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Absence of an anticipated racial disparity in interval breast cancer within a large healthcare organization

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Abstract

PURPOSE—Compared to non-Latina (nL) white women, nL Black women are diagnosed with more aggressive breast cancers, which in turn should be more likely to go undetected on screening mammography and subsequently arise as interval breast cancer (IBC). We sought to estimate the extent of an anticipated racial disparity in IBC within a single, large health care organization.

METHODS—The present analyses focuses on 4,357 breast cancers diagnosed between 2001 and 2012 and within 18 months of a screening mammogram (N=714,218). We used logistic regression with model-based standardization (predictive margins) to estimate adjusted prevalence differences (PD) corresponding to a racial disparity in IBC.

RESULTS—Overall, prevalence of IBC within 18 months was 20.7 percent. Contrary to expectation, in patient-adjusted models, there was no IBC racial disparity (percentage point disparity = -2.1, 95% CI: -4.7, 2.6). However, when controlling for facility characteristics, including proportion nL Black patients, the model coefficient for the IBC disparity reversed sign and changed substantially ($p < 0.0001$) and a racial disparity emerged (percentage point disparity = +5.1, 95% CI: -0.3, 9.9).

CONCLUSIONS—The sorting of patients by race across facilities appears to have mitigated an otherwise anticipated disparity in interval breast cancer. Possible explanations are discussed.

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Keywords

Breast Neoplasms; African Americans; Caucasian Race; Mammography

INTRODUCTION

Mammography screening increases the chances of early detection for breast cancer and the balance of evidence suggests that it also reduces mortality from breast cancer (1–4). Although mammography screening has made a substantial contribution to reducing breast cancer morbidity and mortality, the sensitivity of mammography is inherently limited (varying from 68–93%), especially in young women and women with dense breast tissue (5). Therefore, some breast cancers among screened women are diagnosed as so-called interval breast cancer (IBC); that is, they arise between screens, as the result of a symptom or an indication on a breast physical examination.

Non-Hispanic (nL) black women are more likely than nL whites to be diagnosed with certain, more aggressive forms of breast cancer, including those that are high grade or negative for estrogen and progesterone receptors, and these tumors are more likely to evade detection with mammography (6–8). In addition to having more aggressive tumors, nL Black women also appear to be less likely to have access to the highest quality breast cancer screenings, according to studies of mammography access and quality conducted in Chicago (9–15). A recent analysis from the population-based Breast Cancer Care in Chicago study revealed that nL Black breast cancer patients were more likely than their nL White counterparts to report symptomatic awareness of their breast cancer despite a recent screening mammogram (10). For these reasons, it would be reasonable to expect an excess diagnosis of IBC among nL black women. In the present analysis, we sought to estimate the extent of an anticipated racial difference in IBC within a single large health care organization.

MATERIALS AND METHODS

The study received approval from the Institutional Review Boards at Advocate Health Care, University of Illinois at Chicago and the Illinois Department of Public Health. Data on mammography examinations came from a single large health care delivery organization with healthcare facilities throughout metropolitan Chicago. All sites are connected via a radiology information system developed by PenRad Technologies of Plymouth, MN. The PenRad database is used to enter all breast imaging results, biopsies and pathology results, and related data needed for Mammography Quality Standards Act (MQSA) compliance. For these analyses, a screening mammogram was defined as a bilateral mammogram with a description of screening in the radiology database, in women without a prior history of breast cancer, mastectomy, or breast implants, and without any imaging in the 9 months prior to the screen. We linked 714,218 screening examinations conducted between 2001–2010 to the population-based Illinois State Cancer Registry (ISCR) and identified 4357 breast cancers diagnosed within 18 months of a screen, between 2001 and 2012. The linkage was performed using probabilistic methods and the software Automatch, version 4 (1996)

(16). Automatch is a highly flexible linkage software developed by Matchware Technologies, Inc. Through comparison with known breast cancers diagnosed from hospital tumor registries, approximately 99% of the breast cancers had a corresponding breast cancer record in ISCR.

Definition of interval breast cancer (IBC)

IBC was defined as an in-situ or invasive breast cancer diagnosed within 18 months following a screening mammogram (the “index” mammogram) with a negative finding (BIRADS 1, 2), but prior to a next screen. A breast cancer was defined as a screen-detected breast cancer if it was diagnosed within 18 months of a screening mammogram with a negative finding but ultimately diagnosed after a second screen with an abnormal finding.

Patient and clinical factors

Race/ethnicity was self-reported as nL White, nL Black, Latina, other, and unknown. Age at exam was defined in years and categorized as <40, 40–49, 50–59, 60–69, 70–79, and 80+. Body mass index (BMI) was categorized based on self-reported height and weight at screening exam as underweight (BMI<20) normal weight (20–24.99) over weight (25–29.99) obese (30–34.99) and morbidly obese (BMI>35). Breast density was recorded in the radiology database using the Breast Imaging Reporting and Data Systems (BIRADS) 4th edition categories of fatty, scattered fibroglandular, heterogeneously dense, and extremely dense. Family history of breast cancer was defined as none (no first or second degree relatives affected), weak (only second degree relatives affected), moderate (one first degree relatives over age 50 affected), and strong (multiple first degree relatives affected or at least one under age 50). Time between the two most recent screens prior to diagnosis was calculated as the difference in the date of the index screening mammogram and most recent prior screening mammogram and categorized as 9–18, 19–24, 25–36, 37–48, >48 months or first screen in the database. Presence or absence of a comparison film during interpretation of the index screen was available in the database. Two measures of socioeconomic status that were based on each woman’s census tract of residence (concentrated disadvantage and concentrated affluence) were also calculated (11).

Facility characteristics

We defined a variable to represent each screening facility’s proportion of patients that was nL black. Each mammography screening facility was as also categorized as either a stand-alone site, situated within a hospital that was not a comprehensive breast center, or that was situated within a comprehensive breast center. In addition, each screening exam was defined as either screen film (analog) or full field digital mammography (FFDM).

Tumor characteristics

Estrogen receptor and progesterone receptor status were each defined as negative or positive based on information from tumor registries. Likewise, histologic grade was defined as low, intermediate and high, and stage at diagnosis was categorized into American Joint Committee on Cancer (AJCC) categories of 0, I, II, III, and IV.

Statistical analyses

Ordinal and continuous variables were categorized for descriptive analyses of IBC predictors. We tabulated the distribution of patient clinical characteristics as well as facility and tumor characteristics separately for nL black and nL white patients. We also tabulated the percentage of breast cancers following screening mammography that were IBC by these same characteristics. In both instances, we obtained a p-value for differences in IBC (by race) from a Chi-Squared test (for nominal covariates) or from a test for trend for ordered covariates.

Next, a series of multivariable logistic regression models were conducted with IBC as the dependent variable. For these we restricted our sample to screening mammograms conducted on nL Black and nL White patients, of which there were 3810 breast cancers diagnosed within 18 months of a screening mammogram. Likelihood ratio tests were conducted to compare fit across nested models. Manual backwards selection (type 3 analysis using an $\alpha=0.10$) was used to identify potentially important patient and clinical characteristics beyond age, to control for in all subsequent models (results not shown). Based on these results, breast density, BMI, time since last screen, availability of a comparison film and type of mammogram (analog or digital) were identified as covariates in addition to age and family history (included a-priori) for the mediation analyses described below.

Mediation analyses

We used two approaches in order to examine the potential mediation of a racial disparity in IBC. First, we conducted logistic regression with model-based standardization (predictive margins) in order to estimate the prevalence difference and 95% confidence interval (CI) in IBC prevalence by race (17, 18). Separate models controlled for (1) age, (2) age and patient characteristics, and (3) age, patient, and facility characteristics (facility type and proportion nL black). We used the predictive margins from these models to estimate a series of average controlled direct associations in the form of prevalence differences to estimate what the racial disparity in IBC prevalence might be if the distributions of patient and/or facility characteristics were equalized within race (11). We expressed associations for the black-white disparity as prevalence (percentage-point) differences that were on a scale that is more relevant for public health interpretation than risk ratios or odds ratios are (19, 20). We estimated bias-corrected, bootstrapped 95% confidence intervals for these measures.

Second, we compared rescaled coefficients from probit regression models representing the racial difference in IBC prevalence before and after adjusting for facility characteristics (21). The method equalizes the variances and allows for a fair comparison of the magnitude of coefficients between a “reduced” model (without a set of hypothesized mediators) and a “full” model (with the mediators of interest). The p-value from the difference in the race coefficient from reduced and full models was used to indicate statistical evidence for mediation by facility characteristics on the racial disparity in IBC (18). All analyses were conducted using Stata statistical software, version 12 (Stata Corp, College Station, TX). All p-values are two-sided.

RESULTS

Racial differences in patient, facility and tumor characteristics

The distribution of age was similar for nL Black and nL White patients. NL Black patients were considerably more likely to reside in more disadvantaged and less affluent census tracts. Compared with nL blacks, nL white patients were slightly more likely have dense breasts, more likely to have obtain a digital as opposed to an analog mammogram and to have their screen interpreted in the context of a comparison film, and considerably more likely to be screened at hospital sites (Table 1). NL Black patients were more likely than their nL White counterparts to be diagnosed with more aggressive tumors that were ER negative, PR negative and higher grade. There was no apparent disparity in stage at diagnosis among this sample of screened women (Table 1).

IBC associations with patient, facility, and tumor characteristics

Overall, prevalence of IBC within 18 months was 20.7 percent. Table 2 presents associations with respect to prevalence of IBC. Contrary to expectation, prevalence of IBC was slightly lower for nL Black vs. nL white patients. As expected, younger age and denser breasts were each associated with increased prevalence of IBC. Prevalence of IBC was greater for patients with a shorter time between screens and for patients whose index screen was interpreted with the aid of a comparison film (Table 2). More aggressive tumors (ER/PR negative and higher grade) were more likely to be diagnosed as IBC. In addition, tumors with a lobular histology were more likely to be diagnosed as IBC. IBC was strongly associated with later stage at diagnosis (Table 2). Contrary to expectation, prevalence of IBC was greater at comprehensive breast centers compared to non-academic hospitals and standalone sites. IBC prevalence was greatest for patients screened at facilities with the lowest proportion of nL Black patients (23%) and IBC prevalence was lowest for patients screened at facilities with the highest proportion of nL Black patients (17%) ($p<0.0001$) (Table 2).

Mediation of the black-white disparity in IBC by facility characteristics

In a baseline model adjusting for age (and before adjusting for patient or facility characteristics), nL black patients were roughly two percentage points less likely than nL White patients to experience an interval breast cancer; after adjusting for facility characteristics nL black patients appeared to be roughly five percentage points more likely than nL White patients to experience an interval breast cancer (Table 3). Before adjusting for facility characteristics there was no disparity in the prevalence of interval breast cancer, but after adjusting for facility characteristics a disparity emerged. When we repeated these analyses for patients with data on BMI (which reduced our sample from $N=3778$ to $N=2263$ patients) results were qualitatively similar, except that the disparity began to emerge with adjustment for patient factors including BMI, and again the disparity was magnified with additional adjustment for facility level factors.

We conducted exploratory analyses to examine the hypothesis that nL black patients were being screened disproportionately at facilities with higher false positive rates which in turn might be associated with lower interval cancer prevalence. We aggregated records in the

patient-level dataset by facility and calendar year and calculated the mean interval cancer prevalence, mean false positive rate, and mean cancer detection rate for each combination of facility and calendar year. We compared false positive rates across facilities and calendar years by patient race, and created scatter plots to compare cancer detection rates, false positive rates, and interval breast cancer prevalence across facilities and calendar years (Figure 1). NL Black patients were more likely than nL Whites to be screened at facilities and calendar years with higher false positive rates (Panel A). Higher false positive rates, in turn, were strongly associated with higher cancer detection rates (Panel B) which in turn were associated with lower interval cancer prevalence (Panel B).

DISCUSSION

We anticipated that, since nL Black patients tend to be diagnosed with more aggressive forms of breast cancer, including those that are high grade or negative for estrogen and progesterone receptors, they would likewise be more likely than nL whites to be diagnosed with interval breast cancer. In addition, the expectation of a racial disparity was based on prior research conducted in Chicago showing that, compared to their nL white counterparts, nL Black women may not have the same level of access to high quality breast cancer screening and diagnostic services, which might lead to an exacerbation of expected disparities in the prevalence of interval breast cancer (9–15). Within this single, large healthcare organization a racial disparity in interval breast cancer was not readily apparent. However, an underlying racial disparity might have been masked by the way in which patients of different racial/ethnic backgrounds were distributed across facilities, perhaps due to geographic proximity or referral. A variable representing the proportion of nL Black patients screened at each facility proved to be strongly associated with prevalence of IBC and appeared to account for the lack of an observed racial disparity in IBC; that is, when we included this variable in our models of IBC an otherwise absent disparity emerged. Patients screened at facilities with higher proportions of nL Black patients were more likely to avoid an interval cancer, but it is not clear what specific (unmeasured) aspects of either patients or facilities might account for this. NL White patients were more likely to be screened at a comprehensive breast center which in turn (contrary to expectation) was associated with increased prevalence of IBC, despite the higher quality screening imaging and interpretation that we would anticipate at comprehensive breast centers (22, 23). Perhaps there is an increased focus on reducing false positives at comprehensive sites, which might come with the unanticipated consequence of somewhat higher interval cancer prevalence. In additional exploratory analyses using measures aggregated at the facility and calendar year, we found that NL Black patients were more likely than nL Whites to be screened at facilities and calendar years with higher false positive rates which in turn was associated with higher cancer detection rates and lower interval cancer prevalence.

NL Black women were less likely to have a comparison film available at screening interpretation which in turn was associated with lower prevalence of interval breast cancer. Perhaps the benefit of having a comparison film with respect to reducing callback rates and false positive screens was somewhat offset by an increased tendency to overlook lesions that might later arise as breast cancer, and therefore nL Black women may have experienced a lower likelihood of interval breast cancer at the expense of a higher likelihood of a false

positive screen. During this time period in this organization nL Black women were also more likely to have been screened with an analog as opposed to a digital machine and being screened with an analog machine was associated with lower interval breast cancer prevalence.

Our study has certain limitations. While the sample of women included in this study did encompass the entire mammography screening population within a single, large healthcare organization, including multiple urban and suburban, hospital and non-hospital based locations across metropolitan Chicago, it was not a population-based sample. We lacked detailed measures of individual facilities that could potentially be markers of the quality of screening that might impact IBC prevalence, and had to rely on broad institution type and patient mix with respect to race.

In conclusion, the sorting of patients by race across facilities appears to have mitigated an otherwise anticipated disparity in interval breast cancer. NL Black patients were more likely than nL Whites to be screened at facilities with higher false positive rates which in turn were associated with higher cancer detection rates and less interval breast cancer. This appears to partially explain the lack of an anticipated disparity in IBC.

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FIGURE 1.

All data are aggregated at the facility and calendar year level (one observation for each combination of facility and calendar year). Panel A: Boxplot comparing false positive rates for nH White and nH Black patients. Panel B: Scatter plot where each dot represents a aggregate data for cancer detection rate and false positive rate for a specific facility and calendar year, along with a best fitting linear projection from a regression of cancer detection rate regressed on false positive rate. Panel C: Scatter plot where each dot represents a aggregate data for interval breast cancer prevalence and cancer detection rate for a specific facility and calendar year, along with a best fitting linear projection from a regression of interval breast cancer prevalence regressed on cancer detection rate.

Table 1

Distribution of demographic/clinical, facility, and tumor characteristics by patient race for 3810 nL white and nL Black breast cancer patients screened from 2001–2010 and diagnosed between 2001–2012.

Characteristics	nL White		nL Black		P- Value
	No.	%	No.	%	
Age group					0.005
40 – 49	584	22	204	17	
50 – 59	743	28	333	28	
60–69	724	28	372	32	
70 – 79	581	22	269	23	
BMI					<0.0001
Under weight	66	4	11	1	
Normal weight	426	28	92	12	
Over weight	494	33	214	29	
Obese	328	22	207	28	
Morbidly Obese	205	13	220	30	
Family history					
None	1469	56	713	61	
Weak	510	19	176	15	
Moderate	431	16	202	17	
Strong	222	8	87	7	
Breast Density					0.003
Fatty	244	9	83	7	
Scattered	926	35	511	43	
Heterogeneous	1235	47	529	45	
Dense	225	9	53	4	
Time since last screen					
9 – 14.9 months	945	36	400	34	
15 – 20.9 months	288	11	182	15	
21 – 29.9 months	198	8	122	10	
30+ months	1201	46	474	40	

Characteristics	nL White		nL Black		P- Value
	No.	%	No.	%	
Comparison Film					<0.0001
None	405	15	305	26	
Yes	2227	85	873	74	
Imaging Modality					<0.0001
Analog	1348	51	818	69	
Digital	1284	49	360	31	
Screened at hospital site					<0.0001
No	932	35	720	61	
Yes	1700	65	458	39	
Comprehensive breast center					<0.0001
No	1787	68	1064	90	
Yes	845	32	114	10	
ER Status					<0.0001
Negative	316	12	216	18	
Positive	1886	72	770	65	
Missing	430	16	192	16	
Tumor Grade					<0.0001
Low	622	24	200	17	
Moderate	1092	41	490	42	
High	752	29	401	34	
Missing	166	6	87	7	
Stage at Diagnosis					
0	678	26	326	28	
I	1225	47	483	41	
II	446	17	234	20	
III	233	9	107	9	
IV	35	1	13	1	
Missing	15	1	15	1	

P-values >0.01 are suppressed

Table 2

Patient/clinical, facility, and tumor characteristics and associations with interval breast cancer (IBC) among 3810 nL white and nL Black breast cancer patients and 547 other patients screened from 2001–2010 and diagnosed between 2001 – 2012.

Characteristics	<u>IBC within 18 mos. of screen</u>		
	No.	%	P-Value
Race/ethnicity			0.09
nL White	2632	21	
nL Black	1178	19	
Other/missing	547	24	
Age group			0.0003
40–49	935	25	
50–59	1244	22	
60–69	1245	18	
70–79	933	20	
BMI ^a			0.001
Under weight	87	26	
Normal weight	596	23	
Over weight	799	19	
Obese	585	19	
Morbidly Obese	448	16	
Family history			
None	2570	21	
Weak	764	22	
Moderate	681	20	
Strong	342	20	
Breast Density			<0.0001
Fatty	388	10	
Scattered	1607	17	
Heterogeneous	2019	24	
Dense	339	34	
Time since last screen			<0.0001
9–14.9 months	1504	28	
15–20.9 months	520	24	
21–29.9 months	367	19	
30+ months	1966	15	
Comparison Film			<0.0001
None	836	12	
Yes	3521	23	
Imaging Modality			<0.0001
Analog	2477	18	
Digital	1880	26	

Characteristics	IBC within 18 mos. of screen		
	No.	%	P-Value
Screening site			<0.0001
Stand alone	1952	21	
Non-academic hospital	1303	18	
Comprehensive Breast Centers	1102	26	
Proportion nL Black			<0.0001
Low	3071	23	
Moderate	294	20	
High	992	17	
ER Status			<0.0001
Negative	604	30	
Positive	3016	21	
Tumor Grade			0.0005
Low	938	20	
Moderate	1797	19	
High	1325	25	

P-values >0.10 are suppressed

^a BMI is missing for roughly half the sample.

Table 3

The role of measured facility characteristics versus individual facilities in mediating the racial disparity (nL Black vs. nL White) in the prevalence of interval breast cancer diagnosed within 18 months of a screening mammogram.

	N	PD (95% CI) ¹	(P-value) ³
All available data			
Baseline adjust for age	3788	– 2.1 (–4.7, 2.6)	
Add patient characteristics except BMI ⁴	3788	0.0 (–3.0, 3.4)	<0.0001
Add facility-level factors ⁵	3788	4.5 (–1.0, 9.7)	<0.0001
Add both patient and facility-level factors	3788	5.1 (0.3, 9.9)	<0.0001
For patients with data on BMI			
Baseline adjust for age	2238	– 0.1 (–3.3, 2.3)	
Add patient characteristics except BMI ⁴	2238	1.6 (–1.8, 5.0)	<0.0001
Add patient characteristics including BMI ⁴	2238	2.8 (–0.11, 6.8)	<0.0001
Add facility-level factors ⁵	2238	8.7 (2.9, 14.9)	<0.0001
Add both patient and facility-level factors	2238	9.5 (4.4, 17.7)	<0.0001

¹PD Prevalence difference for the Black White disparity in interval breast cancer within 18 months of a screening mammogram, estimated via logistic regression with marginal standardization, 95% CI via bias-corrected bootstrap methods.

³P-value from a test of the difference in rescaled coefficients compared to the baseline model.

⁴BMI, analog vs. digital mammogram, availability of a comparison film, breast density and time since last screen.

⁵Facility type (stand-alone, hospital, non-comprehensive, or comprehensive breast center) and proportion of patients that were nL Black.