Original Study

Time-Related Changes in Yield and Harms of Screening Breast Magnetic Resonance Imaging

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Abstract

Among high-risk women being followed over time with breast magnetic resonance imaging (MRI), the harms from MRI decrease over time, whereas cancer detection does not. This study supports the practice of serial breast MRI for screening women at high risk for breast cancer.

Purpose: Breast magnetic resonance imaging (MRI) is accepted as a useful adjunct to screening mammography for women at high risk for breast cancer. Nevertheless, concerns about false-positive findings remain, and data about MRI harms and yields are limited. The aim of this study was to quantify harms and yields of breast MRI over time in a large series of patients. **Methods:** A retrospective review was performed of patients at increased risk for breast cancer who underwent annual screening digital mammography and MRI from 2007 to 2013. Harms were defined as events not producing a breast cancer diagnosis (ultrasonography [US], imaging-guided core or surgical biopsy procedure, recommendation for short-term follow-up, or a combination). **Results:** Of 350 high-risk patients offered MRI screening, 320 underwent 757 screening MRI procedures over time. The median age at the first MRI was 48 years. All patients met American Cancer Society criteria for annual screening breast MRI. Total harms were highest with the first MRI procedure and decreased with subsequent MRI screening. Of 75 biopsy procedures performed, including 58 US- or MRI-guided core biopsy procedures and 17 surgical biopsy procedures, 6 specimens were found to be malignant, including 2 resulting from biopsy procedures performed based on findings from the first MRI scan, 0 from the second MRI scan, 3 from the third MRI scan, and 1 from the fourth MRI scan. **Conclusion:** Among women followed with screening MRI, the number of harms was shown to decrease over time. Breast cancer continued to be detected in MRI studies performed over time. This study demonstrates the utility of MRI screening performed over time in high-risk women.

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Introduction

Over the past 25 years, tremendous advances have been made in the technology and interpretation of breast magnetic resonance imaging (MRI). The accuracy of MRI screening and diagnostic tests more generally are a function of both sensitivity (ability to detect true-positive results) and specificity (ability to exclude false-positive results). Although the sensitivity of screening breast MRI has been shown to be superior to that of mammography, it is limited by lower specificity, high false-positive rates, and increased need for additional imaging or biopsy procedures.[1-5]

Studies conducted in the 1990s for patients at high risk for the development of breast cancer found that the sensitivity approximately doubled for MRI compared with mammography, although specificity was variable.[1-6] The need for additional imaging to confirm findings identified on MRI ranged from 8% to 17%, whereas biopsy rates ranged from 3% to 15%. Across a series of 9 studies in which 4485 high-risk women were screened with mammography and MRI, the supplemental yield of MRI was 24 cancers per 1000 women screened, with initial screening MRIs producing the highest rates of false-positive findings.[2-11]

In 2007, the American Cancer Society updated its breast cancer screening guidelines, recommending MRI as an adjunct to mammography in certain high-risk women.[12] Specifically, annual

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MRI was recommended for women known to carry a *BRCA* mutation (or other mutations that confer increased breast cancer risk), untested first-degree relatives of *BRCA* mutation carriers, women who had received chest irradiation between the ages of 10 and 30 years, and women whose lifetime risk was 20% to 25% or greater, as defined by BRCAPRO or other models that are largely dependent on family history. Recent studies have suggested that breast MRI may be particularly useful for breast cancer detection in younger women or women with increased breast density, or for both these groups.[13,14]

Rising health care costs have prompted an increased focus on providing high-value cost-conscious care.[15,16] Furthermore, there are concerns about possible harms that may result from extra testing and biopsy procedures for women who are not subsequently found to have breast cancer and how those harms may contribute to breast cancer screening decision making.[17]

The primary aim of this study was to quantify harms and yields of supplemental breast MRI in high-risk patients and evaluate how those harms and yields change over time. We hypothesized that harms of screening MRI would decrease over time, whereas rates of cancer detection (yields) would remain stable. The findings of this study may assist high-risk women and providers in the decision to use MRI as a supplement to screening mammography.

Methods

We conducted a retrospective chart review in a Cleveland Clinic Institutional Review Board–approved study that identified women at high risk for the development of breast cancer who were seen by 1 breast cancer specialist with expertise in the management of women at increased risk for breast cancer at the Cleveland Clinic Breast Center from April 2007 to January 2013. Patients were included in the study if they met the American Cancer Society criteria for screening breast MRI[12] or had a personal history of breast cancer or ductal carcinoma in situ (DCIS) and were then offered annual screening mammography and supplemental breast MRI 6 months apart—a protocol similar to that practiced in other institutions.[18,19] Data regarding patient characteristics, breast cancer risk variables, breast density on mammography, estimated lifetime risk, need for additional imaging or biopsy procedures (or both), and biopsy outcomes were collected. Rates of radiology callbacks for second-look ultrasonography (US) for enhancement on MRI were compared between the earlier years of the study and the later years.

Harms of screening MRI were defined as the total number of second-look US procedures, US- or MRI-guided core biopsies, surgical biopsies, and short-interval follow-up studies that did not result in a cancer diagnosis. Specific harms resulting from each individual MRI procedure were totaled. Yields of screening MRI were defined as an MRI procedure that resulted in a diagnosis of previously unknown invasive breast cancer or DCIS identified on any core biopsy specimen or surgical procedure that was performed because of the MRI finding. A false-positive biopsy result was a benign finding on any core biopsy or surgical procedure that was performed because of suspicious MRI enhancement.

Reliability of radiologists' US assessments were evaluated using the split-half method. Results of radiologists' second-look US assessments were divided into 2 periods: the first 3 years of the study period and the second 3 years of the study period. The 2 periods were compared to assess consistency of results over time.

We used a modified version of the Breast Imaging Reporting and Data System (BI-RADS) to categorize breast density. We collapsed the 4 standard categories—(1) almost entirely fatty, (2) scattered fibroglandular densities, (3) heterogeneously dense, and (4) extremely dense—into 2 categories, ie, extremely dense (4) and not extremely dense (1-3). This modification was made in an effort to avoid issues with small numbers of observations in some levels of the original breast density variable.

Categorical variables were summarized using counts and percentages. Continuous variables were summarized using means, standard deviations, and 5-number summaries (minimum, first quartile, median, third quartile and maximum). Tests for differences in percentages between categorical variables were done by using the Pearson χ^2 test or the Fisher exact test. The latter was used in situations in which the assumptions of the χ^2 test were violated. Tests for differences in location of continuous variables by levels of a factor were performed using the Wilcoxon rank sum test, accompanied by interquartile ranges. Tests for associations involving ordinal factors and continuous variables were performed by using the Spearman rank correlation, with associated 95% confidence intervals. All analyses were performed using R software, version 2.15.1 (The R Project for Statistical Computing, Vienna, Austria). Statistical significance was defined as a P value $< .05$.

Table 1 Patient Characteristics

Age (mean ± SD)	48 ± 9.1
Race	
White	93%
Black	5.5%
Other	1.5%
BMI (mean ± SD)	26 ± 5.4
Premenopausal Status	62%
Postmenopausal Status	38%
Received Hormone Replacement Therapy	88.4%
First-Degree Relative with Breast Cancer	78%
***BRCA* Mutation or Other Genetic Mutation**	25%
Family History of Invasive Breast Cancer	14%
Personal History of Invasive Breast Cancer or DCIS	17%
Lobular Carcinoma In Situ	7%
ADH or ALH	26%
Tissue Density	
Extremely dense (BI-RADS 4 density)	18%
Not extremely dense (BI-RADS < 4 density)	82%
Median Lifetime Breast Cancer Risk	
Gail lifetime risk (n = 150)	25%
Claus lifetime risk (n = 41)	28%
Tyrer-Cuzick lifetime risk (n = 27)	23%

Abbreviations: ADH = atypical ductal hyperplasia; ALH = atypical lobular hyperplasia; BI-RADS = breast imaging reporting and data system; BMI = body mass index; DCIS = ductal carcinoma in situ.