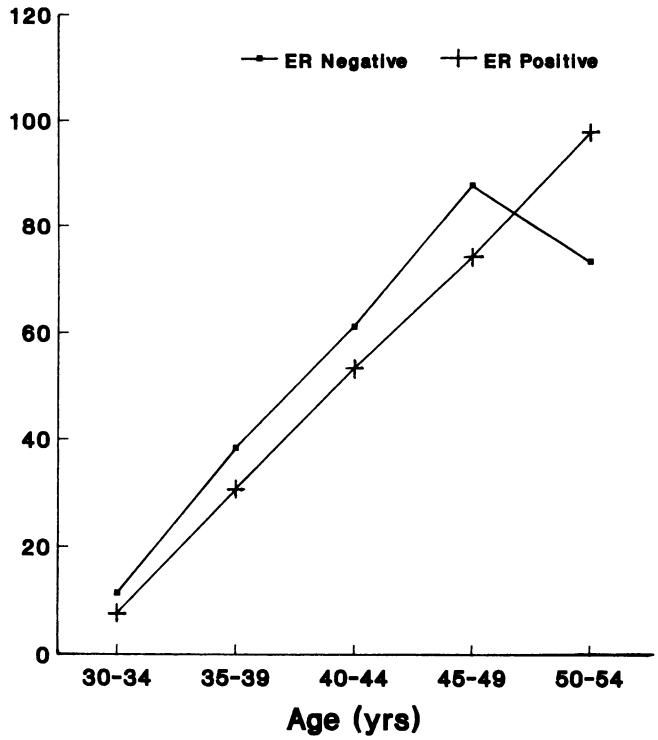

FIGURE 1—Average Annual Age-Specific Breast Cancer Incidence per 100,000 White Women

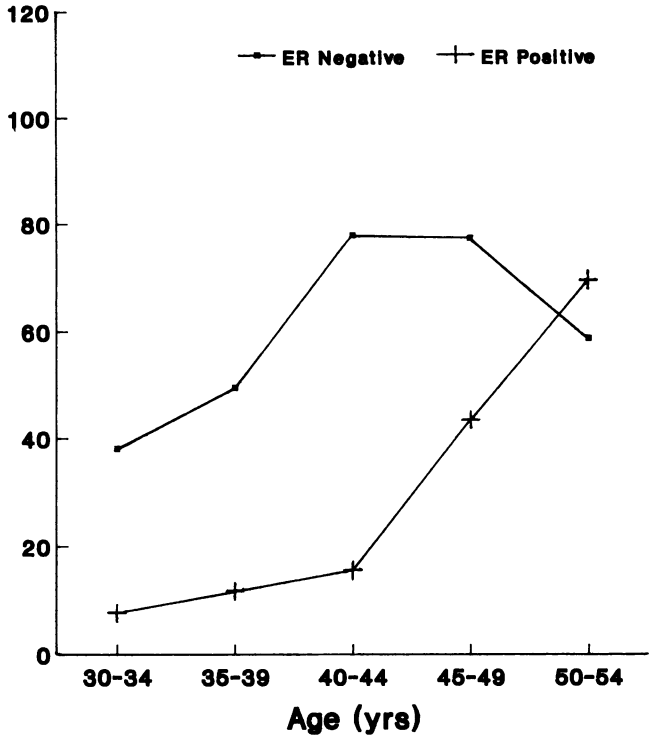

FIGURE 2—Average Annual Age-Specific Breast Cancer Incidence per 100,000 Black Women

CI = 1.2, 3.1) and did not change materially after adjustment for stage of disease at diagnosis or laboratory where the receptor assay was performed.

Discussion

The results of this study may have been influenced by a number of factors. Estrogen receptor results were unavailable for 17.6 per cent of the cases identified for study, but the age and race distributions of these cases did not differ substantially from those of cases included in the analysis. Exclusion of women with unknown receptor values resulted in slightly lower age-specific incidence rates for Whites and Blacks. If women with unknown receptor status had a distribution of estrogen receptor results similar to those with known status, the age-specific incidence patterns would be similar to those presented here.

Laboratory variability was not a factor. The majority of tumor specimens (for both Whites and Blacks) in this series of cases were analyzed at the same laboratory utilizing the same methodology. Furthermore, based on multivariate analyses, Blacks had a higher risk estimate than Whites for estrogen receptor negative (versus receptor positive) cancer, controlling for laboratory.

Multivariate analyses showed a higher risk estimate for estrogen receptor negative cancer (as opposed to estrogen receptor positive cancer) in Blacks compared to Whites after adjusting for age and clinical stage at diagnosis. Thus it does not appear that differences in extent of disease explain the observed differences in White:Black breast cancer rates by age and receptor status.

These age- and race-specific patterns of incidence rates for breast cancer are consistent with prior clinical and epidemiologic observations of an increase in the proportion of estrogen receptor positive cancer with advancing age,[4,5,10,12] and a lower prevalence of estrogen receptor positive breast cancer among Black women compared to White women.[5,8–10] The data suggest that younger women and Black women may be more likely to develop a more aggressive form of breast cancer, i.e., estrogen receptor negative disease.

Estrogen receptor negativity is associated with shorter disease-free intervals and survival in some cases.[1,2,15] In addition, Black women apparently have a lower proportion of receptor positive breast cancer compared to their White counterparts, in pre- and postmenopausal groups,[6,10,16] partly because they have more advanced disease at diagnosis and a higher proportion of poorly differentiated tumors.[6,16,17] The present analysis suggests that Blacks are at higher risk of estrogen receptor negative (as opposed to receptor positive) breast cancer than Whites, after adjustment for age and stage of disease at diagnosis.

Racial variation in estrogen receptor results has been

TABLE 2—White:Black Incidence Rate Ratios* by Age and Estrogen Receptor Status, Atlanta, Georgia, 1980–82

	Estrogen Receptor Status			
	Positive		Negative	
Age (years)	Point Estimate	(95% CI)**	Point Estimate	(95% CI)**
30–34	0.99	(0.31, 3.17)	0.30	(0.16, 0.56)
35–39	2.63	(0.97, 7.16)	0.77	(0.44, 1.37)
40–44	3.43	(1.31, 9.00)	0.79	(0.47, 1.33)
45–49	1.71	(0.85, 3.44)	1.14	(0.65, 1.98)
50–54	1.41	(0.78, 2.55)	1.25	(0.65, 2.40)

*Rate per 100,000 women per year in Whites divided by rate in Blacks.
**Test-based 95% confidence intervals.

hypothesized as one explanation for the observed Black-White differences in breast cancer survival.[6,8,16,18] The present data provide further evidence that receptor negative breast cancer in Black women may be a contributing factor to their survival disadvantage. Future studies of Black-White differences in breast cancer survival should account for tumor estrogen receptor status.

ACKNOWLEDGMENTS

This study was conducted under an interagency agreement between the National Institute of Child Health and Human Development and the Centers for Disease Control, Atlanta, Georgia, with additional support from the National Cancer Institute, Bethesda, Maryland; and with contracts from CDC (200-80-0556) and NCI (N01-CN-61027 and N01-CN-55429) to the Georgia Center for Cancer Statistics.

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Bowel Function and Breast Cancer in US Women

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Abstract: We studied bowel function in relation to 123 breast cancer cases among 7,702 women from the US NHANES I Epidemiologic Follow-up Study. Results suggest a slight increased risk of breast cancer for both decreased frequency of bowel movements (relative risk = 1.5, 95% confidence interval = 0.8, 2.7) and firm stool consistency (RR = 1.8, 95% CI = 1.0, 3.2.) These observations are consistent with an hypothesized association between constipation and increased risk of breast cancer. (*Am J Public Health* 1989; 79: 73–75.)

Introduction

There is indirect evidence that bowel function may be related to breast cancer risk. Petrakis and King found severe constipation (fewer than three bowel movements per week) to be associated with cytologic abnormalities in epithelial cells from breast fluid,[1] which are related to epithelial dysplasia in breast tissue.[2] Atypical proliferative breast disease is a significant risk factor for breast cancer in women; we, and others, have shown the risk to increase with increasing degree of epithelial atypia.[3,4]

Putative mutagens and carcinogens have also been detected in nipple aspirates of breast fluid.[5] Although the precise origin and mechanism of carcinogen delivery to the breast tissue are unknown, involvement of fecal mutagens, bowel function, and the enterohepatic circulation has been hypothesized. Intestinal bacteria produce carcinogens and mutagens, presumably through their actions on dietary constituents and/or bile acids.[6–8] Breast secretory (apocrine) epithelia selectively absorb and concentrate substances from the circulation originating from the gastrointestinal tract.[1,6,9]

Constipation, which results in greater contact time of stool in the intestine and hard stool consistency, may increase formation and absorption of fecal mutagens into the enterohepatic circulation and delivery to breast tissue.[10,11] We describe the first study relating aspects of bowel function directly to the risk of breast cancer in a cohort of women in the first National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study.

Methods

NHANES I and its augmentation survey were conducted by the National Center for Health Statistics (NCHS) from 1971 to 1975.[12,13] These surveys provided cross-sectional information on medical history, anthropometric, biochemical, clinical, demographic, and nutritional factors in a large sample selected to represent the non-institutionalized popu-

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