

BREAST CANCER RACIAL DIFFERENCES BEFORE AGE 40—IMPLICATIONS FOR SCREENING

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Background: Most authorities advocate mammogram screening for breast cancer beginning at age 40 based on the age-specific distribution and incidence of breast cancer in the general population. This policy has been bolstered by studies that demonstrate that, for the *general* population, mammography in the 40–49 age bracket reduces mortality. However, it also has been reported that African-American breast cancer patients are diagnosed more often than white patients below the age of 40. Young African-American women are also more likely to have advanced disease at the time of diagnosis with predictably higher mortality. The purpose of this investigation is to explore the question, whether a subset of African-American women, age 30–39, by virtue of increased vulnerability, would benefit from early mammogram screening.

Study Design: The age-specific distribution (age 30–84) of African-American and white breast cancer patients in five State cancer registries were compared. Prognostic indicators (tumor size and nodal status) in two of the five registries in African-American and white breast cancer cases below the age of 40 were compared. Age-specific incidence in the 30–39 age group and the relative populations of black and white women in the United States were noted in the Surveillance Epidemiology and End Report (SEER) (1994–1998) and The U.S. Census 2000.

Results: The differences of age-specific distribution and age-specific incidence of African-American and white breast cancer patients were found to be significant. More than 10% of African-American women with breast cancer were diagnosed before age 40 compared to 5% of white patients. The incidence of breast cancer (SEER Report 1994–1998) in the 30–39-age bracket for African-American and white women was 48.9 and 40.2 at the 95% confidence level, while the proportion of African-American and white women reported by the Census Bureau was not too dissimilar, 15.8% and 14.6% respectively. Prognostic indicators (tumor size and nodal status) support the notion that young African-American women are more likely to have advanced disease at diagnosis.

Conclusions: African-American women in the 30–39 age group have twice the age-specific distribution, have a higher incidence compared to their white counterparts, and exhibit more ominous prognostic signs. This study provides evidence that African-American women in the 30–39 age category represent a high-risk group that may benefit from efforts at earlier detection. Although mammography remains the preferred screening modality, investigators have pointed out difficulties encountered when using mammography in young women, including low sensitivity, high breast density, cost/benefit concerns, and low positive predictive value. Nevertheless, the increasing mortality and persistent racial inci-

dence gap in young African-American women, age 30–39, argue for considering early screening mammography in spite of recognized concerns. (*J Natl Med Assoc.* 2002;94:149–156.)

Key Words: breast cancer ♦
mammogram ♦ screening guidelines ♦
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The guidelines for mammogram screening have been vigorously debated for the past several years.^{1–3} Although screening after the age of 50 will clearly reduce mortality, only recently, with the Swedish two-county study and meta-analysis reviews has the screening of women in the 40–49 age bracket been proven to favorably impact mortality.^{4–5} As a result, annual mammogram screening beginning at age 40 has been endorsed by The American College of Radiology and many of the major medical institutions in this country. It is reported that 18% of the breast cancer cases found in the general population are diagnosed in the 40–49 year age group.^{6–7}

In women younger than age 40, the breast cancer incidence in the *general* population is so low (only 4% of breast cancers occur in women younger than 35 years of age) that screening would not be cost effective.⁸

Therefore, young women below age 40 are not *routinely* screened with mammography. They are urged by the American Cancer Society and other responsible health care bodies to perform monthly breast self examination (BSE) and undergo yearly clinical breast examination (CBE) by a health professional to uncover breast cancer. Only under certain circumstances, such as excessive radiation exposure or strong genetic predisposition, is mammography examination before age 40 recommended by most oncologists.

At the same time, it has been noted, breast cancer is diagnosed before age 40 more frequently in African-American women compared to the *general* population. Some authors speculate that this is related to early menarche, a known risk factor. Others believe the apparent higher frequency is a function of age-specific distribution. Because African-American women succumb to a variety of diseases in later life, it only appears that relatively more breast cancer occurs in younger age groups. Investigators reason that white women show increased distribution of breast cancer in later years, probably because white women generally live longer, with a longer exposure to risk factors.^{9–12}

Regardless of the reason for the difference in age distribution, there is no disagreement that the majority of African-American women that do contract breast cancer below the age of 40 are diagnosed at Stage II or higher, with a disparate mortality.^{8–9} Even when African-American and white women are matched for Stage and treatment, mortality is disproportionately higher among African-American women at all ages.¹³ These findings suggest that African-American women in general, and young African-American women in particular, may be at high risk and require special scrutiny.

Nevertheless, strategies to uncover breast cancer among African-American women continue to be directed towards emphasizing compliance with the guidelines recommended for the general population. Socioeconomic factors, superstitions, lifestyle factors, diet, co-morbid disease, and poor communication skills are often cited as plausible reasons for delayed diagnosis and the resulting high mortality in the African-American community.^{14–17}

The purpose of this paper is to investigate whether or not African-American women in the

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30–39 year age bracket represent a special risk category that may benefit from mammogram screening in *addition* to the accepted techniques of early detection.

MATERIALS AND METHODS

Information was gleaned from five State cancer registries with large African-American populations, including California (1988–1995), Michigan (1988–1995), New York (1990–1994), Illinois (1986–1995), and Florida (1995–1996). These State registries are part of the Centers for Disease Control National Program of Cancer Registries, and each is a member of the North American Association of Cancer Registries. This provides assurance that data collecting and processing are of the highest standards.

In the State registries studied, race was categorized as black, white, white with Spanish surname, Hispanic, Asian, and other. For this investigation, only *invasive* breast cancers in black and white women were included.

In each of the five registries, breast cancer distributions in African-American and white women were compared (age 30–84 in five year intervals). The mean age and variance of the registries (data not shown) were almost identical, and therefore the information from the five registries was combined (Figure 1A and B).

Two of the State cancer registries (Florida and California) had ample TNM classification data to provide statistically significant information regarding prognostic indicators (nodal status and tumor size). Three of the State cancer registries (Illinois, New York and Michigan) either did not collect such information or were in various stages of compiling data. Therefore, prognostic indicators (nodal status and tumor size) of African-American and white women age 17–39 (the only age bracket under age 40 provided) were compared using the combined data from Florida and California (Table I).

The Surveillance Epidemiology and End Results (SEER) of 1994–1998¹⁸ provided the age-specific breast cancer incidence of African-American and white women 30–39 years of age

and 70–79 years of age (Table II). Also in Table II, the relative proportions of African-American and white women age 30–39 and 70–79 were extracted from U.S. Census 2000 data and recorded for comparison.

RESULTS

Figure 1 depicts the same data in two forms for clarity. The average mean age for African-American women in the five data bases (California, Michigan, New York, Illinois, Florida) was 57, and the average mean age for white women was 62. There is an obvious distinct distribution pattern, with African-American women in younger age groups and white women shifted to older age groups. More than 10% of breast cancers in African-American women are diagnosed younger than 40 years of age, compared to 5% for white women (Student's *t* test; $p < .001$).

Prognostic Indicators (Table I) in African-American and white women age 17–39 in the combined two Cancer registries (Florida and California) differed significantly χ^2 test; $p < .001$). The data indicates that in the 17–39 age bracket, African-American women present with larger tumors and more often have axillary metastases.

In Table II, the age-specific incidence (per 100,000) of breast cancer in African-American and white women age 30–39 in the SEER Report 1994–1998 indicates that young African-American women with an incidence rate of 48.36/100,000 (CI, 44.78–52.15) are at a significantly greater risk for breast cancer than young white women with an incidence rate of 40.79 (CI, 39.45–42.18). Census data (Census 2000) is included to illustrate that the proportion of African-American and white women in the 30–39 age group is very similar, 15.8% and 14.6% respectively, a difference of 7.6%. On the other hand, the racial proportions in the 70–79 age groups differ by 81%. This may account in part for the greater incidence of breast cancer in older white women, but the high breast cancer incidence in young African-

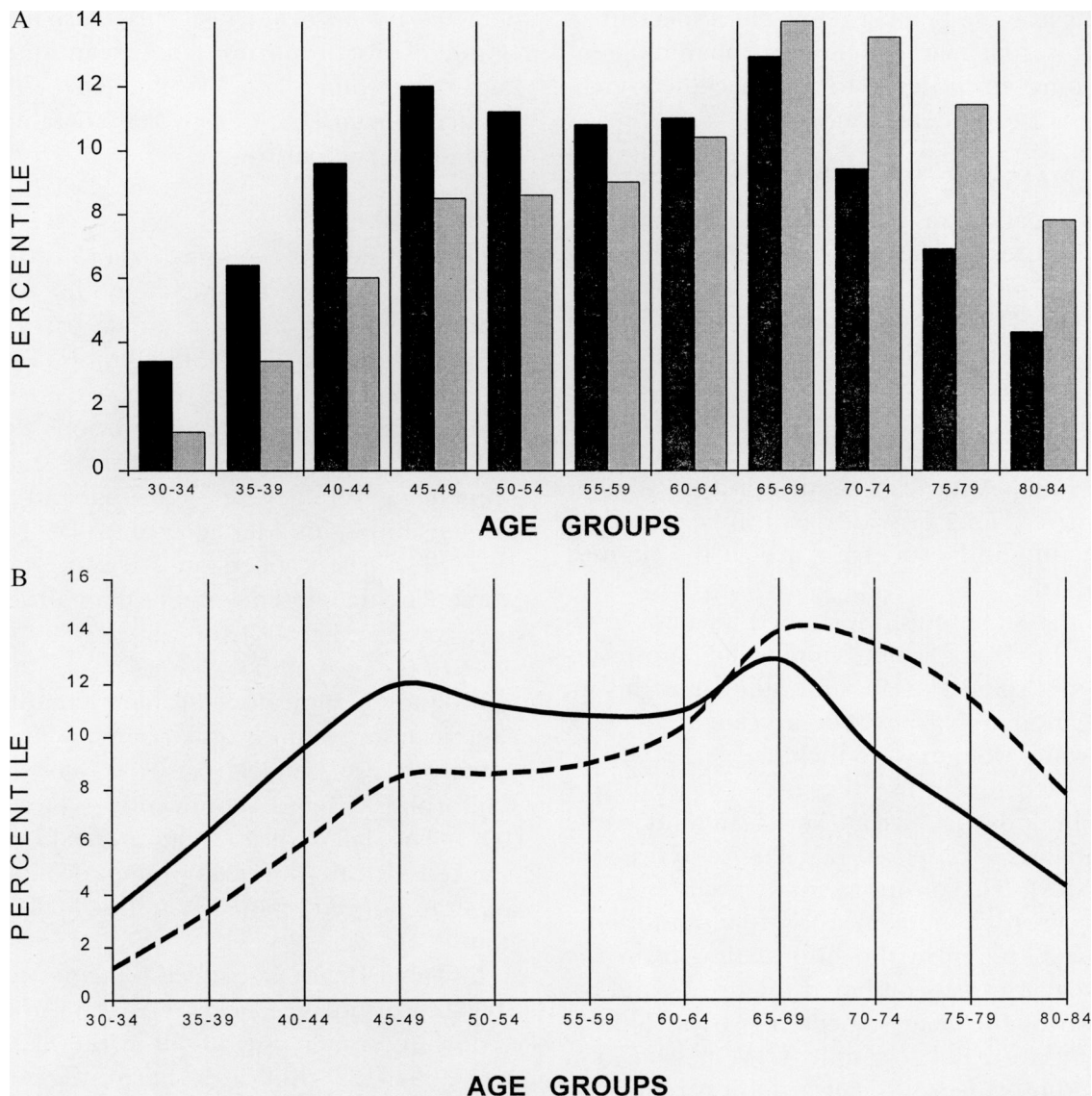


Figure 1. Age-specific distribution of breast cancer. Five state cancer Registries combined (Florida, California, Michigan, Illinois, and New York). A: ■, African-American women (mean age 57 years); ▨, white women (mean age 62 years); $P < 0.001$. B: —, African-American women (mean age 57 years); ----, white women (mean age 62 years); $P < 0.001$.

American women can not be explained on the basis of a higher population proportion.

DISCUSSION

The age-specific distribution of breast cancer in black women found in five State cancer registries (age 30–84 years), and prognostic indicators from two State cancer registries (age 17–39) describe a gaping difference in racial

incidence and an ominous prognosis for young African-American women with breast cancer. The similar overall racial proportions in the 17–39 age bracket in the face of a significantly higher breast cancer incidence supports the notion of increased vulnerability in young African-American women. This is compatible with other reports that conclude that black women have a significantly higher breast cancer incidence and mortality before age 40.^{9,19-23}

Table 1. Prognostic Indicators: California and Florida Cancer Registries Combined

Axillary Lymph Nodes			
Age Group 17-39	No Nodes present	Nodes present	Totals
White Women	2631 (54)*	2222 (46)	4853 (100)
African-American Women	372 (47)	416 (53)	788 (100)
			$p < .001$
Size of Tumor			
Age Group 17-39	Up to 2 cm	More than 2 cm	Totals
White Women	807 (32)	1703 (68)	2510 (100)
African-American Women	116 (26)	334 (72)	450 (100)
			$p < .01$

*Percentages in parenthesis

The SEER Review reported that between 1973 and 1998, breast cancer in African-American women in all age groups combined increased from 68.0 to 99.2/100,000 an increase of almost 49%. In the same period, the incidence of breast cancer in white women increased from 82.5 to 121.3/100,000, an increase of 32%. During the same period, mortality in African-American women increased from 26.3 to 29.6/100,000, an increase of 19%, while mortality in white women actually decreased 6%.¹⁸ These findings are consistent with the trending increase in breast cancer incidence and the persistent mortality gap between the races over the past 30 years.

Many risk factors have been identified that

contribute to the racial gap of breast cancer morbidity and mortality, for example, the lack of health insurance, the reluctance of the gatekeeper to recommend mammography, the lack of follow-up on the patients' part, and the delay in diagnosing and treatment ascribed to the health care system.²⁴⁻²⁵ All of these issues demand attention.

A more difficult problem being studied is an apparent biologically more aggressive cancer in some African-American women. High-grade tumors with atypia are more common in African-American women.²⁶⁻²⁹ Nevertheless, Dignam and Colleagues contends that if cancer were diagnosed earlier in African-American women, in spite of perceived biological differences, the

Table 2. African-American and White Female Populations* and Breast Cancer Incidence**

Black Women				White Women		
AGE	Population	Percent of Total African-American Female Population	Breast Cancer Incidence per 100,000	Population	Percent of Total White Female Population	Breast Cancer Incidence per 100,000
30-39	2,876,899	15.8%	48.36	14,472,210	14.6%	40.79
70-79	782,519	4.3%	407.9	7,764,026	7.8%	500.95
All Ages	18,193,005	100%	103.3	99,395,043	100%	117.9

*U.S. Census—Census 2000
 **Incidence (per 100,000) SEER Report 1994-1998 (95% confidence level)

outcomes would be similar to the general population.³⁰

Searching for cancer *earlier* with the best tools available would seem prudent, and mammography is the only screening modality that has been proven to save lives. There is no evidence that breast self examination and yearly clinical examination actually affect mortality.³¹⁻³³

Be this as it may, there are several difficulties associated with mammogram screening before age 40. Foremost is the problem of low sensitivity. However, breast self examination and yearly clinical examination, currently offered to this high risk population, have an even lower sensitivity and clearly can not find cancer at a more propitious Stage than mammography. Investigators disagree on the relation of breast density and sensitivity in women under age 40. Jeffries reported that density of the young breast did not hinder mammogram recognition of disease.³⁴ Kerlikowski found increased breast density in young women, but demonstrated that density did not correlate with detection of breast cancer in women under age 40.³⁵

Opponents of early screening contend that in young women, mammography may pick up less aggressive, relatively harmless cancers while overlooking more deadly cancers. However, Cowan and coworkers demonstrated that regardless of the circumstances of detection, all cancers had similar characteristics except that mammographically screened cancers are found at an earlier Stage.³⁶

Nonpalpable breast lesions discovered by mammography that lead to biopsy have a low positive predictive value (PPV₂) in young women. PPV₂ is defined as the number of biopsies positive for cancer divided by the number of biopsies performed. Sickles and his colleagues at the University of California, San Francisco showed the PPV₂ is directly related to age. In the 40-49, 50-59, 60-69, and 70+ age groups, the PPV₂ was 22%, 36%, 45%, and 49%, respectively. I suspect the PPV₂ in the 30-39 age group would be approximately 20%.

It should be noted, however, that the low PPV₂ is offset by the fact that these nonpalpable cancers are more often noninvasive compared to palpable lesions (32% vs 4%), and less often associated with metastasis (15% vs 33%).³⁷

Data from the five cancer registries in this report show that 10% of breast cancer in the African-American community strikes before the age of 40. Table I demonstrates that breast cancer in young African-American women, more often than not, is diagnosed at Stage II and higher.

In spite of the perceived increased vulnerability of this subset of young black women, the data gleaned from the five cancer registries does not certify that mammography screening would be beneficial. Only randomized prospective clinical trials (RPCT), comparing mammogram-screened young women with a matched cohort that were not offered mammograms, would give the answer for sure. To date, there are no outcome studies that address this question.

Taber suggests that to justify mammogram screening to reduce mortality significantly: 1) the breast cancer incidence should be at least three times the expected incidence in the absence of screening; 2) 70% of the cancers detected should be lymph node negative; 3) 50% of the invasive cancers should be 1.5 cm or smaller; and 4) at least 15% should be noninvasive cancers.³⁸

Using the StatCalc Program (EpiInfo Version 6) it is estimated that 270,000 participants divided in two matched cohorts would be required to give sufficient power and confidence level to determine if mammography beginning at age 30 would justify screening, according to Taber's criteria.

Ethical issues would also require thought and resolution. If we accept the notion that early detection saves lives and mammography remains our most efficacious tool to uncover early breast cancer, recruitment into such a study may be difficult.

Nevertheless, the disproportionate incidence of breast cancer in young African-Amer-

ican women, and the fact that more than half are diagnosed at Stage II and beyond with an unacceptable mortality, argues in favor of case-controlled cohort studies of mammogram screening, beginning at age 30. Participants would be observed for differences in Stage at diagnosis, and mortality, over the next 10 to 20 years. This testing, though not foolproof as in RPCT, would give some assurance of the validity of early screening.

Of course, there are biases to contend with: selection bias, lead time bias, and length bias. These must be taken into account when designing any screening protocol; but similar studies have led to the adoption of Pap screening for cervical cancer, periodic colonoscopy to uncover colon cancer, and the PSA test to screen for prostate cancer.

The financial cost of screening young African-American women should not be part of this discussion of medical need. Such a cost evaluation would best be determined by the economists and politicians. However, it has been reported that detection of early breast cancer by mammogram screening is more cost effective than treatment of breast cancer at advanced Stages.³⁹

CONCLUSIONS

The data presented in this study, taken from five State cancer registries and the SEER Report 1994–1998, is in agreement with the medical literature, which reflects racial distinctions in breast cancer incidence and distribution in young African-American women and the disparate prognostic indicators, particularly in the 39 and younger age bracket.

This paper offers evidence, but not proof, that screening mammography should be considered in black women in the fourth decade of life, in spite of issues of specificity, breast density, cost factors, and low positive predictive value.

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