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Potential missed detection with screening mammography: does the quality of radiologist's interpretation vary by patient socioeconomic advantage/disadvantage

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Abstract

PURPOSE—We examined whether quality of mammography interpretation as performed by the original reading radiologist varied by patient sociodemographic characteristics.

METHODS—For 149 patients residing in Chicago and diagnosed in 2005-2008, we obtained the original index mammogram that detected the breast cancer and at least one prior mammogram that did not detect the cancer performed within 2 years of the index mammogram. A single breast imaging specialist performed a blinded review of the prior mammogram. Potentially missed detection was defined as an actionable lesion seen during a blinded review of the prior mammogram that was in the same quadrant as the cancer on the index mammogram.

RESULTS—Of 149 prior mammograms originally read as non-malignant, 46% (N=68) had a potentially detectable lesion. In unadjusted analyses, potentially missed detection was greater among minority patients (54% vs. 39%, p=0.07), for patients with incomes below $30,000 (65% vs. 36%, p<0.01), with less education (58% vs. 39%, p=0.02), and lacking private health insurance (63% vs. 40%, p=0.02). Likelihood ratio tests for the inclusion of socioeconomic variables in multivariable logistic regression models were highly significant (p<=0.02).

CONCLUSIONS—Disadvantaged socioeconomic status appears to be associated with potentially missed detection of breast cancer at mammography screening.

Keywords

breast cancer; health care disparities; screening; mammography; socioeconomic status

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INTRODUCTION

In the United States there is evidence that non-Hispanic (nH) Black women are more likely to die from breast cancer compared to their nH White counterparts, despite being less likely to be diagnosed with breast cancer. This mortality disparity is especially high in Chicago, where most recent available data suggests that nH Black women die from breast cancer at a two thirds higher rate than nH Whites [1].

The goal of these analyses was to examine whether variation in the quality of mammography interpretation as performed by the original reading radiologist varied by patient sociodemographic characteristics. Prior data from Chicago suggest that nH Black and Hispanic women were less likely than nH Whites to obtain screening mammography at facilities with characteristics suggesting high quality screening [2]. These included academic medical centers and those that relied on breast imaging specialists. Academic settings provide breast radiologists with opportunities to advance or sustain their skill level in ways that non-academic facilities generally cannot [3]. In addition, radiologists who specialize in breast imaging are more successful in detecting early stage cancers than are general radiologists [4, 5]. Lower-resource institutions may tend to rely more on generalists as opposed to specialists, and may be less likely to be academic medical centers. As a result, radiologists at these lower-resource institutions may read screening mammograms with less sensitivity and this may contribute to a higher false negative screening rate than at other higher-resource institutions. Therefore, we hypothesized that the rate of potentially missed detection would be greater in more disadvantaged patient groups (nH Black and Hispanic patients, those lacking private health insurance, and those with lower income and education).

We define a “potentially missed detection” as a scenario where the lesion corresponding to breast cancer is not identified as abnormal and actionable during the original screening mammogram interpretation, but is subsequently identified as abnormal and actionable upon re-examination by a single expert imaging specialist who is blinded to tumor, patient and radiologist characteristics.

MATERIALS AND METHODS

Sample and Procedure

Patients for this study were recruited from the parent study, “Breast Cancer Care in Chicago”. Details of this study have been published elsewhere [6]. Briefly, eligible female patients were between 30 and 79 years of age at diagnosis, resided in Chicago, had a first primary in situ or invasive breast cancer, were diagnosed between March 1, 2005 and February 31, 2008, and self-identified as either non-Hispanic White, non-Hispanic Black or Hispanic. All diagnosing facilities in the greater Chicago area (N=56) were visited on a monthly basis and all eligible newly diagnosed cases were ascertained. Certified tumor registrars employed by the Illinois State Cancer Registry (ISCR) reviewed pathology records, the hospital tumor registry or both, depending on the protocol at each hospital. Patients were further screened for eligibility and scheduled for interviews if eligible and interested. The 90 minute interview was administered either in English or Spanish as appropriate using computer-assisted personal interview (CAPI) procedures. The final interview response rate was 56% representing 989 completed interviews among eligible patients (397 non-Hispanic White, 411 non-Hispanic Black, 181 Hispanic, response rates 51%, 59% and 66%, respectively) [7]. Upon completion of the interview, patients were asked to provide consent to allow abstraction of their medical records for information pertaining to their breast cancer diagnosis, and asked to allow the study to obtain original breast screening and diagnostic images for the mammography review substudy.

Mammogram review substudy

Patients reporting either initial awareness of their breast cancer through a screening mammogram and/or a prior mammogram within 2 years of detection were eligible for this substudy (N=597). Of these 597 eligible patients, 369 (62%) consented to a review of their mammogram and other breast images involved in their screening and diagnosis. Original mammograms and diagnostic follow-up images and corresponding reports were requested from screening and diagnostic facilities. Often, multiple facilities were involved for a single patient. We received images on 273 patients; for 149 patients (91 non-Hispanic White, 47 non-Hispanic Black, 23 Hispanic) we were able to obtain the index mammogram (that detected the breast cancer) and at least one prior mammogram (that did not detect the cancer). Participants were less likely to be minority compared to non-participants (18% vs. 30%, p<0.0005), but did not differ with respect to income, education, insurance, age, mode of detection, hormone receptor status or tumor grade.

Blinded review

A single breast imaging expert (EC) performed a blinded review of the prior mammogram that had been originally interpreted as normal. All reviews were blinded to details of the original interpretation and all other subsequent screening and diagnostic images and results. All reviews were also blinded to patient age, race/ethnicity and other sociodemographic characteristics. Potentially missed detection (PMD) was defined as the discovery during blinded review of an actionable lesion (BI-RADs category 0, 4 or 5) that was located in the same breast and quadrant as the subsequent breast cancer that was detected on the index mammogram.

Analysis variables

Measures of race/ethnicity and socioeconomic disadvantage—Race and ethnicity were self-reported at interview. Ethnicity was defined as Hispanic if the patient self-identified as Hispanic, reported a Latin American country of origin, or reported a Latin American country of origin for both biological parents. Race and ethnicity were used to categorize patients as non-Hispanic White, non-Hispanic Black or Hispanic. Socioeconomic disadvantage was defined using three binary measures based on annual household income, educational attainment, and health insurance status. Choice of cut-points was based on subject matter and sample size considerations. Annual household income was categorized as not exceeding versus exceeding $30,000. Reported level of education was categorized as not exceeding a high-school degree versus some post-secondary education. Health insurance status was categorized as lacking private health insurance versus having any private health insurance.

Potential indicators of higher quality mammography—The individual mammogram images were defined as either digital or analog (film screen). Mammography facilities were defined as either: (a) public, (b) private non-academic, or (c) private, academic (universityaffiliated) institutions. Using data from a concurrent mammography facility survey of Chicago [2], we defined a variable for reliance on breast imaging specialists based on the number of general radiologists and breast imaging specialists interpreting mammography studies at each facility in 2007. A breast imaging specialist was defined as a radiologist who dedicated at least 75% of his or her working time to breast imaging, regardless of fellowship training. Facility reliance on breast imaging specialists was defined as none (no dedicated breast imagers), partial (some but not complete reliance on breast imagers), or sole reliance on specialists. Our measure of facility reliance on breast imaging specialists was not an attribute of the image, but rather a more general measure of a facility’s reliance on specialists.

Other covariates—The time interval between the prior mammogram (that did not detect breast cancer) and the index mammogram (that detected the breast cancer) was examined as a continuous variable and was also dichotomized at less than or equal to versus greater than 11 months. The reason for this dichotomization was to account for the possibility that a short interval between mammograms (less than annual) might indicate the detection of a more rapidly growing breast cancer that was less likely to be a potentially missed detection and more likely to be a true interval cancer that could not have been detected on the prior mammogram. Breast density was abstracted from mammogram reports and dichotomized by collapsing the two lower density (almost entirely fat and scattered fibroglandular densities) and higher density (heterogeneously dense and extremely dense) categories. Estrogen and progesterone receptor status was abstracted from patient medical records as either both negative or at least one positive result. Histologic grade was defined as recorded in patient medical records as low, intermediate and high. Stage at diagnosis is a potential downstream consequence of a potentially missed detection, and as such was not considered as a covariate in these analyses.

Statistical analyses

Statistical analyses were conducted using SAS version 9 (SAS Institute, Cary NC) and Stata version 11 (Statacorp, College Station, Texas). We tabulated the percentage with PMD by patient, mammography practice and tumor characteristics, and reported associated p-values from Pearson Chi-Squared tests. We estimated a series of nested logistic regression models and conducted likelihood ratio tests for the inclusion of sociodemographic variables in the models. We began with a model containing all 13 covariates from Table 1 and compared this to a model after dropping the 4 sociodemographic covariates (minority ethnicity, lower income, lower education, and lacking private health insurance) from the model, using a likelihood ratio test. We repeated these analyses by estimating similar nested models that included only those non-sociodemographic covariates with crude pvalues of <0.50 and 0.20, respectively (Table 2).

Next, we estimated separate associations for minority ethnicity, lower income, lower education, and lacking private health insurance, with PMD. In general these four variables have complex causal relations among them that are hard to disentangle, and for which mutual adjustment would tend to bias associations towards the null. Therefore, four separate estimation models were conducted in logistic regression. Each model included only one sociodemographic variable at a time, and also included the significant predictors mode of detection, interval between prior and index mammogram, and breast density as covariates. Model-based standardization was used to estimate average risk differences for the relation of each sociodemographic variable with risk of PMD [8].

Sensitivity analysis for selection bias

In order to assess the sensitivity of our results to potential selection bias, we conducted multiple imputation and analyzed the multiply imputed datasets. First, we created a dataset with the 753 potentially eligible patients that either reported a recent mammogram prior to breast cancer detection and/or reported an asymptomatic, mammogram-detected breast cancer. Of these 753 patients, 149 patients contributed data on PMD and were included in our main analysis. Using the method of chained equations (ICE) as implemented by the ice command in Stata, we multiply imputed missing values for PMD, our sociodemographic variables and the model covariates from our main analyses. ICE enables the analyst to choose an imputation model suitable for the distribution of each variable (e.g. logistic regression for binary variables), and to tailor the choice of predictor variables to each variable being imputed, including the use of additional, auxilliary variables [9]. All binary variables were modeled in logistic regression, while ordinal logistic regression was used for imputation models for income category and education level.

We ran initial exploratory models to identify predictors of study inclusion (149 out of 753), as well as models to identify predictors of our main dependent variable (PMD), main independent variables with missing data (low income, low education, no private insurance) and important covariates (breast density, mode of detection, and time between prior and index mammogram). Very briefly, in addition to all of our analysis variables defined earlier, the following additional auxilliary variables were considered for use in imputing our final analysis variables: ordinal versions of income and education, attitudinal scores for cultural beliefs about breast cancer and trust in providers, variables for recency of prior mammogram, clinical breast exam, and routine physical examination, and census tract variables pertaining to concentrated disadvantage and concentrated affluence. We used an automated stepwise selection procedure with an alpha of 0.2 for a predictor to enter and remain in the model. From these exploratory models we constructed our final imputation models and conducted multiple imputation to create 20 imputed datasets of size 753. We then re-estimated our analysis models using Rubin's rules for combined estimation results across multiply imputed datasets [10].

RESULTS

During blinded review of 149 prior mammograms, a total of 72 actionable lesions were identified, of which 68 were in the same breast and quadrant as the subsequent breast cancer (PMD = 68/149 or 46%). There was no difference in the mean number of days between prior and index mammogram when comparing patients with potentially missed detection to those without (391 vs. 409 days, p-value = 0.55 via Wilcoxon Rank Sum test). The probability of PMD was greater for minority compared to nH White patients, for patients reporting annual household incomes below $30,000 compared to higher income patients, for patients not exceeding a high-school education compared to patients with at least some college, and for patients lacking private health insurance compared to those with private insurance (Table 1). Sociodemographic variables when considered as a group in likelihood ratio tests for nested models were retained as significant predictors of PMD (Table 2). In sensitivity analyses, the result of this likelihood ratio (LR) test remained significant regardless of whether we included all 9 covariates a-priori (p-value for LR test=0.02), or identified important covariates via stepwise regression at an alpha of 0.50 (p-value for LR test=0. 008) or at an alpha of 0.20 (p-value for LR test=0.008).

In adjusted models that considered each sociodemographic variable separately, each was associated with PMD (Table 3). Ethnic minority patients were 17 percentage-points more likely to have a potentially missed detection (PMD) than nH Whites (RD=0.17, 95% CI: 0.00, 0.31). Patients with annual household incomes above $30,000 were 26 percentage-points more likely to have a PMD than patients with lower incomes. Patients with no more than a high-school degree were 19 percentage-points more likely than patients with at least some college to have a PMD, and patients lacking any form of private health insurance were more than 30 percentage-points more likely to have a PMD than patients with private insurance (Table 3).

Sensitivity analysis for selection bias

When analyzing our multiply imputed datasets, the association of PMD with low education was attenuated and no longer significant, and the association of PMD with low income was somewhat attenuated but remained highly significant. Risk differences pertaining to minority ethnicity and lacking private health insurance were essentially unchanged. (Table 3).

DISCUSSION

In the present study, we found evidence that rates of potentially missed breast cancer on screening mammography were higher for more socioeconomically disadvantaged patients, in particular for those with lower incomes and lacking private health insurance. It should be emphasized here that this was not a study of mammography performance characteristics, nor a study of interval breast cancer (i.e. breast cancers that present after a normal screening). All of the participants in this study were recently diagnosed with breast cancer and contributed both an index mammogram that detected the breast cancer and a prior screening mammogram on which the breast cancer had not been detected. Potentially missed detection was indicated if our expert reader called the prior mammogram as abnormal and identified an abnormal lesion in the same quadrant and breast as the eventual breast cancer diagnosed. For this scenario to occur, a lesion would have to be truly detectable on the prior screen (since it was detected upon expert re-assessment) but missed by the original interpreter.

This was a study of breast cancer patients, and our expert was aware that she was reviewing images from women who were subsequently diagnosed with breast cancer. We anticipated that this study design would likely result in an overly sensitive definition of potentially missed detection. In the present study, nearly half of all prior screening mammograms had a lesion identified by our expert in the same breast and quadrant as the eventual breast cancer diagnosis. Unlike radiologists reading mammograms in a practice setting, our expert did not have to be concerned with balancing increased sensitivity with the potential for a corresponding increase in false positives. As such, this sort of detection bias was anticipated as a result of the study design. An improvement upon our study design would have been to perhaps include among our sample of images an equal number of screening mammograms from women not subsequently diagnosed with breast cancer. However, because this study originated as a study of breast cancer patients and was population-based, involving dozens of facilities, such a design would have still been infeasible from a budgetary and administrative perspective.

Despite the inevitable overdetection bias that was anticipated in this study, we see no reason to suspect that overdetection by our expert would be related to patient socioeconomic disadvantage, since our expert reviewer was blinded to patient characteristics. As such, we believe that the observed racial/ethnic and socioeconomic disparities in potentially missed detection shed light on differences in the quality of interpretation for different racial/ethnic and sociodemographic groups.

Many prior studies have found associations between radiologist characteristics, practice characteristics, image characteristics, patient characteristics, and likelihood of interval cancer/mammography accuracy [11-16]. Fellowship training has been associated with greater cancer detection rates [11,12]. Other radiologist characteristics that have been associated with performance are volume read per year, years of experience, and a focus on screening compared to diagnostic mammography [13,14]. Screening performance can also vary by facility characteristics, including whether facilities offer screening alone vs. screening and diagnostic mammograms, whether facilities relied on breast imaging specialists, and frequency of audit reviews [15,16]. With this in mind, we anticipated that academic institutions and those that relied on breast imaging specialists would show lower levels of potentially missed detection. However, this was generally not apparent. One possibility is that our relatively crude measures did not adequately capture the true variation in performance across facilities that might otherwise be associated with potentially missed detection. For example, lack of available information on fellowship training may have limited the usefulness of our measure regarding specialization in breast imaging. The relatively small sample size of our study may have also contributed to the apparent lack of associations between practice characteristics and potentially missed detection.

Despite the study's relatively small sample size, we detected substantial disparities in rates of potentially missed detection. The inability to include a larger proportion of eligible patients, however, does raise the possibility of a selection bias if participants and non-participants differed in important ways such that our associations might be affected. Results of analyses of multiply imputed datasets were essentially unchanged from analyses that did not attempt to take into account missing data influences (results not shown). While re-assuring, we cannot rule out a potential influence of differential selection bias that multiple imputation might not have accounted for.

In conclusion, in this sample of urban, recently diagnosed breast cancer patients, disadvantaged socioeconomic status was associated with potentially missed detection of breast cancer at mammography screening. Our results suggest that socioeconomically disadvantaged women are less likely to have malignant lesions interpreted as malignant by their reading radiologist.

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List of abbreviations and acronyms

BI-RADS	Breast Imaging-Reporting and Data System
CAPI	computer-assisted personal interview
ICE	imputation by chained equations
ISCR	Illinois State Cancer Registry
nH	non-Hispanic

Table 1

Distribution of patient, practice, and tumor characteristics with potentially missed detection (N=149)[1].

	N	% PMD	P-Value
Race/ethnicity (n=149)			0.07
non-Hispanic White	82	39	
Black or Hispanic	67	54	
Annual household income (n=147)			0.001
>$30,000	99	36	
<$30,000	48	65	
Educational attainment (n=149)			0.02
More than high-school	96	39	
High-school degree or less	53	58	
Health insurance status (n=149)			0.02
Some private insurance	114	40	
No private insurance	35	63	
Type of facility (n=149)			0.68
Public or private, non-academic	99	44	
Private, academic	50	48	
Reliance on specialiasts (n=131)			0.56
None	80	40	
Sole	51	45	
Mammogram (n=149)			0.56
Film Screen	115	44	
Digital	34	50	
Mode of detection (n=149)			0.03
Asymptomatic	100	52	
Symptomatic	49	33	
Interval between prior and index (n=149)			0.12
Short	112	42	
Long	37	57	
Age at diagnosis (n=149)			0.09
<50	30	43	
50-59	45	33	
60+	74	54	
Histologic Grade (n=128)			0.83
Low	35	49	
Intermediate	49	49	
High	44	43	
ER/PR Status (n=120)			0.81
Negative	20	45	
Positive	100	48	
Breast density (n=148)			0.18

	N	% PMD	P-Value
Fatty/Scattered Fibroglandular	99	41	
Heterogeneously/extremely dense	49	53	

[1]N<149 for instances with missing data on the variables being examined in relation with PMD.

Table 2

Nested multivariable models of potentially missed detection (PMD)

Covariates Included:	Sociodemographic variables included	N	Chi-Squared (LR test)[1]	P-Value[1]
All variables from Table 1	All four	96	11.6	0.02
All variables from Table 1 with p<0.50	All four	146	13.92	0.008
All variables from Table 1 with p<0.20	All four	146	13.92	0.008

[1]Comparing two models, with versus without the sociodemographic variables mentioned.

Table 3

Odds ratios and average risks and risk differences for potentially missed detection by patient sociodemographics.

	Original analysis				Multiply Imputed			
	OR	(95% CI)	R[1]	RD[1]	OR	(95% CI)	R[1]	RD[1]
Race/ethnicity								
non-Hispanic White			0.38				0.39	
Black or Hispanic	2.2	(1.1, 4.5)	0.55	0.17	2.0	(1.0, 4.0)	0.55	0.16
Annual household income								
>$30,000			0.37				0.42	
<$30,000	3.3	(1.5, 7.1)	0.63	0.26	2.2	(1.3, 3.7)	0.60	0.18
Educational attainment								
More than high-school			0.39				0.45	
High-school degree or less	2.4	(1.1, 5.0)	0.57	0.19	1.4	(0.8, 2.6)	0.53	0.08
Health insurance status								
Some private insurance			0.38				0.40	
No private insurance	4.6	(1.7, 12.3)	0.69	0.31	3.8	(1.5, 9.6)	0.70	0.30

[1] Average risks and risk differences obtained logistic regression with model-based standardization via predictive margins. Each of the four sociodemographic characteristic above are modeled separately, and all of the above estimates are adjusted for age at diagnosis, mode of detection, interval between prior and index mammogram, and breast density. Abbreviations: OR, odds ratio; CI, confidence interval; R, average risk; RD, risk difference.