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Preoperative Breast Magnetic Resonance Imaging and Contralateral Breast Cancer Occurrence among Older Women with Ductal Carcinoma in Situ

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Abstract

Purpose—Although preoperative magnetic resonance imaging (MRI) can detect mammographically occult contralateral breast cancers (CBCs) among women with ductal carcinoma in situ (DCIS), the impact of MRI on the incidence of subsequent CBC events is unclear. We examined whether MRI use decreases CBC occurrences and detection of invasive disease among women who develop a CBC.

Methods—Utilizing the Surveillance, Epidemiology, and End Results-Medicare dataset, we assessed overall, synchronous (<6 months after primary cancer diagnosis), and subsequent (≥6 months after diagnosis, i.e. metachronous) CBC occurrence in women ages 67–94 years old diagnosed with DCIS during 2004–2009, with follow-up through 2011. We applied a matched propensity score approach to compare the stage-specific incidence rate of CBC according to MRI use.

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Results—Our sample consisted of 9,166 beneficiaries, 1,258 (13.7%) of whom received preoperative MRI. After propensity score matching, preoperative MRI use was significantly associated with a higher synchronous CBC detection rate (108.6 vs. 29.7 per 1,000 person-years; hazard ratio [HR]=3.65; $p < .001$) with no significant differences in subsequent CBC rate (6.7 vs. 6.8 per 1,000 person-years; HR=0.90; $p=.71$). The 6-year cumulative incidence of any CBC (in situ plus invasive) remained significantly higher among women undergoing MRI, compared with those not undergoing MRI (9% vs. 4%, $p<.001$). Women undergoing MRI also had a higher incidence of invasive CBC (4% vs. 3%, $p=.04$).

Conclusions—MRI use resulted in an increased detection of synchronous CBC but did not prevent subsequent CBC occurrence, suggesting that many of the undetected CBC lesions may not become clinically evident.

Keywords

Ductal carcinoma in situ; magnetic resonance imaging; contralateral breast cancer occurrence; early detection; overdiagnosis

Introduction

The American Cancer Society estimated that more than 60,000 women were diagnosed with ductal carcinoma in situ (DCIS) of the breast in 2009, with an annual incidence rate of 32.5 per 100,000 women.[1, 2] Fortunately, long-term prognosis of DCIS is good, with a reported 10-year cancer-specific survival rate of $> 97\%$.[3] Patients with DCIS generally do not die from breast cancer unless they have subsequent invasive breast cancer, such as ipsilateral recurrence and new ipsilateral or contralateral breast cancer. Thus, strategies to reduce invasive breast cancer are important for optimal DCIS management.

Magnetic resonance imaging (MRI) has been increasingly used among women with newly diagnosed DCIS in the United States.[4–6] Prior literature indicates among women with invasive breast cancer, preoperative MRI detects additional unsuspected ipsilateral lesions, either DCIS or invasive cancer, in approximately 15%[7, 8] and additional occult contralateral breast cancer (CBC) in 3–5%.[9] While preoperative MRI assessment may provide valuable information to define the extent of disease and facilitate surgical planning for women with DCIS, there is little evidence regarding the impact of preoperative MRI on clinical outcomes.[10] Indeed, several studies have demonstrated that MRI use among DCIS patients increases mastectomy rates and re-excision rates.[11–14] Thus, routine use of preoperative MRI remains controversial.

Some critics argue preoperative MRI is particularly useful for DCIS patients because of the early detection of occult CBC.[15] Preoperative MRI provides an opportunity to identify and treat synchronous CBCs and thus reduce subsequent (i.e., metachronous) CBC occurrence. Additionally, by detecting the CBC earlier, it is possible the stage at which those CBCs are diagnosed would be improved. A study reported for patients with DCIS, the development of invasive CBC was the most common event in a short follow-up period,[16] suggesting that these CBCs were present but undetected at the time of the initial DCIS diagnosis.[17] Therefore, MRI use could result in early detection and improve survival for patients with

DCIS.[15] Conversely, a body of literature has demonstrated that early detection may lead to overdiagnosis.[18–20] For instance, among older women with stage I/II breast cancer, approximately 45% of CBCs detected by MRI were overdiagnosed, indicating an MRI-detected CBC might not become clinically apparent during a patient's lifetime.[20] Understanding the association between MRI use and CBC occurrence as well as corresponding stage can advance our knowledge about the benefits of MRI use for DCIS patients.

This study examined the association between MRI and CBC occurrences among female Medicare beneficiaries with DCIS. We hypothesized that MRI use would increase synchronous CBC detection (within 6 months after primary diagnosis) and potentially decrease subsequent (i.e., metachronous) CBC occurrence. We further examined whether MRI use would be able to reduce overall invasive CBC occurrences.

Methods

Study design and data source

This was a retrospective cohort study. Using the Surveillance, Epidemiology, and End Results (SEER)-Medicare database, we applied propensity score matching methodology to assess the relationship between MRI use and CBC occurrences. We specifically distinguished the corresponding stage of synchronous and subsequent CBCs. The SEER registries currently cover approximately 30% of the U.S. population.[21] We used SEER data to identify CBC occurrences and stage of occurrence, along with patient sociodemographic and tumor characteristics. We used Medicare claims to identify receipt of MRI, type of breast cancer surgery, and additional indicators of interactions with the healthcare system. The Yale Human Investigation Committee determined this study did not directly involve human subjects.

Patients

We identified all women diagnosed with DCIS from 2004–2009 who were 67–94 years old at the time of diagnosis, with follow-up through 2011. We used SEER ICD-O-3 behavior and histology codes to identify patients with DCIS (in situ tumor which is consistent with ductal origin). We limited our sample to women whose tumor laterality was known, who received first breast cancer surgery within 9 months of diagnosis, and who had been enrolled in Medicare Parts A and B 24 months before diagnosis through 12 months after definitive breast cancer surgery. Patients were excluded if they were male, their diagnosis occurred only according to death certificate or autopsy, they had any cancer condition identified from claims in the 3 to 24 months prior to diagnosis, or their income or education by zip code was unknown. To avoid contamination effects, we also excluded women who received MRI between the date of first breast surgery and 180 days after DCIS diagnosis.

Exposure and outcome ascertainment

We identified breast MRI according to the Healthcare Common Procedure Coding System codes 76093–94, 77058–59, and C8903–C8908 between 90 days pre-diagnosis through the date of the first breast surgery. CBC occurrences after primary breast cancer diagnosis and

the corresponding stages were derived from the SEER program when patients had a subsequent breast cancer diagnosis and laterality between primary and subsequent breast cancer events differed. We distinguished the corresponding stage of synchronous and subsequent CBCs, using an a priori cutoff of 6 months after primary cancer diagnosis to separate synchronous from subsequent CBC.[22, 23] We censored CBC occurrences at the earlier of death date or December 1, 2011.

Covariate creation and selection

Patient characteristics included age at diagnosis, race, year of diagnosis, marital status, SEER registry, metro status of residence, comorbidity, and the number of outpatient clinic visits on separate days within 3 to 24 months before primary cancer diagnosis.[24] SEER-Medicare provides census-based estimates of median household income and percentage of adults with high school education or less at the census tract level. We also used Elixhauser comorbidity conditions, adapting an approach that requires either the diagnosis code appear on an inpatient claim or 2 outpatient claims greater than 30 days apart.[25] Tumor characteristics included stage, grade, size, histology, and estrogen receptor (ER) and progesterone receptor status, as reported by SEER. Acknowledging that MRI use may lead to more extensive follow-up, we also assessed breast imaging (mammography, breast ultrasound, breast MRI) that occurred after primary cancer diagnosis using Medicare claims.

Statistical analysis

We used propensity score matching to adjust for baseline characteristics and account for potential treatment selection bias, where those who receive MRI might be systematically different from those who do not. Patients with similar propensity scores should exhibit similar distributions of confounders within the intervention and comparison groups. Using logistic regression, including all covariates listed in the previous section, we estimated the probability of receiving MRI (Appendix Table A1). We used 2 to 1 nearest neighbor matching within 0.2 standard deviations of the logit of the estimated propensity score without replacement.[26] We assessed balance diagnostics by comparing prevalence of baseline characteristics using absolute standardized differences (expressed as a percentage). [27] Prior research has suggested that 2 to 1 matching can improve precision,[28] and a standardized difference ≥ 10 indicates meaningful imbalance in the baseline covariate.[29]

In the matched sample, we used χ^2 tests to evaluate the association between MRI use and CBC occurrence. CBC occurrence was categorized according to timing of the event (overall, synchronous, and subsequent) and by invasiveness of the event (in situ plus invasive, in situ, invasive, and stage specific). We used Cox proportional hazard regression models to describe the association between MRI and time to CBC occurrence. The model is clustered by matched sets to allow for correlation between matched pairs of patients by receipt of MRI. We examined the proportional hazards assumption using the Kolmogorov-type supremum test and observed cumulative martingale residuals.[30] We estimated the cumulative risk of CBC occurrence up to 6 years after primary DCIS diagnosis for the MRI and non-MRI groups. All analyses were conducted using SAS version 9.4 (SAS Institute, Inc., Cary, NC). We used the macro %PSMATCHING to create the propensity score match.[31] Tests were two-sided with an alpha value of .05. Acknowledging that MRI use may lead to more

extensive follow-up, we reported the prevalence of imaging tests according to MRI use (Appendix Table 2). We conducted two sensitivity analyses controlling for follow-up MRI, or excluding patients receiving contralateral prophylactic mastectomy (CPM) among the propensity-score matched sample.

Results

The sample consisted of 9,166 women with breast cancer (mean age 75 years), including 1,258 (13.7%) who received preoperative MRI (Table 1). Women who received MRI tended to be younger, white, and married, live in regions with higher education levels and higher median incomes, and have fewer comorbidities, ($p < .001$ for all except $p = .002$ for race). A total of 1,159 women receiving MRI were successfully matched with 2,156 non-MRI controls (997 women had two controls and 162 women had one control). The remaining 99 women receiving MRI were not matched. After matching, baseline characteristics between those who received MRI and those who did not were balanced, with standardized differences less than 10.

Overall CBC occurrence

In the propensity-score matched cohort (3,315 women with 12,562 person-years of follow-up; median follow-up: 44 months), women who received MRI had a higher rate of overall CBC occurrence, compared with women who did not receive MRI (19.7 vs. 9.6 per 1,000 person-years; HR 2.11; 95% CI 1.53 to 2.92; Table 2). The Kolmogorov-type supremum test indicated that the assumption of proportional hazard was violated for overall CBC, but valid for subsequent CBC. Hence, we reported synchronous and subsequent CBCs separately.

Synchronous CBC occurrence

In the matched sample, MRI use led to an increase of synchronous CBC detection. Among women with DCIS, the synchronous invasive CBC incidence was 5.1% in the MRI group and 1% in the non-MRI group. Women who received MRI had a higher rate of synchronous in situ CBC (53.4 vs. 14.4 per 1,000 person-years; HR 3.61; 95% CI 1.93 to 6.74) and invasive CBC (55.2 vs. 15.3 per 1,000 person-years; HR 3.70; 95% CI 2.02 to 6.79, Table 2; Figure 1). Women who underwent MRI were more likely to have synchronous invasive stage I CBCs (46.0 vs. 12.5 per 1,000 person-years; HR 3.79; 95% CI 1.94 to 7.40), compared with women who did not receive MRI. However, there was no statistically significant association between MRI use and detection of synchronous stage II-IV CBC (7.4 vs. 2.9 per 1,000 person-years; HR 2.67; 95% CI 0.60 to 11.92).

Subsequent CBC occurrence

There was no significant relationship between MRI use and subsequent CBC occurrence (6.7 vs. 6.8 per 1,000 person-years for women with vs. without MRI, respectively; HR 0.90; 95% CI 0.52 to 1.56; Table 2; Figure 1). However, the direction of the association between MRI use and subsequent CBC varied by tumor stage. Women who received MRI tended to have a higher rate of subsequent in situ CBC (3.5 vs. 1.7 per 1,000 person-years; HR 1.23; 95% CI 0.51 to 2.94). In contrast, they tended to have a lower rate of subsequent invasive CBC (3.2 vs. 5.1 per 1,000 person-years; HR 0.75; 95% CI 0.37 to 1.52). The results were

statistically insignificant. There was also no significant relationship between MRI use and subsequent stage I (2.7 vs. 3.0 per 1,000 person-years; HR 1.13; 95% CI 0.49 to 2.64) or stage II-IV (0.5 vs. 1.7 per 1,000 person-years; HR 0.38; 95% CI 0.08 to 1.79) CBC occurrences.

A large proportion of CBC events, especially for women who received MRI, occurred in the first 6 months (i.e. synchronous; Figure 2A), as indicated on the cumulative CBC incidence plot. After 6 years of follow-up, cumulative CBC incidence (both in situ and invasive) for women receiving MRI was approximately two times that of women who did not receive MRI (9% vs. 4%; $p<.001$). Similarly, the 6-year cumulative incidence of invasive CBC remained higher among women receiving MRI than among women who did not receive MRI (4% vs. 3%; $p=.04$; Figure 2B). Sensitivity analyses controlling for follow-up MRI use or excluding patients receiving CPM did not substantially change our results.

Discussion

For women with DCIS, the use of preoperative breast MRI substantially increases detection of synchronous in situ or invasive CBC, but this increase is not offset by a similar decrease in subsequent CBC occurrences. The invasive CBC detection tends to become equal with and without MRI use, whereas MRI use is associated with a substantial increase in in situ CBC detection. These findings suggest undetected CBCs may not become clinically evident. Among Medicare beneficiaries, MRI use may have led to overdiagnosis of CBC, which could also have the consequence of overtreatment.

Our study advances current knowledge about MRI use in DCIS patients in several important ways. First, we provided an estimate of the yield of CBC detection attributed to MRI. Our results of synchronous CBC diagnosis in the two groups (with and without MRI) were 5.1% versus 1.4% respectively, indicating a yield of 3.7% incremental CBC detection. Given that over 60,000 women are diagnosed with DCIS each year, an increase of CBC detection by 4% attributable to MRI use could have a substantial population health impact. Additionally, our results suggest the incremental CBC detection is similar for patients with DCIS and those with invasive breast cancer. A meta-analysis of women with invasive breast cancer reported an identical incremental CBC detection rate by MRI of 4.1% (95% CI 2.7% to 6.0%).^[9] By analyzing SEER-Medicare beneficiaries with invasive breast cancer, we have also demonstrated that synchronous CBC rates in the two groups (with and without MRI) were 5.8% versus 2.1%, suggesting a yield of 3.7% incremental CBC detection.^[20] Our results suggest the incremental CBC detection attributed to MRI use is similar between patients with DCIS and invasive breast cancer.

Second, examining CBC occurrence allowed us to investigate the benefits of MRI regarding occult cancer detection. Unlike ipsilateral recurrence consisting of both “true” recurrence (prescribed local treatment like surgery and radiotherapy which do not eliminate microscopic disease) and “elsewhere” recurrence (distinct breast tumors), CBC occurrence represents an “elsewhere” lesion. Our analysis was intentionally restricted to contralateral disease so that there is no disagreement regarding whether the detection is part of the primary cancer. We found early CBC detection due to MRI use neither decreased overall

invasive CBC occurrences nor shifted CBC to an earlier stage. Researchers have recently proposed top-tier future research needs for management strategies for DCIS.[32] Using the recommended study design, our study provides empirical evidence of the effect of MRI on rates of invasive cancer.

Third, prior research examining the benefits of MRI on long-term CBC outcomes mainly focused on patients with invasive breast cancer,[33] which does not necessarily apply to DCIS patients. For example, patients with DCIS rarely received chemotherapy, which may control occult CBC progression. To date, evidence suggests that preoperative MRI is not associated with improvement in surgical outcomes,[34] yet only one study examined the impact of preoperative MRI on clinical outcomes among DCIS patients. Analyzing 2,321 DCIS patients (596 of them undergoing MRI) who received BCS with or without RT at Memorial Sloan-Kettering Cancer Center, researchers found similar metachronous CBC rates of 3.5% at 5 years for both MRI and non-MRI groups. The results were based on data from one institute, which may not apply to the general population. Additionally, because the authors excluded patients with synchronous CBC, this study could not compare the effect of MRI use on overall (i.e., synchronous and subsequent) CBC occurrence. We observed that the synchronous CBC rate was much higher than the subsequent CBC rate, thus shedding light on the utility of MRI use for patients with DCIS.

Our study has several advantages compared with previous literature. First, in our analyses, the CBC occurrence and corresponding stages are directly derived from the SEER program, ensuring accurate and consistent determination of our primary outcome measures. Second, our analysis is a population-based Medicare beneficiary cohort, which is a good representation of older women with DCIS in the United States. To our knowledge, we present the largest analysis of outcomes associated with receipt of MRI among DCIS patients to date. Third, we applied propensity score matching on known measurable factors that confound MRI use according to indication. Acknowledging MRI use may change treatment patterns, such as follow-up diagnostic imaging tests, which can influence subsequent CBC occurrence, we explored the magnitude of these changes in our matched cohort. We found that there was not a significant difference in having any follow-up breast imaging test between the MRI and the non-MRI groups (87% vs. 85%) within one to two years after primary cancer diagnosis (Appendix Table 2). However, women who received preoperative MRI were more likely to receive additional MRI and ultrasound during the follow-up period until 6 years after diagnosis, suggesting MRI use is associated with more downstream healthcare utilization. Future research examining the utility of follow-up MRI for DCIS patients is warranted.

Our study, however, has some limitations. First, the median follow up time is 44 months in our sample, which may not apply to younger women who have longer life expectancies or those with more aggressive DCIS. Future research focusing on the younger population with longer follow-up times is necessary. Second, approximately 56% of our cohort had an ER-positive DCIS, and therefore were likely to receive hormone therapy. If MRI use were associated with a higher likelihood of hormone therapy, our estimates of higher CBC occurrence in the MRI group would be biased towards the null. Thus, we may underestimate overdiagnosis attributable to MRI use. Third, we did not find a significant association

between MRI use and subsequent CBC occurrence, which may be due to insufficient power. However, even if this result were significant, the absolute benefit attributed to MRI is very small - a decrease of 1.7 per 1,000 person-years for subsequent stage II-IV CBC. Fourth, we did not examine ipsilateral recurrence, because SEER does not routinely collect ipsilateral recurrence information. Some experts are advocating for less aggressive treatment for DCIS, [35, 36] including BCS without RT. For DCIS patients who omitted RT, MRI use might be beneficial if it could identify patients in whom microscopic foci of residual disease was not present.[37] Future studies should investigate whether MRI use reduces ipsilateral recurrences, especially for patients who receive BCS without RT. Finally, our study is not a randomized trial. While we applied a propensity score matching method to reduce selection bias, we were unable to control for unobserved factors.

In conclusion, preoperative MRI use led to a higher detection rate for synchronous CBC but there is a lack of evidence that MRI use decreases subsequent CBC occurrence or improves the stage of subsequent CBC. Our results indicate that using preoperative MRI to detect occult CBC may be causing more harm than good for older women with DCIS. As MRI use becomes more common in clinical practice, it is critical to consider the impact of MRI on patient health outcomes. More judicious use of preoperative MRI in this population is necessary.

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Appendix

Appendix Table 1

Logistic regression model: predictors of breast MRI utilization

Characteristics	Adjusted OR (95% CI)	Adjusted P-value
Age		
67–69	Reference	<.001
70–74	0.85 (0.71–1.01)	

Characteristics	Adjusted OR (95% CI)	Adjusted P-value
75–79	0.60 (0.50–0.73)	
80–84	0.39 (0.31–0.50)	
85+	0.18 (0.11–0.27)	
Race		
White	Reference	.49
Black	1.00 (0.75–1.32)	
Other	0.83 (0.60–1.13)	
Marital Status		
Married	Reference	.002
Unmarried	0.80 (0.69–0.92)	
Other	0.68 (0.49–0.95)	
Median income of census tract		
< \$30,000	Reference	.41
\$33,000–40,000	1.19 (0.90–1.58)	
\$40,000–50,000	1.15 (0.87–1.51)	
\$50,000–63,000	1.02 (0.76–1.37)	
\$63,000	1.19 (0.86–1.64)	
Percent HS education or less of census tract		
< 30 %	Reference	<.001
30 to 40%	0.82 (0.67–0.99)	
40 to 50 %	0.54 (0.43–0.68)	
50 to 60%	0.54 (0.42–0.71)	
60%	0.41 (0.30–0.55)	
Metro		
Non-metro	Reference	.17
Metro	1.20 (0.93–1.55)	
Elixhauser Comorbidity		
None	Reference	<.001
1 to 2	0.72 (0.62–0.83)	
3 or more	0.50 (0.40–0.64)	
Grade		
Well differentiated	Reference	.051
Moderately differentiated	1.06 (0.85–1.33)	
Poorly differentiated	0.94 (0.74–1.19)	
Undifferentiated	1.27 (0.95–1.69)	
Unknown	1.22 (0.94–1.57)	
Tumor size		
<2.0 cm	Reference	.004
2.0–5.0 cm	1.26 (1.05–1.51)	

Characteristics	Adjusted OR (95% CI)	Adjusted P-value
>5.0 cm	1.34 (0.91–1.98)	
Missing	0.87 (0.74–1.02)	
Lymph node involvement		
No nodes examined	0.48 (0.42–0.55)	<.001
No positive nodes (also includes missing/unknown)	Reference	
Hormone receptors		
ER+ or PR+	Reference	.003
ER– and PR–	1.22 (0.99–1.49)	
Missing	0.81 (0.68–0.96)	
Comedocarcinoma		
Yes	0.64 (0.49–0.84)	.001
No	Reference	
Year of Diagnosis		
2004	Reference	<.001
2005	1.85 (1.29–2.66)	
2006	3.02 (2.15–4.24)	
2007	6.34 (4.59–8.77)	
2008	10.24 (7.46–14.05)	
2009	10.29 (7.48–14.14)	
SEER Registry		
San Francisco	0.46 (0.31–0.68)	<.001
Connecticut	1.04 (0.79–1.37)	
Detroit	0.47 (0.32–0.67)	
Hawaii	0.15 (0.05–0.44)	
Iowa	0.42 (0.28–0.61)	
New Mexico	2.61 (1.67–4.09)	
Seattle	1.44 (1.11–1.88)	
Utah	0.34 (0.19–0.60)	
San Jose	0.35 (0.21–0.58)	
Los Angeles	1.01 (0.77–1.33)	
Greater California	Reference	
Kentucky	0.29 (0.19–0.44)	
Louisiana	0.63 (0.45–0.88)	
New Jersey	1.06 (0.84–1.35)	
All Georgia	0.42 (0.32–0.56)	
Physician visits (24–3 months pre-diagnosis)		
<7 visits	Reference	.006
7–11 visits	1.18 (0.98–1.43)	
12–19 visits	1.25 (1.02–1.52)	

Characteristics	Adjusted OR (95% CI)	Adjusted P-value
>19 visits	1.46 (1.18–1.81)	

MRI: Magnetic resonance imaging; OR: Odds ratio; CI: Confidence interval; ER: Estrogen receptor; PR: Progesterone receptor

Appendix Table 2

Follow-up Imaging Tests According Preoperative MRI Use

	Time after initial diagnosis				
	1–2yr	2–3yr	3–4yr	4–5yr	5–6yr
	Number at Risk				
Preoperative MRI	1,089	1,052	728	443	238
No preoperative MRI	2,101	2,006	1,410	899	485
	Subsequent MRI				
Preoperative MRI	14.0%	8.7%	6.9%	6.3%	5.0%
No preoperative MRI	2.3%	1.6%	1.8%	1.3%	<2.3%
P-value	<.001	<.001	<.001	<.001	<.001
	Subsequent ultrasound				
Preoperative MRI	21.6%	15.5%	13.0%	13.5%	12.2%
No preoperative MRI	13.0%	10.8%	7.9%	6.0%	6.0%
P-value	<.001	<.001	<.001	<.001	0.004
	Subsequent mammography				
Preoperative MRI	86.2%	73.4%	65.7%	60.0%	48.7%
No preoperative MRI	84.4%	72.7%	66.2%	59.0%	54.2%
P-value	0.17	0.68	0.79	0.70	0.17
	Subsequent imaging (MRI, ultrasound or mammography)				
Preoperative MRI	87.3%	74.9%	67.4%	61.6%	50.4%
No preoperative MRI	85.1%	73.8%	66.8%	59.6%	55.3%
P-value	0.08	0.50	0.77	0.48	0.22

Cell values less than 11 were not reported per SEER-Medicare DUA to protect the privacy of human subjects. MRI: Magnetic resonance imaging

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Fig. 1. Stage- and time-specific incidence rate of contralateral breast cancer (CBC) according to MRI status^a

^aEach bar indicates a stage-specific incidence rate of contralateral breast cancer occurrence, according to MRI status and within vs. after 6 months of primary breast cancer diagnosis.

MRI: magnetic resonance imaging

Fig. 2. Cumulative incidence of CBC according to breast MRI, propensity-score matched cohort: A. in situ and invasive CBC; B. invasive CBC^a

Months from diagnosis	0	6	12	24	36	48	60	72
N at Risk	3315	3219	3192	3152	2221	1342	724	362

^aThe difference in CBC occurrence was significant ($P < .001$, for in situ and invasive CBC, and $P = .04$ for invasive CBC; log-rank). The vertical line indicates the cutoff point (6 months) between synchronous and subsequent events. DCIS: ductal carcinoma in situ; MRI: magnetic resonance imaging; CBC: contralateral breast cancer

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Months from diagnosis	0	6	12	24	36	48	60	72
N at Risk	3315	3219	3192	3152	2221	1342	724	362

Table 1

Selected characteristics of DCIS patients, according to MRI status in original sample and propensity-score matched cohort^a

	Original Sample			Propensity-matched cohort		
	MRI (N=1,258)	No MRI (N=7,908)	St. Dif. ^b	MRI (N=1,159)	No MRI (N=2,156)	St. Dif. ^b
Age						
67–69	27.6%	18.7%	21.1	26.1%	25.4%	1.7
70–74	36.5%	29.4%	15.2	36.7%	35.9%	1.6
75–79	23.4%	26.4%	–7.0	23.8%	24.7%	–2.1
80–84	10.5%	17.5%	–20.2	11.1%	11.7%	–1.9
85+	2.1%	8.0%	–27.5	2.2%	2.2%	0.1
Race						
White	89.0%	85.8%	9.5	88.4%	87.8%	1.6
Black	6.0%	9.0%	–11.5	6.4%	7.1%	–2.8
Other	5.1%	5.2%	–0.6	5.3%	5.1%	0.9
Marital Status						
Married	56.4%	44.6%	23.8	54.4%	52.5%	3.7
Unmarried	39.3%	50.2%	–21.9	41.2%	42.6%	–2.8
Other	4.2%	5.2%	–4.6	4.4%	4.9%	–2.2
Median income of census tract						
< \$33,000	10.3%	19.9%	–27.0	11.0%	12.0%	–3.0
\$33,000–40,000	11.3%	14.9%	–10.8	11.9%	11.6%	0.8
\$40,000–50,000	18.5%	20.5%	–5.0	19.2%	19.9%	–1.5
\$50,000–63,000	21.5%	20.4%	2.8	21.3%	21.4%	–0.3
\$63,000	38.3%	24.2%	30.7	36.5%	35.1%	3.0
Percent HS education or less of census tract						
< 30 %	40.9%	24.5%	35.5	38.5%	36.0%	5.1
30 to 40%	21.4%	16.6%	12.1	21.5%	21.8%	–0.9
40 to 50 %	14.5%	18.1%	–9.7	15.3%	15.5%	–0.6
50 to 60%	12.6%	17.8%	–14.4	13.4%	14.3%	–2.8

	Original Sample		Propensity-matched cohort		
	MRI (N=1,258)	No MRI (N=7,908)	MRI (N=1,159)	No MRI (N=2,156)	St. Dif. ^b
60%	10.5%	22.9%	11.4%	12.3%	-2.8
Metro					
Non-Metro	8.6%	16.0%	9.1%	9.6%	1.6
Metro	91.4%	84.0%	90.9%	90.4%	-1.6
Elixhauser Comorbidity					
None	53.3%	44.5%	52.2%	50.2%	4.0
1 to 2	37.0%	40.9%	37.5%	39.4%	-3.9
3 or more	9.7%	14.6%	10.3%	10.4%	-0.4
Grade					
Well differentiated	11.3%	14.5%	11.6%	12.3%	-2.3
Moderately differentiated	34.3%	32.6%	34.7%	32.8%	3.9
Poorly differentiated	26.9%	26.4%	27.1%	27.8%	-1.5
Undifferentiated	12.6%	9.8%	11.6%	11.7%	-0.1
Unknown	14.9%	16.6%	15.0%	15.4%	-1.1
Tumor size					
<2.0 cm	52.8%	53.2%	52.6%	51.1%	3.1
2.0–5.0 cm	19.3%	13.5%	18.4%	18.6%	-0.7
>5.0 cm	3.7%	2.2%	3.5%	3.0%	2.5
Missing	24.2%	31.2%	25.5%	27.3%	-3.9
Hormone receptors					
ER+ or PR+	65.4%	57.7%	64.9%	64.1%	1.7
ER– and PR–	15.5%	11.3%	15.1%	14.0%	3.2
Missing	19.1%	31.0%	20.0%	22.0%	-4.8
Lymph node involvement					
No nodes examined	57.2%	73.0%	60.0%	62.2%	-4.5
No positive nodes (also includes missing/unknown)	42.8%	27.0%	40.0%	37.8%	4.5
Comedocarcinoma					
Yes	6.6%	9.6%	6.6%	7.1%	2.3

	Original Sample			Propensity-matched cohort		
	MRI (N=1,258)	No MRI (N=7,908)	St. Dif. ^b	MRI (N=1,159)	No MRI (N=2,156)	St. Dif. ^b
No	93.4%	90.4%	11.0	93.4%	92.9%	-2.3
Physician visits (24–3 months pre-diagnosis)						
<7 visits	23.1%	23.3%	-0.4	23.2%	23.4%	-0.5
7–11 visits	25.4%	25.6%	-0.3	25.4%	25.7%	-0.9
12–18 visits	25.0%	25.5%	-1.0	24.9%	25.6%	-1.5
>18 visits	26.4%	25.6%	1.7	26.5%	25.2%	2.9

^a Other variables in the propensity-score matching included SEER registries, year of diagnosis and number of physician outpatient visits prior to breast cancer diagnosis

^b Standardized difference is the mean difference divided by the pooled standard deviation, expressed as a percentage MRI: magnetic resonance imaging; ER: estrogen receptor; PR: progesterone receptor

Table 2

Contralateral breast cancer (CBC) incidence, according to MRI status after propensity-score adjustment

	CBC Incidence (per 1,000 Person-Years)		Incidence Rate Ratio (95% CI)	P-value
	MRI	No MRI		
Overall CBC				
Any	19.7	9.6	2.11 (1.53–2.92)	<.001
In situ	9.9	3.3	2.52 (1.54–4.15)	<.001
Invasive	9.9	6.4	1.84 (1.20–2.84)	.006
Synchronous CBC (<6 months)				
Any	108.6	29.7	3.65 (2.36–5.65)	<.001
In situ	53.4	14.4	3.61 (1.93–6.74)	<.001
Invasive	55.2	15.3	3.70 (2.02–6.79)	<.001
Subsequent CBC (≥ 6 months)				
Any	6.7	6.8	0.90 (0.52–1.56)	.71
In situ	3.5	1.7	1.23 (0.51–2.94)	.65
Invasive	3.2	5.1	0.75 (0.37–1.52)	.42

MRI: magnetic resonance imaging; CI: confidence interval