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CLINICAL TRIAL

Regular screening mammography before the diagnosis of breast cancer reduces black:white breast cancer differences and modifies negative biological prognostic factors

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Abstract Black women present with later stage breast cancers compared to white women, and their cancers are more likely to be larger, receptor negative, and undifferentiated. This study evaluated black:white differences in the stage and biology of breast cancer among women who had a screening mammogram at one of two Chicago academic medical centers within two years of the breast cancer diagnosis (regularly screened) and compared them to the black:white differences in the stage and biology of breast cancer in women who had not received mammographic screening within two years of a breast cancer diagnosis (irregularly screened.) There were no significant black:white differences in the proportion of early breast cancers (black = 74 %; white = 69 %, p = NS) in the regularly screened population or in the irregularly screened group (black = 60 %; white = 68 %, p = NS.) The regularly screened population received significantly more mammograms (58 % ≥4 mammograms) compared to the irregularly screened population (41 % ≥4 mammograms.) Black women in the regularly screened population were less likely than irregularly screened black women to have estrogen negative breast cancers (26 vs. 36 %, $p < .05$), progesterone negative breast cancers (35 vs. 46 %, $p < .05$), and poorly differentiated breast cancers (39 vs. 53 %, $p < .05$.) White women in the irregularly screened population also had worse prognostic factors than white women in the regularly screened population, though these were not statistically significant. Regular mammographic screening can contribute to the narrowing of black:white differences in presentation of breast cancer.

Keywords Breast cancer · Disparity · Mammography · Receptors

Introduction

While the healthy people initiative, in place for three decades, has been calling for the reduction [1] and elimination [2] of health disparities, black:white disparity in breast cancer mortality in the US has expanded from a rate ratio (RR) of near unity in 1980 to 1.37 in 2009 [3]. In Chicago, the black:white breast cancer mortality RR is among the highest in the nation. The black:white RR for breast cancer mortality in Chicago was 1 in 1980, 1.68 in 2003, and 1.98 in 2005 [4–6].

Stage is the foremost predictor of breast cancer mortality and black women in the US present with later stage cancers compared to white women [7, 8]. Breast cancers in black women are also more likely to be receptor negative and more undifferentiated compared to those in white women and these factors also contribute to poorer prognosis [8–10]. These facts have been conflated to imply that the poor

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prognostic cancer biological factors are responsible for the later stage and the black:white breast cancer mortality differential [11–13]. An alternative hypothesis is that remediable factors including access to care, the quality of mammography, as well as the quality of treatment underlie the racial breast cancer mortality disparity [5, 6, 14–16].

This study was conducted to test the hypothesis that under circumstances of equivalent access to screening mammography, the stage at diagnosis of breast cancer would be equivalent for black and white women, regardless of other prognostic factors.

Methods

A retrospective study was conducted on women diagnosed with breast cancer from January 2001 through December 2006 at Northwestern Memorial Hospital (NMH) or Rush University Medical Center (Rush). These institutions were chosen because their mammography quality audits demonstrated that they exceeded the quality standards recommended by the American College of Radiology [17]. Cases were identified from the cancer registries at each institution. Data were collected regarding age, race, mammogram history, detection manner, diagnosis date, subtype of breast cancer and pathology (including grade, stage, estrogen, progesterone, Her-2 receptor status), total screening and diagnostic mammograms in the 5 years preceding diagnosis, number of weeks from diagnosis to first treatment, and status of subject at time of study (living or expired). The pathological stage of the breast cancers found was categorized as early if they were Stage 0 or 1 and late if they were Stage 2, 3, or 4. Node status was also analyzed.

Non-hispanic black and non-hispanic white women, ages 40 years and older, were included in the study. Women were categorized as regularly screened (Population 1) if they had at least one normal screening mammogram at Rush or NMH within 2 years of the diagnosis of breast cancer at either institution. Women were classified as irregularly screened (Population 2) if they had not received a screening mammogram before their breast cancer diagnosis or if they had a previous screening mammogram, but that mammogram was obtained more than 2 years prior to the diagnosis of breast cancer. Data were collected on a total of 1,702 subjects (1,074 at NMH and 628 at Rush) out of which 1,642 met criteria to be included in one of the two analyses populations. Population 1 included 980 women who had been regularly screened. Population 2 included 662 women who had been irregularly screened. Measurements of association were conducted by the pearson χ^2 analysis (SAS version 9.2, SAS Institute, Cary NC).

Results

The results are presented in Tables 1 and 2. The age distribution of cancer diagnosis was similar between black and white women. Of the 980 women who had received regular screening prior to the breast cancer diagnosis, 726 were white and 254 were black. Of the 662 women who did not receive regular screening, 492 were white and 170 were black. There was a significant association ($p \leq .05$) between race and Stage 0 (in situ) cancers, pathological grade, progesterone and estrogen receptor status, triple negative status, and time from diagnosis to treatment in the regularly screened population. Specifically, a higher proportion of regularly screened (Population 1) black women compared to regularly screened white women were diagnosed with in situ breast cancer, had poorly differentiated cancer (ER−, PR−, ER/PR/Her-2−), and had greater than 30 days pass between diagnosis and treatment. There was no significant difference in early stage breast cancers (Stage 0 and 1 combined), node status, Her-2 status or institution, and race within either population.

Within the irregularly screened population (Population 2), there was a significant association between race and pathological grade, progesterone and estrogen receptor status, triple negative status, and time from diagnosis to treatment. Similar to Population 1, there was a higher proportion of black women compared to white women who had poorly differentiated cancer, were ER (−), PR (−), ER/PR/Her2 (−), and had a greater than 30 days pass between diagnosis and treatment. Compared to the regularly screened women (Population 1), women who were irregularly screened (Population 2) regardless of race were more likely to have poorly differentiated cancer, estrogen negative, progesterone negative, and triple negative breast cancer.

There was no significant difference in the overall lymph node positivity status either within or between regularly screened women and irregularly screened women (regularly screened $p = .12$, unscreened $p = .06$, comparing populations $p = .07$). However, a higher proportion of irregularly screened black women were lymph node positive as compared to black women who were regularly screened ($p = .003$). This was not true for white women ($p = .76$.)

Discussion

When women received regular or irregular mammographic breast cancer screening at either of two Chicago academic medical centers, there were no black-white differences in the early pathological stage of breast cancer at diagnosis. Black women who were regularly screened were

Table 1 Population characteristics

	Population 1 Regularly screened ($n = 980$)	Population 2 Irregularly screened ($n = 662$)
Race		
Black	254 (26 %)	170 (26 %)
White	726 (74 %)	492 (74 %)
Age		
40–49	229 (23 %)	159 (25 %)
50–59	308 (32 %)	200 (31 %)
60–69	251 (26 %)	145 (22 %)
70+	186 (19 %)	143 (22 %)
Prior mammograms *($p < .0001$)		
Prior mammograms ≤3	416 (42 %)	387 (59 %)
Prior mammograms ≥4	564 (58 %)	273 (41 %)

* Prior mammograms refer to both prior screening and diagnostic mammograms

significantly less likely to have invasive breast cancer than white women, a positive prognostic indicator. Black women were more likely than white women to have undifferentiated and receptor negative breast cancer, poorer prognostic indicators. They were also significantly more likely to experience delay from diagnosis to treatment. However, when comparing Population 1 (women screened regularly before breast cancer diagnosis) with Population 2 (women screened irregularly before breast cancer diagnosis), those women screened regularly were more likely to have well-differentiated and receptor positive breast cancers than those not screened regularly, regardless of race, though this positive modulation of biological prognostic factors was more profound among black women. While racial differences in the pathologic stage of breast cancer (early vs. late) were not statistically different in either the regularly screened or the irregularly screened populations, black women who were regularly screened were more likely to be lymph node negative than black women who were irregularly screened. As stage and biological characteristics of breast cancer at diagnosis are the most important predictors of long-term breast cancer survival [7], the results of this study reinforce the importance of routine and regular mammographic screening as a key tool to reduce black-white disparity in breast cancer mortality. It also suggests that poor prognostic biological factors such as receptor status and grade may be ameliorated by regular mammography screening. This is a unique finding that will require further exploration.

This study had some limitations. This study is retrospective and was conducted at two Chicago academic medical centers, which may limit generalizability to other types of screening facilities. Sample size was also a limitation, especially with regard to within sample comparisons; the numbers of deaths was small and was not age-adjusted, so we are unable to comment on survival. While there was no direct measure of mammography quality at the two academic medical centers, a review of the mammography audits at NMH (PG) and Rush (DA) found that they exceeded the American College of Radiology standards for cancers detected per thousand screened and the percent early (Stage 0 and 1) cancers, proxies for quality. The criteria for the regularly screened sample (a screening mammogram within 2 years of the breast cancer diagnosis) was consistent with national norms. However, the irregularly screened sample had received a significant number of mammograms as well. Had we examined the breast cancer stage and biological factor distribution in a non-screened population, the black breast cancer outcome improvements seen with the regular screening mammography might have been greater.

This study takes on additional meaning given that Chicago has among the worst reported black:white breast cancer mortality disparity in the United States [4–6]. The finding that there are no stage differences between black and white women whose breast cancers are detected after regular screening mammography suggests that the inequity in racial breast cancer outcomes could be modified with access to routine and regular screening like that provided at these two academic medical centers. In addition, the diminution of negative prognostic factors such as estrogen and progesterone receptor negativity and the proportion of poorly differentiated breast cancers in the regularly screened population has never been reported before. It is postulated that women who reside in high poverty areas [18] and those with non-screened detected cancers [19] have cancers with more negative prognostic biological characteristics. Our study is the first to suggest that in black women greater than 40 years of age, regular mammographic screening can modify these negative biological risk factors.

This study reinforces the fact that racial gaps in breast cancer outcomes can be improved. The Metropolitan Chicago Breast Cancer Taskforce was established to eliminate racial disparity in breast cancer mortality in Chicago [14]. The Taskforce initiated a "Chicago Breast Cancer Quality Consortium [5]" to improve mammography quality at Chicago area institutions and found wide variability in mammography quality in the first year of data collection [20]. Brawley wrote that black:white breast cancer mortality disparity "remains an unsettling truth… The solutions are not simple, but we must try [21]." This study suggests that one solution is within reach and that is simple access to routine and regular mammography screening.

Table 2 Outcomes in breast cancer by race and population

	Population 1 Regularly screened ($n = 980$)		Population 2 Irregularly screened ($n = 662$)		Population 1 vs. 2 ($n = 1642$)
	Black	White	Black	White	
Diagnosis[+]	($n = 247$)	($n = 717$)	($n = 160$)	($n = 487$)	($n = 1611$)
In situ	99 (40 %)	203 (28 %)	48 (30 %)	137 (28 %)	
Infiltrating	148 (60 %)	514(72 %)	112 (70 %)	350 (72 %)	
Pathological stage	($n = 219$)	($n = 612$)	($n = 138$)	($n = 406$)	($n = 1375$)
Early	163 (74 %)	422 (69 %)	83 (60 %)	276 (68 %)	
Late	56 (26 %)	190 (31 %)	55 (39 %)	130 (32 %)	
Pathological grade[+,&,*]	($n = 228$)	($n = 704$)	($n = 150$)	($n = 457$)	($n = 1539$)
Well-differentiated	38 (17 %)	233 (33 %)	18 (12 %)	135 (30 %)	
Moderately differentiated	101 (44 %)	306 (44 %)	53 (35 %)	174 (38 %)	
Poorly differentiated	89 (39 %)	165 (23 %)	79 (53 %)	148 (32 %)	
Node status	($n = 215$)	($n = 611$)	($n = 137$)	($n = 402$)	($n = 1365$)
Positive	34 (16 %)	126 (21 %)	40 (29 %)	86 (21 %)	
Negative	181 (84 %)	485 (79 %)	97 (71 %)	316 (79 %)	
Progesterone receptor status[+,&,*]	($n = 227$)	($n = 652$)	($n = 157$)	($n = 447$)	($n = 1483$)
Positive	148 (65 %)	479 (73 %)	87 (55 %)	304 (68 %)	
Negative	79 (35 %)	173 (27 %)	70 (46 %)	143 (32 %)	
Estrogen receptor status[+,&,*]	($n = 240$)	($n = 711$)	($n = 163$)	($n = 478$)	($n = 1592$)
Positive	177 (74 %)	576 (81 %)	104 (64 %)	370 (77 %)	
Negative	63 (26 %)	135 (19 %)	59 (36 %)	108 (23 %)	
Her2 receptor status	($n = 145$)	($n = 482$)	($n = 113$)	($n = 329$)	($n = 1069$)
Positive	16 (11 %)	65 (13 %)	20 (18 %)	42 (13 %)	
Negative	129 (89 %)	417 (87 %)	93 (82 %)	287 (87 %)	
Triple negative[+,&,*]	($n = 145$)	($n = 482$)	($n = 112$)	($n = 329$)	($n = 1068$)
Yes	36 (25 %)	40 (8 %)	31 (28 %)	41 (12 %)	
No	109 (75 %)	442 (92 %)	81 (72 %)	288 (88 %)	
Time from diagnosis to treatment[+,&]	($n = 254$)	($n = 726$)	($n = 170$)	($n = 492$)	($n = 1642$)
30 days or less	159 (63 %)	556 (77 %)	110 (65 %)	371 (75 %)	
Greater than 30 days	95 (37 %)	170 (23 %)	60 (35 %)	121 (25 %)	
Status[&,*]	($n = 252$)	($n = 725$)	($n = 168$)	($n = 486$)	($n = 1631$)
Living	240 (95 %)	706 (97 %)	145 (86 %)	458 (94 %)	
Expired	12 (5 %)	19 (3 %)	23 (14 %)	28 (6 %)	

[+] Indicates a significant association ($p \leq .05$) between race and outcome in Population 1

[&] Indicates a significant association ($p \leq .05$) between race and outcome in Population 2

* Indicates a significant association ($p \leq .05$) between populations (1 and 2) and outcome

Conflict of interest None.

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