Radiology

ORIGINAL RESEARCH • BREAST IMAGING

Preoperative Breast MRI and Survival Outcomes in Women 50 Years or Younger with Breast Cancer

Heera Yoen, MD[*1] • *Hee-Chul Shin, MD, PhD*[*2] • *Kyung-Hwak Yoon, MD*[2] • *Jeong Hun Oh, MD*[2] • *Jiwon Park, MS*[3] • *Yunhee Choi, PhD*[3] • *Wonshik Han, MD, PhD*[4,5] • *Nariya Cho, MD, PhD*[1,6,7] • *Woo Kyung Moon, MD, PhD*[1,6,7] • *Su Min Ha, MD, PhD*[**1,6,7] • *Hong-Kyu Kim, MD, PhD*[**4,5]

* H.Y. and H.C.S. contributed equally to this work.

** S.M.H. and H.K.K. are co–senior authors.

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Background: Data on the impact of preoperative MRI on long-term outcomes in young patients with breast cancer are insufficient.

Purpose: To investigate the associations of preoperative MRI with recurrence and survival outcomes in patients 50 years or younger with newly diagnosed breast cancer, and the impact of hormone receptor status on these associations.

Materials and Methods: This retrospective study included patients aged 50 years or younger with newly diagnosed unilateral breast cancer who underwent surgery at one of two tertiary hospitals between January 2011 and December 2017. Patients who underwent preoperative MRI (MRI group) were balanced with patients who did not (no-MRI group) using inverse probability of treatment weighting (IPTW). Recurrence and death were compared between the MRI and no-MRI groups using hazard ratios (HRs) with 95% CIs. *P* values were obtained using Fine and Gray models for recurrence and Cox proportional hazards models for death, both adjusted with IPTW. Patients were followed up for a median of 7.7 years.

Results: Of the 4414 women included (mean age, 43.2 years ± 5.2 [SD]), 4118 (93.3%) underwent preoperative MRI, and 296 (6.7%) did not. A total of 342 patients (7.7%) experienced recurrence. The 5-year cumulative incidence of ipsilateral in-breast recurrence was lower in the MRI group than in the no-MRI group (1.6% vs 3.3%; subdistribution hazard ratio [sHR], 0.49; *P* = .04). However, there was no evidence of a difference in total recurrence between the MRI and no-MRI groups (sHR, 0.70 [95% CI: 0.43, 1.13]; *P* = .15). In patients with hormone receptor–negative cancer, the 5-year cumulative incidence of recurrence was lower in the MRI group than the no-MRI group (8.2% vs 20.7%; sHR, 0.40 [95% CI: 0.19, 0.82]; *P* = .04), as was the incidence of ipsilateral in-breast recurrence (sHR, 0.28 [95% CI: 0.10, 0.76]). There was no evidence of a difference in overall survival (HR, 0.62 [95% CI: 0.26, 1.50]; *P* = .58).

Conclusion: Preoperative MRI was associated with reduced risk of ipsilateral breast cancer recurrence in patients 50 years or younger, with the greatest benefit in those with hormone receptor–negative cancers.

Supplemental material is available for this article.

Breast MRI is the most sensitive imaging modality for evaluating tumor extent and detecting additional lesions that may be missed at mammography or US in patients with breast cancer (1). However, the use of preoperative MRI is controversial, as it can lead to false-positive biopsies, increase patient anxiety and costs, and cause treatment delays (1,2). Thus, there is an ongoing debate regarding the effects of preoperative MRI on short-term and long-term outcomes and the appropriate selection of patients who would benefit from its use (3). With respect to short-term surgical outcomes, systematic reviews have shown increased mastectomy rates with MRI use (4,5), whereas other studies have reported reduced reoperation rates without increased mastectomy rates (6,7).

For long-term outcomes, the impact of preoperative MRI remains heterogeneous. One retrospective study reported that preoperative MRI was associated with a lower local recurrence rate (1.2% vs 6.8%) and contralateral breast recurrence rate (1.7% vs 4.0%) (8). Another study found that unilateral preoperative MRI was associated with improved disease-free survival for local-regional recurrence, and bilateral preoperative MRI was associated with improved disease-free survival for contralateral breast recurrence, compared with no MRI (9). In contrast, other studies with 8- and 15-year follow-up periods reported comparable ipsilateral and contralateral recurrence rates between MRI and no-MRI groups (10,11). Recently, a meta-analysis evaluating recurrence rates after breast-conserving surgery reported that some studies found lower ipsilateral tumor recurrence with preoperative MRI, whereas others did not; overall, the analysis concluded that there was no conclusive evidence supporting the utility of preoperative MRI (12). Given these conflicting results, some clinicians advocate the use of preoperative MRI only in younger patients, those with dense breasts, or those with lobular breast cancer (13). However, the use of MRI varies widely and is influenced by patient factors and surgeon preferences (14), with approximately 40% of surgeons routinely ordering MRI before surgery, according to data published in 2013 (15).

Breast cancer diagnosis is often delayed in younger patients owing to their lower levels of concern and awareness of breast disease, as well as the lower sensitivity of screening mammography in dense breast tissue (16). Several national guidelines, including those of the National Comprehensive Cancer Network (17) and the European Society of Breast Imaging (18), suggest potential benefits and indications for preoperative MRI; however, there are no clear recommendations specifically for young patients.

Abbreviations

HR = hazard ratio, IPTW = inverse probability of treatment weighting, sHR = subdistribution HR

Summary

Undergoing preoperative MRI was associated with reduced risk of ipsilateral in-breast recurrence in patients 50 years or younger with breast cancer, with the greatest benefit observed in those with hormone receptor–negative cancers.

Key Results

- In a retrospective study of 4414 women aged 50 years or younger with unilateral breast cancer, preoperative MRI was associated with a lower cumulative incidence of ipsilateral in-breast recurrence (subdistribution hazard ratio [sHR], 0.49; $P = .04$).
- There was an interaction effect between preoperative MRI and hormone receptor status ($P = .04$): MRI was associated with a lower cumulative incidence of recurrence for hormone receptor–negative cancers than for hormone receptor–positive cancers (sHR, 0.40; $P = .04$).
- Preoperative MRI showed no association with overall survival (hazard ratio, 0.62; $P = .58$).

Considering the higher prevalence of dense breasts in younger women, along with the fact that younger women with breast cancer have a higher local recurrence rate, increased cancer-related morbidity and mortality over time, and increased likelihood that their cancer involves genetic susceptibility (19–21), investigating the possible benefits of preoperative MRI in young patients is highly important. Furthermore, the incidence of breast cancer has recently increased among young patients (22).

The prognostic value of preoperative MRI in young patients with breast cancer has been investigated in recent studies (6,19,23); however, its impact on long-term outcomes in patients with different subtypes of breast cancer remains unclear. Compared with hormone receptor–negative subtypes, hormone receptor–positive subtypes (ie, estrogen receptor or progesterone receptor positive) are associated with more favorable outcomes (24). Given the knowledge gap about the impact of preoperative MRI in young women with different subtypes of breast cancer, the aim of this study was to evaluate the associations between preoperative MRI and long-term outcomes, including recurrence and survival outcomes, in patients aged 50 years or younger with newly diagnosed breast cancer, and to determine the impact of hormone receptor status on these associations.

Materials and Methods

Study Population and Data Collection

This multicenter retrospective study was approved by the institutional review boards of the two tertiary institutions involved in the study, and the requirement for written patient consent was waived. The breast cancer surgery department databases at each institution were searched for consecutive patients aged 50 years or younger who were diagnosed with unilateral breast cancer and underwent upfront surgery between January 2011 and December 2017. Patients were included if they received treatment with curative intent, with or without preoperative MRI, for American Joint Committee on Cancer stage 0–III breast cancer (25). Patients with stage IV cancer, patients who received neoadjuvant chemotherapy, and patients without a final pathologic diagnosis or with insufficient follow-up (<5 years) were excluded. Demographic information was collected from department databases at each institution. Breast density at mammography was recorded according to the Breast Imaging Reporting and Data System, 5th edition (26). Data were collected on method of operation, receipt of adjuvant therapy, and pathologic findings, including estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 status. Tumors with 1% or more of cells staining positive for estrogen receptor and/or progesterone receptor were classified as hormone receptor positive. Tumors with less than 1% of cells staining positive for both receptors were classified as hormone receptor negative.

Preoperative Evaluation and Postoperative Imaging Surveillance

Preoperative staging involved clinical breast examinations, digital mammography, handheld US, and/or MRI. The detailed MRI imaging protocol is provided in Appendix S1. For the first 5 years following breast cancer treatment, annual mammography and US or MRI were offered (27). Chest radiography, chest CT, bone scanning, and/or whole-body fluorine 18 fluorodeoxyglucose PET were used for distant metastasis surveillance.

Outcome Measures

The date of last data collection was March 31, 2024. The follow-up interval was calculated from the date of surgery to the last date of follow-up or to the date of recurrence. Site of first recurrence was categorized as local-regional (ipsilateral in-breast and/or regional lymph nodes), contralateral breast, or distant metastasis (other areas of the body). Total recurrence was defined as the combination of local-regional recurrence, contralateral breast recurrence, and distant metastasis. Within the category of local-regional recurrence, the first recurrence within the ipsilateral breast was considered separately, referred to as ipsilateral in-breast recurrence.

Statistical Analysis

To balance patients who underwent preoperative MRI (MRI group) and those who did not (no-MRI group), stabilized inverse probability of treatment weighting (IPTW) was used (28). The probability of undergoing MRI was calculated using a logistic regression model that included the variables shown in Table 1. The stabilized inverse probability was applied to each data point as a weight. The balance between the MRI and no-MRI groups was assessed via the standardized difference, using a cutoff value recommended by Austin (29): An absolute standardized difference less than 0.12 was considered indicative of balance between the two groups. The χ^2 test or Fisher exact test was used to compare categorical variables between the groups, and the independent *t* test and Wilcoxon rank sum test were used to compare mean and median age, respectively. The cumulative incidence of recurrence was estimated via the cumulative incidence function to account for death before recurrence as a competing event and was compared via the Fine and Gray subdistribution hazard model; the subdistribution hazard ratio (sHR) was estimated with 95% CIs. Overall survival and hazard ratios (HRs) with 95% CIs were estimated using a Cox proportional hazards regression model after

Table 1: Patient and Tumor Characteristics before and after IPTW Adjustment

	Before IPTW Adjustment			After IPTW Adjustment*			
Variable	No MRI (*n* = 296)	MRI (*n* = 4118)	*P* Value	No MRI (*n* = 294)	MRI (*n* = 4118)	*P* Value	Standardized Difference†
Mean age (y)‡	43.8 ± 5.0 (20–50)	43.2 ± 5.2 (19–50)	.06	43.6 ± 5.0 (20–50)	43.2 ± 5.2 (19–50)	.28	−0.060
Median age (y)§	45 (41–48)	44 (40–47)	.06	44 (40–48)	44 (40–47)	.33	
Menopausal status			<.001			.91	0.033
Premenopausal	209 (70.6)	3463 (84.1)		242 (82.3)	3425 (83.2)		
Postmenopausal	18 (6.1)	289 (7.0)		22 (7.5)	287 (7.0)		
Unknown	69 (23.3)	366 (8.9)		30 (10.2)	407 (9.9)		
First-degree family history of breast cancer			.29			.98	0.002
No	277 (93.6)	3782 (91.8)		271 (92.2)	3787 (92.0)		
Yes	19 (6.4)	336 (8.2)		24 (8.2)	331 (8.0)		
Symptoms at diagnosis			<.001			.60	−0.031
No	183 (61.8)	2019 (49.0)		142 (48.3)	2054 (49.9)		
Yes	113 (38.2)	2099 (51.0)		152 (51.7)	2065 (50.1)		
Breast density			.57			.58	−0.035
Nondense (A, B)	11 (3.7)	182 (4.4)		11 (3.7)	180 (4.4)		
Dense (C, D)	285 (96.3)	3936 (95.6)		283 (96.3)	3939 (95.7)		
Histologic type			<.001			>.99	0.044
DCIS	114 (38.5)	620 (15.1)		48 (16.3)	685 (16.6)		
Invasive ductal	154 (52.0)	2987 (72.5)		209 (71.1)	2930 (71.2)		
Invasive lobular	11 (3.7)	216 (5.2)		16 (5.4)	212 (5.1)		
Other invasive‖	17 (5.7)	295 (7.2)		21 (7.1)	291 (7.1)		
Pathologic stage			<.001			.65	−0.027
Stage 0 or I	228 (77.0)	2716 (66.0)		192 (65.3)	2747 (66.7)		
Stage II or III	68 (23.0)	1402 (34.0)		102 (34.7)	1372 (33.3)		
Tumor size			<.001			.75	−0.019
≤2 cm	235 (79.4)	2864 (69.5)		204 (69.4)	2892 (70.2)		
>2 cm	61 (20.6)	1254 (30.5)		90 (30.6)	1227 (29.8)		
Lymph node status			.007			.77	−0.018
No metastasis	246 (83.1)	3142 (76.3)		224 (76.2)	3161 (76.8)		
Metastasis	50 (16.9)	976 (23.7)		71 (24.1)	957 (23.2)		
Tumor grade			.06			.33	0.082
Low or intermediate	207 (69.9)	2615 (63.5)		176 (59.9)	2632 (63.9)		
High	87 (29.4)	1486 (36.1)		116 (39.5)	1468 (35.6)		
Not reported	2 (0.7)	17 (0.4)		2 (0.7)	18 (0.4)		
Hormone receptor status#			.15			.34	0.057
Negative	57 (19.3)	942 (22.9)		74 (25.2)	932 (22.6)		
Positive	239 (80.7)	3176 (77.1)		221 (75.2)	3186 (77.4)		
HER2#			.90			.79	−0.016
Negative	279 (94.3)	3889 (94.4)		277 (94.2)	3890 (94.5)		
Positive	17 (5.7)	229 (5.6)		17 (5.8)	229 (5.6)		
Lymphovascular invasion			<.001			.98	<0.001
No	217 (73.3)	2773 (67.3)		199 (67.7)	2790 (67.8)		
Yes	44 (14.9)	1144 (27.8)		80 (27.2)	1108 (26.9)		
Not reported	35 (11.8)	201 (4.9)		15 (5.1)	220 (5.3)		
Final operation method			.37			.10	−0.099
TM	99 (33.4)	1483 (36.0)		120 (40.8)	1478 (35.9)		
BCS	197 (66.6)	2635 (64.0)		174 (59.2)	2640 (64.1)		
Adjuvant radiation therapy			.74			.05	0.115
No	95 (32.1)	1284 (31.2)		108 (36.7)	1289 (31.3)		
Yes	201 (67.9)	2834 (68.8)		186 (63.3)	2829 (68.7)		
Adjuvant chemotherapy			<.001			.53	0.038
No	211 (71.3)	1998 (48.5)		153 (52.0)	2062 (50.1)		
Yes	85 (28.7)	2120 (51.5)		141 (48.0)	2057 (50.0)		

(Table 1 continues)

Table 1 *(continued)*: Patient and Tumor Characteristics before and after IPTW Adjustment

Variable	Before IPTW Adjustment			After IPTW Adjustment*			
	No MRI (n = 296)	MRI (n = 4118)	P Value	No MRI (n = 294)	MRI (n = 4118)	P Value	Standardized Difference†
Adjuvant hormone therapy			.29			.20	0.076
No	66 (22.3)	814 (19.8)		68 (23.1)	823 (20.0)		
Yes	230 (77.7)	3304 (80.2)		226 (76.9)	3295 (80.0)		

Note.—Except where indicated, data are numbers of patients or cancers, with percentages in parentheses, and P values are from a χ^2 test or Fisher exact test. BCS = breast-conserving surgery, DCIS = ductal carcinoma in situ, HER2 = human epidermal growth factor receptor 2, IPTW = inverse probability of treatment weighting, TM = total mastectomy.

* To compare the two groups with IPTW adjustment, the hypothetical proportions were derived, resulting in a total sample size of 4412 patients (294 in the no-MRI group and 4118 in the MRI group) instead of the original 4414 patients. When each variable was compared, the values were rounded to integers.

† Standardized difference was calculated to evaluate the balance between the two groups after IPTW adjustment. An absolute standardized difference of less than 0.12 was considered to indicate a balanced variable. Based on reference 29, the 95% CI for the standardized difference is $\pm 1.96\sqrt{\frac{n_t + n_c}{n_t n_c}} = \pm 1.96\sqrt{\frac{4118 + 296}{4118 \times 296}} = 0.12$ when the true standardized difference is zero.

‡ Data are mean ± SD, with range in parentheses. P values are from an independent t test.

§ Data in parentheses are IQRs. P values are from a Wilcoxon rank sum test.

‖ *Other invasive* included mucinous carcinoma, mixed ductal and lobular carcinoma, metaplastic carcinoma, papillary carcinoma, tubular carcinoma, invasive cribriform carcinoma, adenoid cystic carcinoma, pleomorphic carcinoma, secretory carcinoma, and adenosquamous carcinoma.

Hormone receptor and HER2 status were not included in the IPTW adjustment.

applying IPTW. The proportional hazards assumption was tested using interaction terms between MRI and time to death (or recurrence), to assess whether the effect of MRI varied over time, and the assumption was found to be satisfied. While hormone receptor status was not included in the initial IPTW calculation, it was later included in the model as an effect modifier of interest to account for the interaction between MRI and breast cancer hormone receptor status. The interaction effects were tested using the Fine and Gray subdistribution hazard model or the Cox proportional hazards model. If the interaction was statistically significant, the effect of MRI was estimated separately for hormone receptor–negative and hormone receptor–positive cancers. Recurrence and death in patients treated for invasive cancers were explored as preplanned secondary analyses. To control for type I error, the Hochberg method was applied to adjust P values for the primary outcomes (the effect of MRI and its interaction with hormone receptor status on recurrence and death). $P < .05$ was considered to indicate a statistically significant difference. Statistical analyses were performed by two authors (J.P. and Y.C.) using SAS software (version 9.4; SAS Institute).

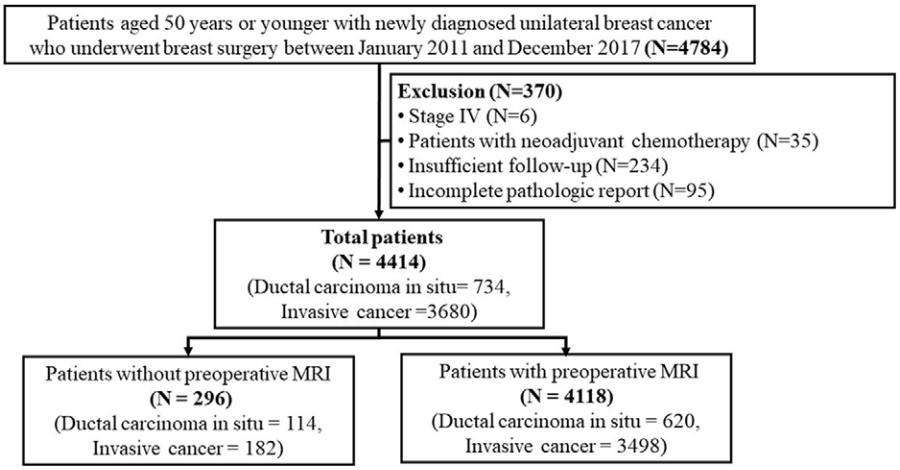

Figure 1: Flowchart of patient inclusion.

Results

Study Population and Patient Demographics

Of 4784 women aged 50 years or younger who were diagnosed with unilateral breast cancer, 370 were excluded, and 4414 were consecutively included (Fig 1). Among the 4414 women included (mean age, 43.2 years ± 5.2 [SD]; age range, 19–50 years), 4118 (93.3%) underwent preoperative MRI, and 296 (6.7%) did not (Fig 1). The maximum follow-up period was 13.2 years (median, 7.7 years [IQR, 6.0–9.7 years]; MRI group: median, 7.7 years [IQR, 6.0–9.8 years]; no-MRI group: median, 6.5 years [IQR, 5.8–8.2 years]). During follow-up, 342 (7.7%) of the 4414 patients experienced recurrence. In 73.1% (250 of 342) of these patients, recurrence occurred within 5 years (IQR, 1.7–3.8 years) after breast cancer treatment, and in 26.9% (92 of 342), recurrence occurred after 5 years (IQR, 6.0–8.2 years). Before group balancing, patients in the MRI group were more likely to be premenopausal (84.1% [3463 of 4118] vs 70.6% [209 of 296]; $P < .001$) and more likely to have symptoms at diagnosis (51.0% [2099 of 4118] vs 38.2% [113 of 296]; $P < .001$) than were those in the no-MRI group. In patients who underwent MRI, cancers were more likely to be invasive (84.9% [3498 of 4118] vs 61.5% [182 of 296]), have a higher

Table 2: Association between Preoperative MRI and Recurrence after Inverse Probability of Treatment Weighting Adjustment

Patient Population and Outcome	No. of Patients with Recurrence*	Subdistribution Hazard Ratio†	*P* Value†
All patients (*n* = 4414)			
Total recurrence (*n* = 342)‡			
No MRI	23/296 (7.8)		
MRI	319/4118 (7.7)	0.70 (0.43, 1.13)	.15
Recurrence according to first site			
Local-regional (*n* = 151)§			
No MRI	11/296 (3.7)		
MRI	140/4118 (3.4)	0.73 (0.37, 1.45)	.37
Ipsilateral in-breast (*n* = 106)§			
No MRI	11/296 (3.7)		
MRI	95/4118 (2.3)	0.49 (0.24, 0.97)	.04
Contralateral breast (*n* = 91)			
No MRI	6/296 (2.0)		
MRI	85/4118 (2.1)	0.73 (0.27, 1.99)	.54
Distant metastasis (*n* = 100)			
No MRI	6/296 (2.0)		
MRI	94/4118 (2.3)	0.64 (0.27, 1.54)	.32
Patients with invasive cancers (*n* = 3680)			
Total recurrence (*n* = 297)‡			
No MRI	17/182 (9.3)		
MRI	280/3498 (8.0)	0.68 (0.40, 1.16)	.16
Recurrence according to first site			
Local-regional (*n* = 128)§			
No MRI	7/182 (3.8)		
MRI	121/3498 (3.5)	0.66 (0.30, 1.47)	.31
Ipsilateral in-breast (*n* = 85)§			
No MRI	7/182 (3.8)		
MRI	78/3498 (2.2)	0.41 (0.18, 0.93)	.03
Contralateral breast (*n* = 71)			
No MRI	4/182 (2.2)		
MRI	67/3498 (1.9)	0.62 (0.20, 1.91)	.40
Distant metastasis (*n* = 98)			
No MRI	6/182 (3.3)		
MRI	92/3498 (2.6)	0.76 (0.31, 1.85)	.55

* Data in parentheses are percentages.

† Subdistribution hazard ratio and *P* values were obtained via Fine and Gray subdistribution hazard model with inverse probability of treatment weighting adjustment. Data in parentheses are 95% CIs.

‡ *Total recurrence* includes local-regional recurrence, contralateral breast recurrence, and distant metastasis.

§ *Local-regional* includes ipsilateral in-breast recurrence and recurrence involving the regional lymph nodes; thus, *ipsilateral in-breast* is a subset of local-regional.

stage (34.0% [1402 of 4118] vs 23.0% [68 of 296]), and exhibit lymphovascular invasion (27.8% [1144 of 4118] vs 14.9% [44 of 296]) (all $P < .001$). After IPTW adjustment, the variables were well balanced between the two groups, and the absolute standardized differences were less than 0.12 (Table 1).

Preoperative MRI and Recurrence Outcomes

The 13-year cumulative incidence of recurrence was 11.4%. Among the 342 recurrences, 151 (44.2%) were local-regional recurrence, 91 (26.6%) were contralateral breast recurrence, and 100 (29.2%) were distant metastasis (Table 2). Among the 151 local-regional recurrences, 106 (70.2%) were ipsilateral in-breast recurrences. Among the 319 recurrences in the MRI group (7.7% of 4118 patients), 140 (44%) were local-regional recurrences (of which 95 [68%] were ipsilateral in-breast recurrences), 85 (27%) were contralateral breast recurrences, and 94 (29%) were distant metastases. Among the 23 recurrences in the no-MRI group (7.8% of 296), 11 (48%) were local-regional recurrences (all of which were ipsilateral in-breast recurrences), six (26%) were contralateral breast recurrences, and six (26%) were distant metastases.

The incidence of ipsilateral in-breast recurrence was lower in the MRI group than in the no-MRI group (5-year cumulative incidence, 1.6% in the MRI group vs 3.3% in the no-MRI group; sHR, 0.49 [95% CI: 0.24, 0.97]; $P = .04$; Table 2, Fig 2). However, there was no evidence of a difference in the risk of total recurrence (sHR, 0.70 [95% CI: 0.43, 1.13]; $P = .15$), local-regional recurrence (sHR, 0.73 [95% CI: 0.37, 1.45]; $P = .37$), contralateral breast recurrence (sHR, 0.73 [95% CI: 0.27, 1.99]; $P = .54$), or distant metastasis (sHR, 0.64 [95% CI: 0.27, 1.54]; $P = .32$) between the MRI and no-MRI groups.

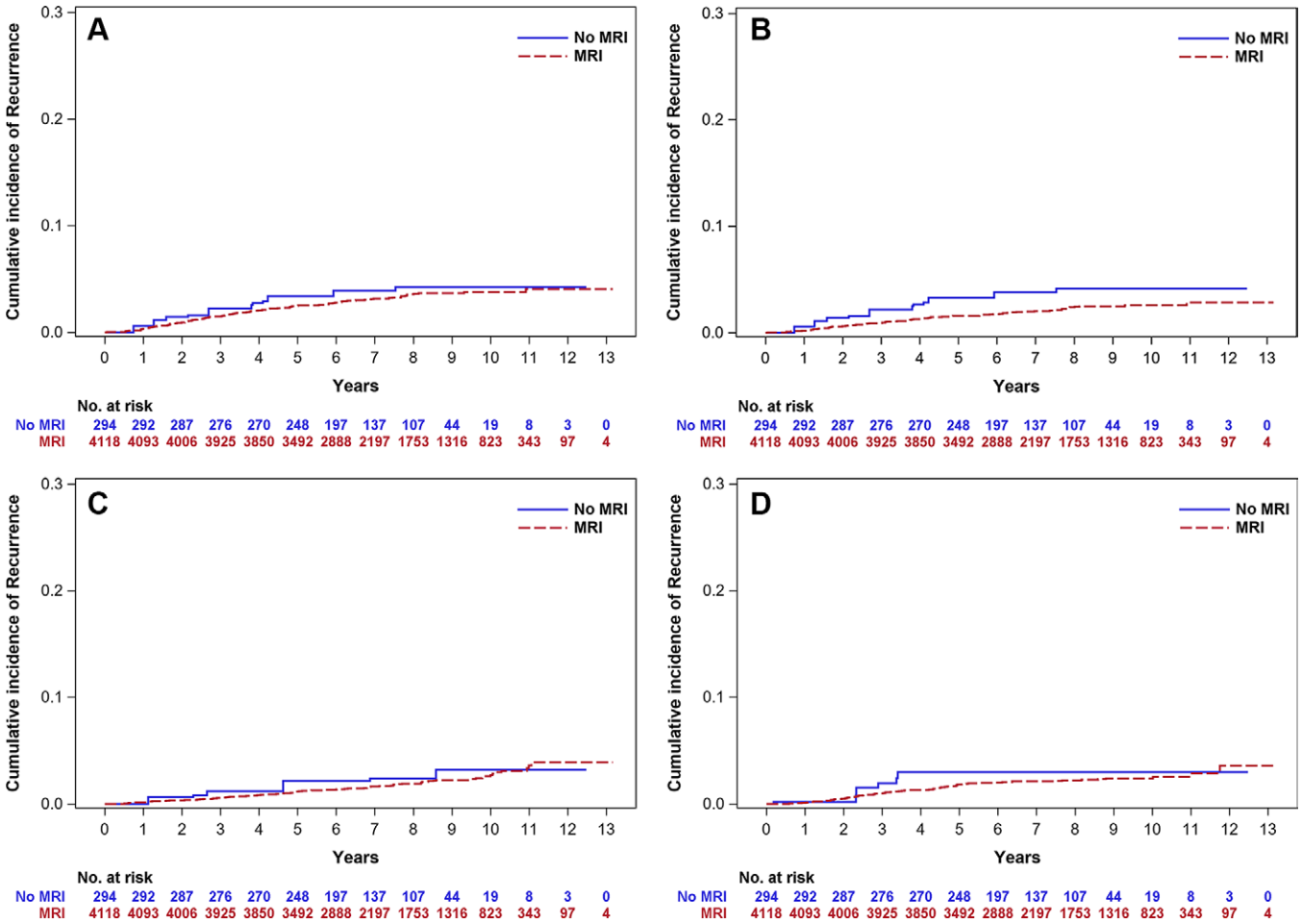

Figure 2: Cumulative incidence of recurrence according to site of first recurrence in the MRI and no-MRI groups, adjusted with inverse probability of treatment weighting. **(A)** Local-regional recurrence (subdistribution hazard ratio [sHR] = 0.73 [95% CI: 0.37, 1.45]; *P* = .37). **(B)** Ipsilateral in-breast recurrence (sHR = 0.49 [95% CI: 0.24, 0.97]; *P* = .04). **(C)** Contralateral breast recurrence (sHR = 0.73 [95% CI: 0.27, 1.99]; *P* = .54). **(D)** Distant metastasis (sHR = 0.64 [95% CI: 0.27, 1.54]; *P* = .32). The number at risk is shown below each panel.

Among the 3680 patients with invasive cancers, 297 (8.1%) experienced recurrence. Among the 128 local-regional recurrences, 85 (66.4%) were ipsilateral in-breast recurrences. The incidence of ipsilateral in-breast recurrence was lower in the MRI group than in the no-MRI group (sHR, 0.41 [95% CI: 0.18, 0.93]; *P* = .03) (Table 2). Similar to the findings for all patients, there was no evidence of a difference in total recurrence (sHR, 0.68 [95% CI: 0.40, 1.16]; *P* = .16), local-regional recurrence (sHR, 0.66 [95% CI: 0.30, 1.47]; *P* = .31), contralateral breast recurrence (sHR, 0.62 [95% CI: 0.20, 1.91]; *P* = .40), or distant metastasis (sHR, 0.76 [95% CI: 0.31, 1.85]; *P* = .55) between the MRI and no-MRI groups in the subgroup of patients with invasive cancers.

Preoperative MRI and Recurrence Outcomes According to Hormone Receptor Status

Among the 999 patients who had been treated for hormone receptor–negative cancers, 109 (10.9%) experienced recurrence, and among the 3415 patients who had been treated for hormone receptor–positive cancers, 233 (6.8%) experienced recurrence. There was an interaction effect between MRI use and hormone receptor status in patients with breast cancer (*P* = .04). For hormone receptor–negative cancers, the total recurrence rate was lower in the MRI group than in the no-MRI group (5-year cumulative incidence, 8.2% vs 20.7%; sHR, 0.40 [95% CI: 0.19, 0.82]; *P* = .04). In the subgroup analyses according to site of first recurrence among patients with hormone receptor–negative cancers, ipsilateral in-breast recurrence was lower in the MRI group than in the no-MRI group (5-year cumulative incidence, 2.9% vs 10.0%; sHR, 0.28 [95% CI: 0.10, 0.76]) (Table 3, Fig 3). In patients with hormone receptor–positive cancers, there was no evidence that MRI reduced the risk of total recurrence (sHR, 1.09 [95% CI: 0.58, 2.03]; *P* = .79).

For hormone receptor–negative invasive cancers, total recurrence was lower in the MRI group than in the no-MRI group (sHR, 0.33 [95% CI: 0.16, 0.69]; *P* = .003), as was ipsilateral in-breast recurrence (sHR, 0.21 [95% CI: 0.08, 0.59]) (Table 3). For hormone receptor–positive invasive cancers, there was no evidence that MRI reduced the risk of total recurrence (sHR, 1.30 [95% CI: 0.61, 2.81]; *P* = .50). Figure 4 presents images in a patient with hormone receptor–positive invasive cancer in the no-MRI group who experienced recurrence.

Survival Outcomes

Among the 4414 patients, the 13-year cumulative rate of death was 3%. The 5-year overall survival was 99.4% in the MRI group and 98.6% in the no-MRI group after IPTW adjustment.

Table 3: Association between Preoperative MRI and Recurrence according to Hormone Receptor Status, after Inverse Probability of Treatment Weighting

Patient Population and Outcome	No. of Patients with Recurrence*	Subdistribution Hazard Ratio†	*P* Value‡
All patients (*n* = 4414)§			
Total recurrence (*n* = 342)‖			.04#
Hormone receptor negative	109/999 (10.9)	0.40 (0.19, 0.82)	.04**
Hormone receptor positive	233/3415 (6.8)	1.09 (0.58, 2.03)	.79**
Recurrence according to first site			
Local-regional (*n* = 151)††			.08#
Hormone receptor negative	51/999 (5.1)	0.39 (0.15, 1.04)	.06
Hormone receptor positive	100/3415 (2.9)	1.31 (0.52, 3.29)	.57
Ipsilateral in-breast (*n* = 106)††			.12#
Hormone receptor negative	39/999 (3.9)	0.28 (0.10, 0.76)	.01
Hormone receptor positive	67/3415 (2.0)	0.83 (0.33, 2.13)	.70
Contralateral breast (*n* = 91)			.21#
Hormone receptor negative	33/999 (3.3)	0.40 (0.10, 1.68)	.21
Hormone receptor positive	58/3415 (1.7)	1.32 (0.41, 4.29)	.64
Distant metastasis (*n* = 100)			.48#
Hormone receptor negative	25/999 (2.5)	0.41 (0.10, 1.78)	.24
Hormone receptor positive	75/3415 (2.2)	0.80 (0.27, 2.35)	.68
Patients with invasive cancers (*n* = 3680)‡‡			
Total recurrence (*n* = 297)‖			.01#
Hormone receptor negative	101/889 (11.4)	0.33 (0.16, 0.69)	.003
Hormone receptor positive	196/2791 (7.0)	1.30 (0.61, 2.81)	.50
Recurrence according to first site			
Local-regional (*n* = 128)††			.07#
Hormone receptor negative	47/889 (5.3)	0.31 (0.11, 0.84)	.02
Hormone receptor positive	81/2791 (2.9)	1.57 (0.38, 6.49)	.53
Ipsilateral in-breast (*n* = 85)††			.10#
Hormone receptor negative	35/889 (3.9)	0.21 (0.08, 0.59)	.003
Hormone receptor positive	50/2791 (1.8)	0.93 (0.22, 3.91)	.92
Contralateral breast (*n* = 71)			.12#
Hormone receptor negative	29/889 (3.3)	0.30 (0.07, 1.23)	.10
Hormone receptor positive	42/2791 (1.5)	1.58 (0.34, 7.35)	.56
Distant metastasis (*n* = 98)			.38#
Hormone receptor negative	25/889 (2.8)	0.44 (0.10, 1.91)	.28
Hormone receptor positive	73/2791 (2.6)	0.99 (0.33, 2.94)	.99

Note.—Hormone receptor–positive cancers were estrogen receptor positive and/or progesterone receptor positive; hormone receptor–negative cancers were estrogen receptor negative, progesterone receptor negative, and human epidermal growth factor receptor 2 positive or negative (ie, triple negative).

* Data in parentheses are percentages.

† Subdistribution hazard ratios were obtained via Fine and Gray subdistribution hazard model with inverse probability of treatment weighting adjustment. Data in parentheses are 95% CIs.

‡ *P* values adjusted with inverse probability of treatment weighting.

§ Number of patients in MRI group, 4118; number of patients in no-MRI group, 296.

‖ *Total recurrence* includes local-regional recurrence, contralateral breast recurrence, and distant metastasis.

P value for interaction between MRI and hormone receptor status of original breast cancer.

** To control for type I error, the Hochberg method was applied to adjust the *P* value.

†† *Local-regional* includes ipsilateral in-breast recurrence and recurrence involving the regional lymph nodes; thus, *ipsilateral in-breast* is a subset of local-regional.

‡‡ Number of patients in MRI group, 3498; number of patients in no-MRI group, 182.

The proportion of patients who died was 2.0% (82 of 4118) in the MRI group and 2.0% (six of 296) in the no-MRI group. There was no evidence that MRI improved overall survival (HR, 0.62 [95% CI: 0.26, 1.50]; *P* = .58) or survival among patients with invasive cancers (HR, 0.67 [95% CI: 0.28, 1.63]; *P* = .38) (Table 4, Fig 5).

Discussion

In our study, preoperative MRI was associated with lower ipsilateral in-breast recurrence (subdistribution hazard ratio [sHR], 0.49; *P* = .04) among patients aged 50 years or younger with breast cancer. Specifically, the 5-year cumulative incidence was 1.6% in those who underwent MRI and 3.3% in those who

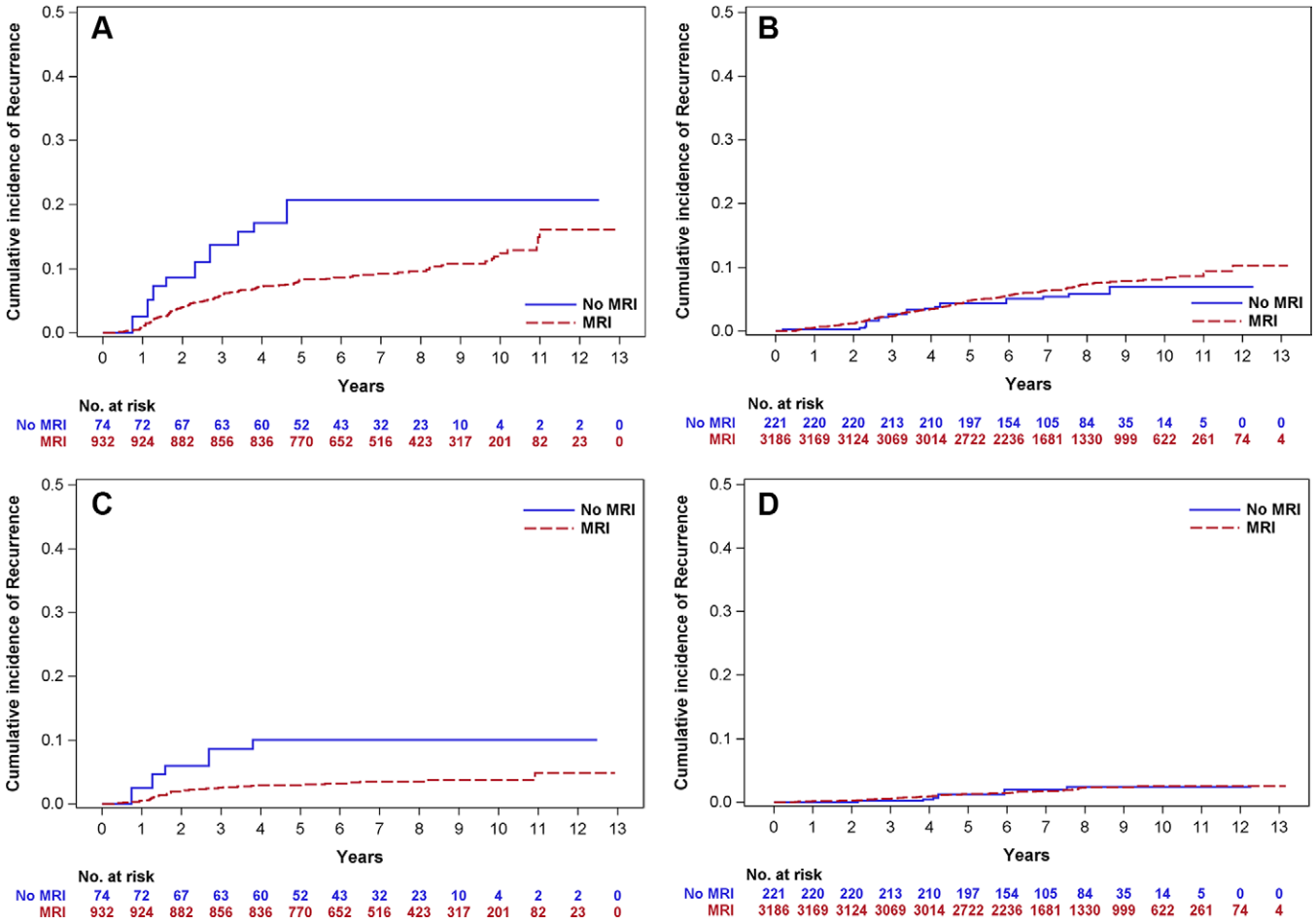

Figure 3: Cumulative incidence of recurrence according to hormone receptor status and site of first recurrence in the MRI and no-MRI groups, adjusted with inverse probability of treatment weighting. **(A)** Total recurrence in hormone receptor–negative cancers (subdistribution hazard ratio [sHR] = 0.40 [95% CI: 0.19, 0.82]; *P* = .04). **(B)** Total recurrence in hormone receptor–positive cancers (sHR = 1.09 [95% CI: 0.58, 2.03]; *P* = .79). **(C)** Ipsilateral in-breast recurrence in hormone receptor–negative cancers (sHR = 0.28 [95% CI: 0.10, 0.76]). **(D)** Ipsilateral in-breast recurrence in hormone receptor–positive cancers (sHR = 0.83 [95% CI: 0.33, 2.13]; *P* = .70). The number at risk is shown below each panel.

did not. In patients with hormone receptor–negative cancers, preoperative MRI was associated with lower total recurrence, which included local-regional recurrence, contralateral breast recurrence, and distant metastasis (5-year cumulative incidence, 8.2% in the MRI group vs 20.7% in the no-MRI group; sHR, 0.40; *P* = .04). Notably, the 5-year cumulative incidence of ipsilateral in-breast recurrence was lower in patients with hormone receptor–negative cancers who underwent MRI than in those who did not undergo MRI (2.9% vs 10.0%; sHR, 0.28).

Young patients with breast cancer are at greater risk of recurrence due to several factors, including a higher incidence of hormone receptor–negative cancers and a greater likelihood of familial mutations (20,21). In addition, with higher rates of dense breasts, young patients may have tumors that are occult at conventional imaging and thus undertreated. Indeed, meta-analyses have shown that preoperative MRI detects 11%–14% of occult tumors not detected at mammography (1,30) and 0.9%–2% of occult tumors not detected at mammography combined with breast US (31). Without preoperative MRI, these undetected lesions might become evident as recurrences, unless effectively managed with adjuvant therapy.

Our study revealed a 5-year cumulative incidence of ipsilateral in-breast recurrence of 1.6% in patients who underwent MRI and 3.3% in patients who did not (*P* = .04). The lower ipsilateral in-breast recurrence rate in the MRI group may be attributable to the high sensitivity of MRI in helping radiologists detect additional findings and accurately assess the extent of the tumor in the treated breast. Notably, the Swedish Preoperative MRI of the Breast (POMB) study randomized young patients to preoperative MRI versus standard imaging and reported lower ipsilateral breast tumor recurrence with MRI (4.9% vs 8.6%; HR, 0.67) (6), which is consistent with our findings. However, in our study, there was no evidence of a difference in total recurrence (sHR, 0.70; *P* = .15), including local-regional recurrence (sHR, 0.73; *P* = .37), contralateral breast recurrence (sHR, 0.73; *P* = .54), or distant metastasis (sHR, 0.64; *P* = .32), between the MRI and no-MRI groups. Zeng et al (19) reported similar local recurrence rates (HR, 1.05; *P* = .89) in premenopausal women who did versus those who did not undergo MRI. Another study found that preoperative MRI did not result in a significant improvement in local-regional recurrence-free survival in patients younger than 35 years (HR, 1.3; *P* = .42) (23). With the increasing incidence of breast cancer in young patients, our results support the selective use of preoperative MRI to lower the risk of ipsilateral in-breast recurrence in patients aged 50 years or younger with newly diagnosed breast cancer who plan to undergo upfront surgery.

In our study, among outcomes according to hormone receptor status, a lower 5-year cumulative incidence of recurrence was

observed with MRI only in hormone receptor–negative cancer (8.2% in MRI group vs 20.7% in no-MRI group for overall recurrence, 2.9% vs 10.0% for ipsilateral in-breast recurrence). This finding aligns with recent studies showing that local-regional recurrence is more common in patients aged 40 years or younger, particularly in those with hormone receptor–negative subtypes such as human epidermal growth factor receptor 2–positive and triple-negative cancers (24,32). The greater benefit of preoperative MRI in patients with hormone receptor–negative tumors may be attributable to the lower responsiveness of these tumors to hormonal therapies and the higher risk of recurrence (21,32). By enabling the early detection of preoperatively occult malignancies, MRI may help reduce postoperative recurrence in this high-risk subgroup. Additionally, when recurrence patterns were examined by site (local-regional, contralateral breast, and distant metastasis), our study revealed notable differences, despite the limited statistical power due to the small number of recurrences in each subgroup. Among patients with hormone receptor–negative cancers, the HRs for recurrence in the MRI group ranged from 0.28 to 0.41, whereas among patients with hormone receptor–positive cancers, they ranged from 0.80 to 1.32. Consistent with our findings, a study that evaluated subsets of women based on primary cancer histopathologic type (invasive vs ductal carcinoma in situ), age (≤50 vs >50 years), and hormonal receptor status reported improved local control in patients with triple-negative cancers who underwent preoperative MRI compared with those who did not (11). By focusing on young patients with breast cancer and stratifying outcomes on the basis of hormone receptor status, our study provides valuable insights into the subgroups that may benefit most from tailored preoperative MRI.

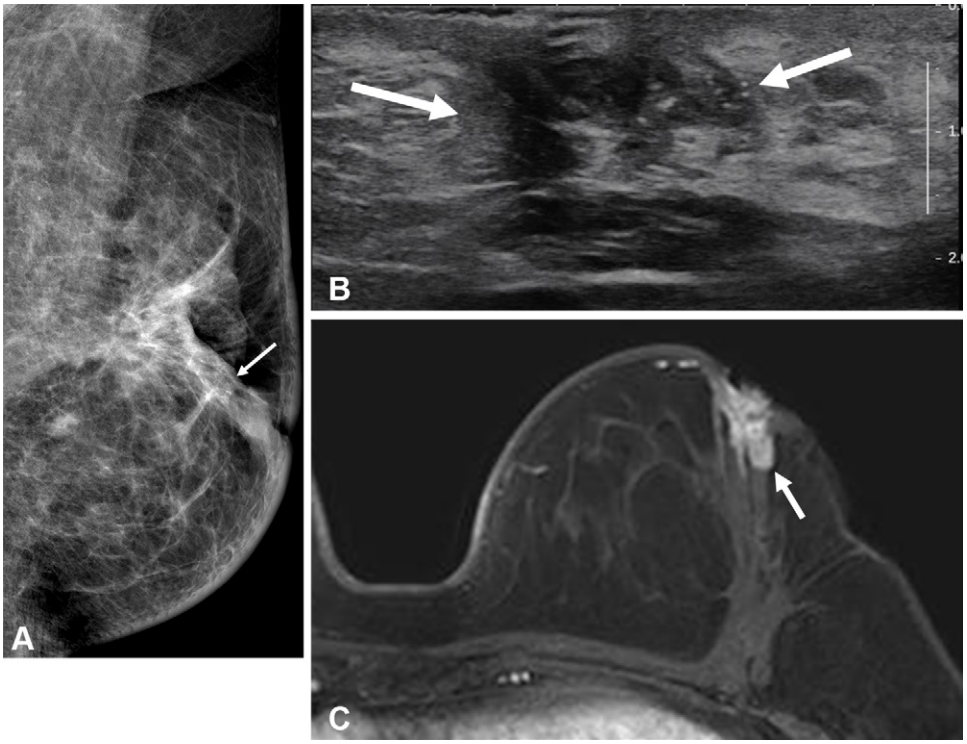

Figure 4: Images in a 49-year-old patient originally treated for hormone receptor–positive invasive cancer without preoperative MRI who developed bloody nipple discharge 2 years after surgery. **(A)** Left mediolateral oblique mammogram shows new grouped pleomorphic calcification (arrow) adjacent to the previous operation site. **(B)** Transverse US image shows a 2.3-cm hypoechoic mass (arrows) with calcifications. **(C)** Axial contrast-enhanced fat-saturated T1-weighted MRI scan shows an irregular, heterogeneously enhancing mass (arrow) in the left breast, adjacent to the operation site. The final pathologic examination confirmed recurrent invasive ductal carcinoma.

Table 4: Association between Preoperative MRI and Overall Survival after Inverse Probability of Treatment Weighting

Outcome	No. of Patients Who Died*	Hazard Ratio†	*P* Value‡
Deaths in all patients (*n* = 4414)			
No MRI	6/296 (2.0)		
MRI	82/4118 (2.0)	0.62 (0.26, 1.50)	.58§
Deaths in patients with invasive cancers (*n* = 3680)			
No MRI	6/182 (3.3)		
MRI	80/3498 (2.3)	0.67 (0.28, 1.63)	.38

* Data in parentheses are percentages.

† Data in parentheses are 95% CIs.

‡ *P* value obtained via Cox proportional hazards model with inverse probability of treatment weighting adjustment.

§ To control for type I error, the Hochberg method was applied to adjust the *P* value.

The strengths of our study include its multicenter design and the use of IPTW to adjust for confounding factors. However, our study had some limitations. First, as this was a retrospective study, there may be selection bias. Indeed, the relatively small size of the no-MRI group may have resulted in excessive weights being assigned to some patients. However, we minimized confounding through matching and used stabilized IPTW. Second, patients treated with neoadjuvant chemotherapy were excluded. This exclusion may limit the generalizability of our findings, as human epidermal growth factor receptor 2–positive and triple-negative tumor subtypes were not included, despite the important role of MRI in assessment of pathologic response and guiding of surgical management in these cancer types (33). Third, we did not investigate the impact of preoperative MRI findings in predicting surgical appropriateness and did not include an analysis of MRI imaging characteristics. Fourth, the

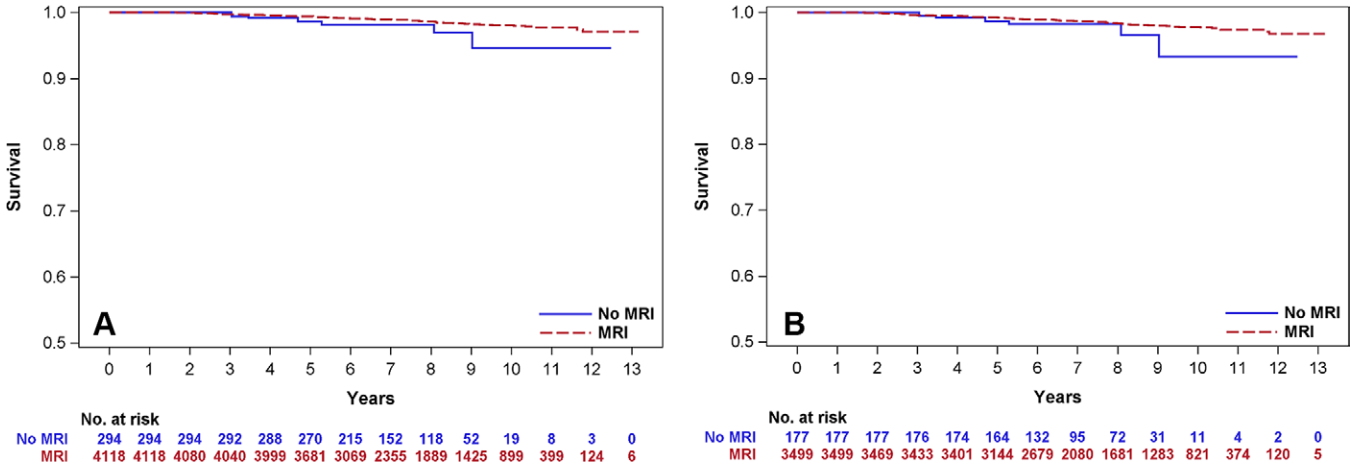

Figure 5: Overall survival outcomes in the MRI and no-MRI groups adjusted with inverse probability of treatment weighting. **(A)** Overall survival in all patients (hazard ratio, 0.62 [95% CI: 0.26, 1.50]; *P* = .58). **(B)** Overall survival in patients with invasive cancers (hazard ratio, 0.67 [95% CI: 0.28, 1.63]; *P* = .38). The number at risk is shown below each panel.

subgroup analyses based on site of first recurrence were exploratory and thus should be interpreted with caution due to the increased risk of type I error. Fifth, the number of deaths in the study may have been too low to evaluate the effect of MRI on survival with adequate statistical power. Given the current sample size of 4414 patients and 88 deaths, the statistical power calculated post hoc was 42.6%. Therefore, it is possible that a statistically significant effect could have been observed with a larger number of deaths.

In conclusion, our findings suggest that preoperative MRI is associated with a lower risk of ipsilateral in-breast recurrence in patients with newly diagnosed breast cancer at age 50 years or younger, with the greatest benefits observed in patients with hormone receptor–negative cancers. Further prospective multicenter studies are needed to validate the effectiveness of preoperative MRI in these young patients with breast cancer.

Deputy Editor: Linda Moy
Scientific Editor: Shannyn Wolfe (AJE)

Author affiliations:

[1] Department of Radiology, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea

[2] Department of Surgery, Seoul National University Bundang Hospital, Seongnam, Republic of Korea

[3] Division of Medical Statistics, Medical Research Collaborating Center, Seoul National University Hospital, Seoul, Republic of Korea

[4] Department of Surgery, Seoul National University Hospital, Seoul, Republic of Korea

[5] Cancer Research Institute, Seoul National University, Seoul, Republic of South Korea

[6] Department of Radiology, Seoul National University College of Medicine, Seoul, Republic of Korea

[7] Institute of Radiation Medicine, Seoul National University Medical Research Center, Seoul, Republic of Korea

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Address correspondence to: S.M.H. (email: su3ha5@snu.ac.kr).

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