

Breast Cancer: Factors Associated With Stage at Diagnosis in Black and White Women

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Background: Numerous studies have reported differences in cancer staging at diagnosis and in survival between Black and White patients with breast cancer. Utilizing data obtained from the National Cancer Institute's (NCI's) Black/White Cancer Survival Study for the period 1985-1986, a new study is presented here that systematically examines multiple explanatory factors (e.g., lack of mammograms) associated with these cancer-staging differences. **Purpose:** We evaluated within a single study the relationship of selected demographic, lifestyle, antecedent medical experiences, and health care access factors to cancer staging at diagnosis in Black and White breast cancer patients. **Methods:** Data utilized in this population-based cohort study of 1222 eligible women (649 Black and 573 White) newly diagnosed for the period 1985-1986 with histologically confirmed primary breast cancer were obtained from the NCI's Black/White Cancer Survival Study. Sources of data included abstracts of hospital medical records, central review of histology slides by a study consultant pathologist, and patient interviews obtained from three metropolitan areas: Atlanta, New Orleans, and San Francisco-Oakland. Within each area, 70% of all Black incident cases were randomly selected, and a sample of White cases, frequency matched by age groups (20-49 years, 50-64 years, and 65-79 years), was selected for comparison. Stage of breast cancer at diagnosis was classified according to the international tumor-lymph node-metastases (TNM) system. Statistical models utilized in this study included the log-linear and polychotomous logistic regression with multiple predictor variables. **Results:** Factors associated with cancer staging were differentially expressed in Blacks and Whites. Indicators of access to health care, a lack of mammograms, and an increased body mass index significantly ($P < .02$) contributed to stage differences in Blacks, whereas income was marginally associated ($P = .06$) with stage for Whites only. Nuclear grade, having a breast examination by a physician, and a history of patient delay explained approximately 50% of the excess risk for stage III-IV cancer versus stage I-II_{N0} cancer among Blacks compared with Whites (odds ratio reduction from 2.19 to

1.68). **Conclusion:** These findings suggest that no single factor or group of factors can explain more than half of the race-stage differences noted in this study with respect to Black and White breast cancer patients. [J Natl Cancer Inst 85:1129-1137, 1993]

Numerous studies have reported differences in disease stage at diagnosis (1-7) and in survival (1,2,8-12) between Black and White female patients with breast cancer. During the last quarter of a century, the National Cancer Institute's (NCI's) End Results Program as well as Surveillance, Epidemiology, and End Results (SEER)¹ data have shown an increase in the 5-year relative rate of survival from breast cancer from 46% to 64% in Blacks and from 63% to 76% in Whites (13,14). Comparative studies in Blacks and Whites by the Commission on Cancer of the American College of Surgeons (1,2), the SEER Program (8), and other investigators (10) indicate that the poorer 5-year relative survival rate in Blacks with breast cancer is due, in part, to the advanced stage of the disease at diagnosis. Advanced stage of breast cancer at diagnosis has been associated with age (15-18), delay in diagnosis (3,19-22), low socioeconomic status (4,23,24), obesity (5,6,25-27), and poor preventive health care practices of patients (21,22,28-31). The contributions of these and other factors to the observed differences in stage distributions between Black and White patients with breast cancer have not been systematically examined.

In 1983, the NCI implemented a study of the differences in survival among Black and White patients with breast cancer in the United States (32). This population-based cohort study examined social, behavioral, lifestyle, and biological factors as well as treatment and health care system factors that may contribute to the observed racial differences in the 5-year relative survival rate among women with breast cancer. One of the study hypotheses was that differences in stage at diagnosis may be due to differential

*See "Notes" section following "References."

behavioral patterns in the races. For example, it was hypothesized that Black patients might report less screening activity, have fewer asymptomatic detections, and have a longer duration of symptoms prior to seeking treatment than White patients (32).

The present investigation by the NCI's Black/White Cancer Survival Study Group is unique in that it assesses in a single study the relationship of sociodemographic, behavioral, clinicopathologic, and health care access factors to differences in stage at diagnosis of breast cancer in Black and White patients.

Patients and Methods

Study Population

Between January 1, 1985, and December 31, 1986, data on eligible women with newly diagnosed, histologically confirmed primary breast cancer were sampled from all hospital pathology records of cases ascertained in three metropolitan areas: 1) Atlanta, Ga., 2) New Orleans, La., and 3) San Francisco-Oakland, Calif. The study design and methods have been described in detail previously (32). Overall, 70% of all Black incident breast cancer cases were randomly selected from each metropolitan area, and a sample of White breast cancer cases, frequency matched by age groups (20-49 years, 50-64 years, and 65-79 years) within each metropolitan area, was selected for comparison to adjust for the tendency of Blacks to be younger than Whites at diagnosis. Monitoring and adjustment of the patient selection rates during the study resulted in an increase in the overall sample size target and a slight imbalance in the race distribution (53% Blacks and 47% Whites) (32). A total of 1222 eligible women (649 Blacks and 573 Whites) was entered in the study.

Sources of Data

Data were collected from three sources: 1) abstracts of hospital medical records ($N = 1222$), 2) central review of histology slides by a study consultant pathologist (R. J. Kurman) ($N = 1200$), and 3) patient interviews ($N = 1013$). Informed consent was obtained from all participants. Trained interviewers administered the questionnaire to patients either at home (85%), in a nonclinical setting (10%), by telephone (4%), or in a hospital or clinic (1%). Eighty-seven percent of interviews were performed within 6 months of diagnosis. Seventeen percent of patients (122 Blacks [18.8%] and 87 Whites [15.2%]) were not interviewed for one of the following reasons: physician refusal (2.9%); physician ill, deceased, or moved (2.0%); patient refusal (7.4%); patient ill, deceased, or moved (3.1%); or other reasons (1.8%). Additional information required for disease staging was obtained by a centralized review of operative and surgical pathology reports and from the physicians' office records.

Staging Criteria

Disease stage at diagnosis was classified according to the international tumor-lymph node-metastases (TNM) system for breast cancer based on postsurgical pathologic evaluation criteria of the American Joint Committee on Cancer (33). The tumor size, number of lymph nodes, degree of chest wall and skin involvement, tumor histology, type of surgical procedure, and the extent of metastatic work-up were evaluated in the assignment of stage. In addition to medical record abstractions, information from the physicians' office records was reviewed to ascertain if, as a minimum, a chest x ray (stage I or II disease) or a chest x ray and a bone scan (stage III or IV disease) had been performed as part of the diagnostic evaluation. A breast cancer staging algorithm incorporating the above-mentioned criteria was developed by a working group on staging of the Black/White Cancer Survival Study Group. Discrepancies were resolved by one of the authors (H. B. Muss).

Variables

The following demographic variables were used in this analysis: marital status, education, and total family income. Lifestyle variables were smoking history and body mass index as described by Abraham (34). The body mass index was based on the patient's reported usual weight (kg)/height ($m^{1.5}$). Overweight women were defined as women with a body mass index of $34 \text{ kg}/m^{1.5}$ or higher. Reproductive history variables were parity and history of use of oral contraceptive pills.

Factors used to measure a patient's preventive health care behavior during the 6 years prior to breast cancer diagnosis were a history of breast self-examination, of breast examination by a physician, and of mammography.

The history of patient delay was defined as the length of time from the patient's recognition of a symptom to her first visit to a physician for evaluation of that symptom. It has four categories: 1) no delay, consisting of asymptomatic patients whose breast abnormality was discovered by routine examination, screening, or evaluation for other illness; 2) symptomatic, with first medical consultation less than 8 weeks after symptom recognition; 3) symptomatic, with first medical consultation 8 or more weeks after symptom recognition; and 4) symptomatic, with unknown time from symptom recognition to first medical consultation.

Comorbidities were the current medical diseases or conditions (e.g., diabetes mellitus, heart disease, hypertension, or other chronic conditions) that the patient had at the time of hospital admission when a diagnosis of breast cancer was made.

The following factors were used to indicate an individual patient's reported access to medical care: the type of health insurance and usual source of medical care (private physician or private clinic, health maintenance organization [HMO], hospital outpatient or emergency room or public clinic, or none).

The following biological parameters of the tumor were used: estrogen receptor levels in femtomoles per milligram cytosol protein (positive, ≥ 10 ; borderline, 3 to 9; negative, 0 to <3); tumor grade (architectural grade [well differentiated, moderately well differentiated, poorly differentiated, or unknown]) and nuclear grades 1, 2, and 3 ranging from best to worst prognosis).

Statistical Methods

Differences between Blacks and Whites in breast cancer stage at diagnosis and the distribution of selected characteristics were evaluated by a chi-square test for independence and, where appropriate, by a chi-square test for trend (35). Analyses of factors associated with stage and race were performed for all stages (in situ, I, II_{N0}, II_{N1}, III, and IV) and for invasive stage cases only. Some analyses were also done in which the group of asymptomatic women with no history of patient delay was excluded. In order to achieve adequate numbers in some analyses, stage levels were collapsed from five to three levels of invasive stage by combining the lymph node-negative patients with stage I disease with lymph node-negative patients with stage II disease as well as combining patients with stage III disease with those with stage IV disease, based on similarity of expected prognosis. The effect of combining these stages was evaluated and found to satisfactorily preserve the relationship between race and stage.

The relationship between each factor and stage was evaluated for Blacks and Whites separately in log-linear models controlling for the effects of metropolitan area of residence and age group on stage and the factor (36). Those factors that showed a statistically significant association with stage at the $P < .10$ level in either Blacks or Whites were further examined in tables cross-classifying race, stage, metropolitan area of residence, age group, and the factor of interest, with nested log-linear models used to assess the association between race and stage controlling for these other variables (36). These models were converted to equivalent polychotomous logistic regression models, with the response variable defined in terms of each stage category with the lowest invasive stage category (I-II_{N0}) as baseline stage (35). Log-linear models were used as an effective way to quickly evaluate many model terms and check for high-order interactions and sparse data problems, whereas logistic models provided a more readily interpretable and simple summary, inasmuch as only those factors associated with stage were explicitly retained in the model. With Whites as

the reference group, adjusted odds ratios with 95% confidence intervals were computed.

Explanatory factors that showed a statistically significant association with stage at diagnosis in both Blacks and Whites were examined further in polychotomous logistic regression models with multiple predictor variables. Initially, these factors were simultaneously included in a model with race, metropolitan area of residence, and age group. Factors were then sequentially eliminated on the basis of the least statistically significant contribution to the explanatory power of the model, as assessed by the difference in log-likelihood chi-square results between models with and without a given factor present.

Results

Disease Stage at Diagnosis

The frequency distribution of the 649 Black and 573 White breast cancer patients by stage at diagnosis is shown in Fig. 1. There was a highly significant association between race and stage at diagnosis ($P < .00005$). Among the 65 cases (5.3%) with incomplete information on stage at diagnosis, 31 were reported as invasive breast cancer with insufficient additional documentation available, 23 had missing data for pathology-defined nodal status, and 11 had unknown tumor size. The percentage with unknown stage differed only slightly between Blacks and Whites, and unknown stage cases ($N = 65$) were excluded from all subsequent analyses.

To evaluate whether differences in the quality of medical evaluation contributed to understaging within a given stage, we examined the completeness of the metastatic evaluation used for staging. The median number of lymph nodes examined at surgery was 16 in both races. More than 95% of patients with invasive cancer ($N = 1065$) had a chest x-ray procedure, with no difference in distribution of chest x rays by race and stage. Overall, 44% of the 799 patients with stage I and II disease had a bone scan compared with 77% of the 266 patients with stage III and IV disease. The use of bone scans to assess extent of disease did not differ by race and stage, except in the 193 patients with stage III disease,

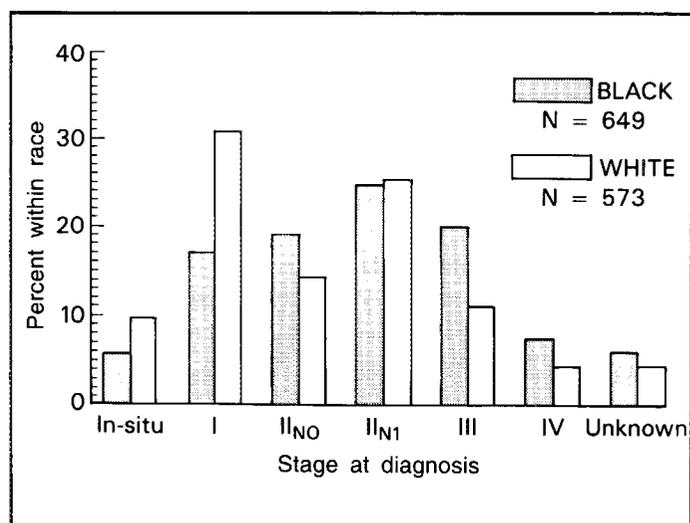


Fig. 1. Distribution of breast cancer stage at diagnosis by race. The association between race and stage at diagnosis had high statistical significance ($P < .00005$).

among whom 71% of Blacks and 83% of Whites had bone scans. There was no indication from the diagnostic parameters examined that understaging within a given stage was likely to account for differences in stage at diagnosis between Black and White breast cancer patients.

Differences between Blacks and Whites in breast cancer stage at diagnosis were also assessed according to interview status, since factors used in these analyses such as income and usual source of medical care were available only for interviewed patients. Blacks had a more advanced disease stage at diagnosis for all case patients and for interviewed case patients. Since women with a more advanced stage of disease might be less willing or able to complete the interview portion of the study, relationships between race, stage, and interview status were examined. There was no statistical association between race and interview status ($P = .40$). There was, however, an association between stage and interview status ($P = .0001$), with the proportion of stage III and IV cases greater among the noninterviewed group in both races. Examination of the effect of race in combination with stage and interview status suggested that the association was independent of race. Odds ratios for race by interview category showed patients with unknown disease stage to be about 3.3 times more likely to be Black in the noninterviewed group and about equally as likely to be Black in the interviewed group.

Metropolitan Area of Residence and Age Group Differences in Stage at Diagnosis

Although we controlled for metropolitan area of residence and age group in the study design, we examined the degree to which the race-stage relationship varied by these factors. Differences observed in the race-stage relationship by metropolitan area of residence adjusted for age group were not statistically significant. Fig. 2 shows odds ratios for Blacks and Whites by age group adjusted for metropolitan area of residence. Among patients younger than 50 years, those with in situ disease were significantly more likely to be White, whereas those with stage III-IV disease were significantly more likely to be Black. For example, the odds ratios for Blacks versus Whites under age 50 years were 0.35 (95% confidence interval = 0.17-0.72) for in situ cancers and 2.01 (95% confidence interval = 1.22-3.33) for stage III-IV disease. Among women aged 65-79 years, no statistically significant differences by race were seen. This variation in the race-stage relationship by age group was marginally significant ($P = .07$).

Comparison of Selected Characteristics of Black and White Patients With Breast Cancer

Table 1 presents the racial distribution of selected demographic, lifestyle, antecedent medical experiences, and health care access characteristics among patients with breast cancer. All of these factors were statistically different between the races ($P < .001$). Compared with Whites, Blacks were more likely to have less than a high school education and a lower total family income as well as to be overweight.

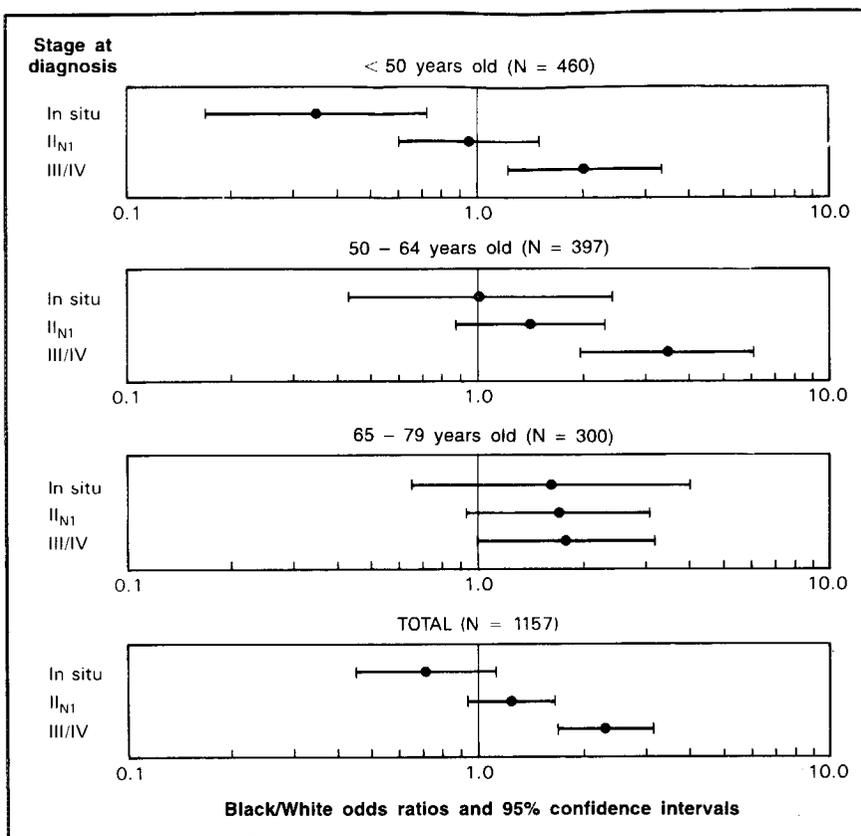


Fig. 2. Age group differences in breast cancer stage at diagnosis for Black and White patients. Odds ratio and 95% confidence interval for Blacks and Whites are shown by age group adjusted for metropolitan area of residence. Odds ratios are from logistic regression model for polychotomous response (35). Each point estimates the ratio of Blacks to Whites in the specified stage divided by the ratio of Blacks to Whites in the reference stage (I/II_{N0}). Horizontal bars indicate 95% confidence intervals. The variation in the race-stage relationship by age groups was marginally significant ($P = .07$).

In addition, Blacks were more frequently never married, were more often current smokers, had a greater history of comorbidities, were more frequently multiparous, and had less history of oral contraceptive use (data not shown). The majority of patients in both races reported coverage by a private health insurer, and the usual source of medical care was provided by a private physician or in a private clinic setting. However, a greater proportion of Blacks than Whites either had no insurance or received health care services through public assistance (Medicaid/welfare). Likewise, for a greater proportion of Blacks, the usual source of medical care was through the hospital outpatient clinic or emergency room or a public clinic facility. Most patients in both races reported practicing breast self-examination (data not shown) and having had a breast examination by a physician. When we excluded asymptomatic patients, the distribution of time from recognition of symptoms related to breast cancer to seeking medical consultation was similar in both races. Fewer Blacks than Whites, however, reported having had previous mammograms.

Also presented in Table 1 are biological characteristics of the breast cancers in the patients. Estrogen receptor data were available for 82% of patients (data not shown). Principal reasons for a lack of estrogen receptor data were related to small tumor size and early stage with insufficient tissue available for examination. The observed proportion of estrogen receptor-positive tumors was somewhat lower, and poorly differentiated tumors and increased nuclear atypia were more frequent among Blacks than among Whites. Except for estrogen receptor status ($P = .07$), the distribution

of all biological features of examined tumors was statistically different between the races at $P < .001$.

Association Between Race and Disease Stage After Controlling for Other Risk Factors

Using a partial association model, we examined the relationship between selected factors and disease stage at diagnosis among Blacks and Whites. Since biological and pathologic markers of the tumor were, in general, only relevant for patients with invasive cancer, separate analyses were conducted for all stages and for invasive stages only. In both races, markers of the biological behavior of the tumor (architectural grade and nuclear grade) were significantly associated with stage ($P < .01$), with an excess of poorly differentiated tumors and increased nuclear atypia found in patients with a higher disease stage. A recent history of a breast examination by a physician was significantly associated (Blacks, $P < .01$; Whites, $P < .04$) with lower disease stage. A history of patient delay was positively related to higher stage in both races ($P < .00005$). The association between history of patient delay and stage remained statistically significant even when we excluded asymptomatic patients diagnosed through screening (Blacks, $P = .0001$; Whites, $P = .01$). Factors associated with limited access to health care (health insurance [$P < .01$] and usual source of medical care [$P < .003$]), larger body mass index ($P < .02$), and lower mammography use history ($P < .004$) were significantly associated with higher disease stage among Blacks only. Lower income was marginally associ-

Table 1. Summary of selected characteristics in Black and White women with breast cancer

Characteristic*	Black patients (N = 610)		White patients (N = 547)	
	No.	%†	No.	%†
Demographic				
Education				
Less than high school	211	42.2	60	13.0
High school	145	29.0	154	33.3
College or above	144	28.8	248	53.7
Unknown	110	(18.0)	85	(15.5)
Total family income				
<\$10000	190	43.1	39	9.2
\$10000-\$19999	120	27.2	87	20.4
\$20000-\$34999	78	17.7	118	27.7
≥\$35000	53	12.0	182	42.7
Unknown	169	(27.7)	121	(22.1)
Lifestyle				
Body mass index, kg/m^{1.5}				
<26	43	8.0	85	17.2
26-27	34	6.4	104	21.0
28-33	206	38.6	231	46.7
≥34	251	47.0	75	15.1
Unknown	76	(12.5)	52	(9.5)
Antecedent medical experiences				
History of patient delay				
No delay‡	32	5.2	82	15.0
Symptomatic, <8 wk	286	47.0	232	42.6
Symptomatic, ≥8 wk	127	20.9	92	16.9
Symptomatic, unknown	164	26.9	139	25.5
Unknown	1	(0.2)	2	(0.4)
Physician breast examination				
Yes	384	77.7	414	89.4
No	110	22.3	49	10.6
Unknown	116	(19.0)	84	(15.4)
Mammography				
Yes	122	24.6	160	34.6
No	374	75.4	302	65.4
Unknown	114	(18.7)	85	(15.5)
Health care access				
Health insurance				
Private insurance only	228	45.5	328	70.9
Medicare/private insurance	67	13.4	101	21.8
Medicare only	67	13.4	8	1.7
Medicaid/welfare	74	14.7	13	2.8
None	65	13.0	13	2.8
Unknown	109	(18.0)	84	(15.4)
Usual source of medical care				
Private physician or private clinic	275	55.1	363	78.4
HMO	64	12.8	42	9.1
Hospital outpatient clinic or emergency room or public clinic	121	24.3	12	2.6
None	39	7.8	46	9.9
Unknown	111	(18.2)	84	(15.4)
Biological features				
Architectural grade§				
Well differentiated	106	20.0	128	27.4
Moderately well differentiated	305	57.7	266	57.0
Poorly differentiated	118	22.3	73	15.6
Unknown	44	(7.7)	25	(5.1)
Nuclear grade§				
1	150	30.0	214	46.7
2	263	52.6	190	41.5
3	87	17.4	54	11.8
Unknown	73	(12.7)	34	(6.9)

*Differences between Blacks and Whites in distribution were significant at $P < .001$ for all characteristics except estrogen receptor status ($P = .07$).

†Values in parentheses are the percents of total cases for the selected characteristic that was unknown. Percents of known responses for each characteristic are calculated by subtracting the unknown response from the total to determine the new denominator; then each categorical proportion is determined (e.g., $610 - 110 = 500$; $211/500 = 42.2\%$; $145/500 = 29.0\%$, etc.)

‡Patients with no delay were asymptomatic women whose breast cancers were found on routine examination, during screening, or during evaluation for an illness.

§Excludes in situ cases.

ated with higher disease stage for Whites only ($P = .06$), and less education was marginally associated with higher disease stage among Blacks only ($P = .07$). Marital status, smoking history, parity, oral contraceptive use, comorbidity, breast self-examination, and estrogen receptor status were not associated with stage at diagnosis in either racial group. When in situ cancers were added to the models (tumor grade [architectural and nuclear] and estrogen receptor status excluded), similar associations of the factors with stage at diagnosis were demonstrated.

The adjusted odds ratios of breast cancer stage among Black versus White patients by stage at diagnosis from the logistic regression model are presented in Fig. 3. Odds ratios (reference group: White, stage I-II_{N0} disease) relating race to stage at diagnosis of invasive cases only (data not shown) were in general similar to those obtained for the analyses incorporating in situ cases. Race-stage associations adjusted for architectural grade or nuclear atypia included only the invasive cases. For patients with stage III-IV disease, all 95% confidence intervals did not include 1.0, indicating that patients with stage III-IV disease were significantly more likely ($P < .05$) to be Black, even after we adjusted for individual factors associated with stage. For stage II_{N1} versus the reference stage, odds ratios were greater than 1.0,

but less than those for the stage III-IV cases. When we adjusted for history of patient delay, the odds ratio was closest to 1.0, indicating that this variable may explain some of the race-stage association. For in situ cancers versus the reference stage, the values were less than 1.0, suggesting that patients with in situ cancers were less likely to be Black. Regardless of which individual factor was controlled, there was little effect on the association between race and stage. For example, all adjusted odds ratios for patients with stage III-IV disease were compatible with at least a twofold increase in the odds ratios for Blacks versus Whites.

Simultaneous inclusion of the factors found to have a statistically significant association with disease stage at diagnosis in both Blacks and Whites into the logistic regression model yielded adjusted odds ratios for race of 1.68 among stage III-IV cases and 1.24 among stage II_{N1} cases (Table 2). Three factors, nuclear grade of the tumor, having a clinical breast examination by a physician in the last 6 years, and history of patient delay, explained approximately half of the excess risk for stage III-IV disease versus stage I-II_{N0} among Black women compared with White women (odds ratio reduction from 2.19 to 1.68). The architectural grade variable was found not to contribute significantly to the model fit. Although the three factors did

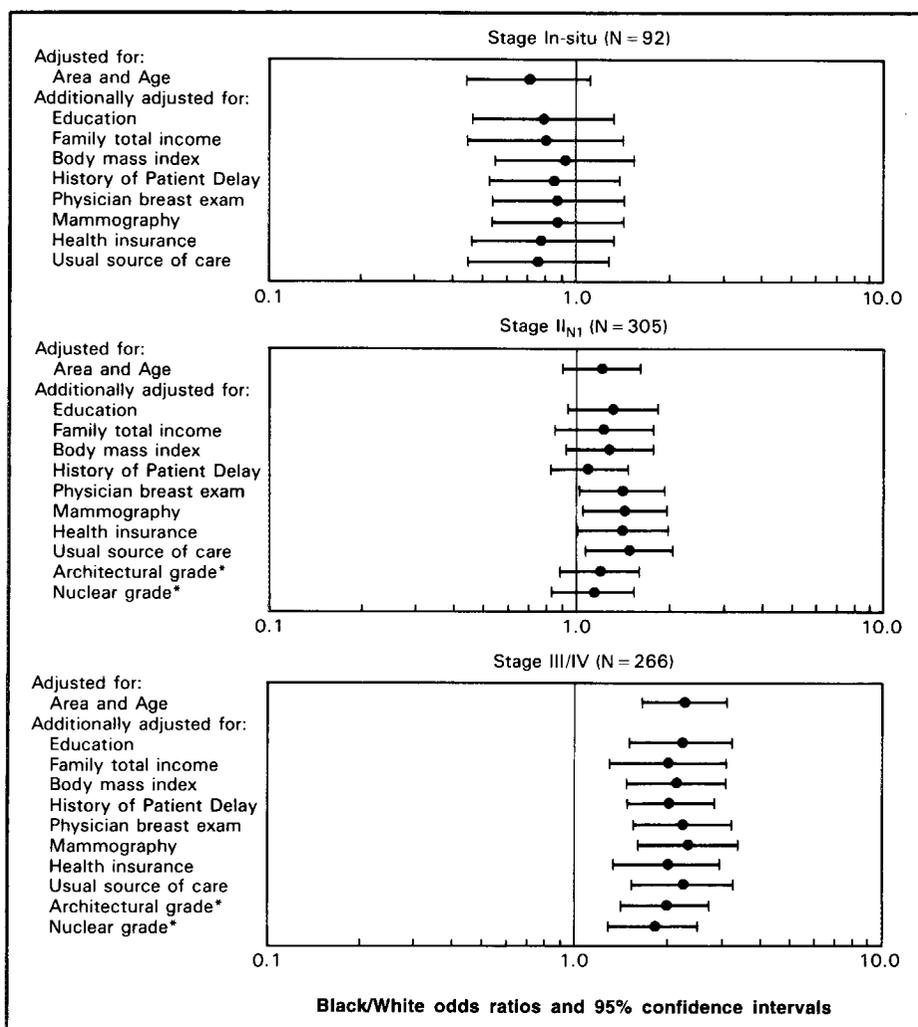


Fig. 3. Black-White odds ratio and 95% confidence interval for breast cancer stage at diagnosis adjusted for metropolitan area of residence (area), age group, and other selected factors. Odds ratios are from logistical regression model for polychotomous response (35). Each point estimates the ratio of Blacks to Whites in the specified stage divided by the ratio of Blacks to Whites in the reference stage (I/II_{N0}). Horizontal bars indicate 95% confidence intervals. * = based on invasive cancers only.

Table 2. Black-White odds ratio and 95% confidence interval for breast cancer stage at diagnosis*

Model	Variable	Degree of freedom	Likelihood ratio	Statistical significance of factor removed, P value	Odds ratios (95% confidence intervals) for Blacks versus Whites†		
					Stage I-II _{N0}	Stage II _{N1}	Stage III-IV
<i>All patients with invasive stage disease (N = 1065)</i>							
1	Race, metropolitan area of residence, age, metropolitan area of residence × age	16	18.80		1.00	1.25 (0.94-1.67)	2.30 (1.68-3.15)
<i>Subset with complete data (N = 799)</i>							
1	Race, metropolitan area of residence, age, metropolitan area of residence × age, architectural grade, physician's breast examination in the last 6 y, nuclear grade, history of patient delay	652	710.57		1.00	1.24 (0.88-1.76)	1.68 (1.13-2.49)
2	Model 1 minus architectural grade	656	711.58	.91	1.00	1.25 (0.88-1.76)	1.67 (1.12-2.48)
3	Model 2 minus physician's breast examination	658	719.31	.02	1.00	1.23 (0.87-1.73)	1.77 (1.20-2.62)
4	Model 3 minus nuclear grade	662	734.05	.01	1.00	1.32 (0.94-1.85)	1.96 (1.34-2.89)
5	Model 4 minus history of patient delay	668	785.21	.00005	1.00	1.46 (1.05-2.03)	2.19 (1.51-3.18)

*Polychotomous logistic regression with multiple predictor variables (backward elimination).

†Reference group: White patients with stage I and II_{N0} disease.

explain some of the observed race-stage relationship, 95% confidence intervals for odds ratios still did not overlap 1.0 for the stage III-IV cases, indicating that the inclusion of these explanatory factors did not adequately explain the excess of Blacks among the patients with higher stage disease at diagnosis.

Discussion

This study confirms the results of earlier studies (1-7) that demonstrated more advanced stages of cancer at diagnosis in Blacks than in Whites. One of our study objectives was to examine if Blacks would be understaged more frequently than Whites due, in part, to less thorough staging procedures (32). Previous studies from population-based registries (4) and from national surveys (2,7) comparing large samples of Blacks and Whites were limited by imprecise staging information to define the extent of disease as well as by few detailed reports on the extent of diagnostic work-up. Our data on stage differ uniquely from these previously reported studies. We made extensive efforts to determine, through a systematic approach, the extent and results of the diagnostic evaluation for cancer. Our findings indicate that unequal diagnostic evaluation is unlikely to be a major factor in stage assignment at diagnosis between the races, since the extent of diagnostic evaluation, in general, is comparable.

Our results show that some factors associated with stage at diagnosis are differentially expressed in Blacks and Whites. Among Blacks only, we observed that access to health care, lifestyle, and other antecedent medical experiences influence disease stage at diagnosis. Whites from lower socioeconomic income strata also tended to have more advanced disease at diagnosis. Those patients with higher total family income and medical care through private

physicians, private clinics, or HMOs presented with earlier stage cancers. These findings suggest that the advanced stage of breast cancer at diagnosis is related, in part, to the poorer access to health care common to socioeconomically disadvantaged populations. These observations also demonstrate the complexity of the race-stage association and indicate the need for a greater understanding of social and health care environmental issues that may impact on the design of intervention strategies in these populations.

To our knowledge, this is the first report from a population-based study that systematically examined multiple explanatory factors and their relationship to disease stage at diagnosis. In this investigation, the relationship between race and disease stage at diagnosis was evaluated after we adjusted for potential confounding factors and controlled for the design effects of age group and metropolitan area of residence. Adjustment for individual factors produced relatively modest modifications of the race-by-stage association, indicating that this relationship cannot be adequately explained by any single factor. Analyses of multiple predictor variables common to both races suggested that up to 50% of the excess risk for late stage at diagnosis of breast cancer in Black women compared with White women may be accounted for by the intrinsic tumor biology and by the lack of application of current knowledge and practices in breast cancer prevention. Whereas the relationship between the cellular differentiation of the tumor and advanced-stage disease at diagnosis requires further elucidation, the lack of a breast examination by a physician and delay in seeking medical attention among symptomatic patients point to areas where specific intervention strategies can be directed.

These findings also confirm other reports of an age-stage relationship and an increased risk of advanced stages of breast cancer at diagnosis in older women, particularly

Blacks (15-18). The heterogeneity in the race-stage associations by age strata observed in this study may be due to differences in preventive health care practices, surgery, insurance, medical care evaluations, and concurrent medical problems, and it suggests the need to investigate explanatory factors separately within age groups. In an earlier analysis of symptomatic women with known time from symptom recognition to medical consultation (37), only a borderline statistically significant relationship with stage was reported. When the full spectrum of women was analyzed, a positive association between history of patient delay and stage was observed in our study.

The effect of socioeconomic status on disease stage at diagnosis has been described (4,23,24), and one may infer from reports of cancer in low socioeconomic and minority populations that limited access to health care contributed to the late stages of the breast cancers observed at diagnosis (23,24,38,39). The present data clearly demonstrated an association between specific indicators of access to medical care and certain health care characteristics of patients and stage at diagnosis. Similar to the findings of other studies (40-44), we observed no association between estrogen receptor levels and stage; however, we were able to demonstrate a relationship between tumor grade (architectural and nuclear) and stage.

Although the association between race and interview status was not statistically significant in our study, the noninterviewed subjects had more advanced stages of cancer at diagnosis and were more frequently Black. If an interview bias exists, however, the strength of the underlying associations between race and stage at diagnosis reported in this study may actually be greater than that observed in these analyses.

Certain limitations were encountered in our analysis due to sparseness in data. In addition, some factors were highly associated with the stratification variables, particularly metropolitan area of residence. For example, it is difficult to disentangle the confounding effects of some of the medical care variables from other effects related to geographic area of residence, since sources of medical care, such as HMOs, covaried strongly with geographic area. Similarly, but to a lesser extent, it may be difficult to separate the effects of race from those of low socioeconomic status.

The major findings of this study on factors associated with stage at diagnosis in Black and White breast cancer patients may be summarized as follows: 1) The extent of diagnostic evaluation is similar in both races and does not account for stage differences; 2) factors associated with stage are differentially expressed in Blacks and in Whites, with the indicators of access to health care, lack of mammography use, and increased body mass index contributing significantly to stage differences in Blacks and income being marginally associated with stage in Whites; and 3) having a breast examination by a physician, a history of patient delay, and nuclear grade of the tumor may explain up to 50% of the excess risk of stage III-IV cancers versus stage I-II_{N0} in Black women compared with White women.

These observations point to a need to formulate and test more concrete hypotheses about possible causal pathways

from race to differences in stage of disease at diagnosis, so that factors of primary importance can be identified more readily and quantified. Identifying these causal pathways is especially important for the ultimate goal of end points for interventions so that racial differences in disease stage at diagnosis and survival can be reduced or eliminated.

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Notes

¹Ed. note: SEER is a set of geographically defined, population-based central tumor registries in the United States, operated by local nonprofit organizations under contract to the NCI. Each registry annually submits its cases to the NCI on a computer tape. These computer tapes are then edited by the NCI and made available for analysis.

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