The Utility of Short-Interval Follow-Up for Baseline High-Risk Screening Breast MRI

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Abstract

Objective: Patients with a high lifetime risk of developing breast cancer undergo annual screening magnetic resonance imaging (MRI) starting at age 30. A proportion of these patients are subsequently required to undergo short-interval follow-up MRI 6 months after their baseline examination. The purpose of this study was to evaluate the utility and outcome of these short-interval follow-up examinations in this population. Methods: A retrospective review was performed of 523 patients who received their baseline high-risk breast screening MRI at our institution between 2013 and 2017. The proportion of patients who received a short-interval follow-up MRI at 6 months was recorded. The findings at baseline and follow-up MRI were recorded, as well as the outcomes and results of any interventions performed. Results: Ninety-six (17.6%) patients (age range: 25-67, mean age: 41) received a short-interval follow-up MRI following their baseline screening examination. Indications for follow-up included moderate to marked background parenchymal enhancement, nonmass enhancement, and likely benign enhancing mass. Of the 92 patients, 5 (5.4%) went on to have a biopsy, with none revealing a malignant pathology. The remainder either returned to routine screening (91.3%) or received further imaging in the form of ultrasound or additional follow-up MRI (3.3%). Conclusion: Short-interval follow-up breast MRI in high-risk patients after a baseline screening study with likely benign findings is unlikely to yield clinically significant findings. This retrospective study can be considered a starting point for additional future work looking at the rate, indications, and yield of short-interval follow-up following baseline high-risk screening breast MRI studies.

Résumé

Objectif : Les patientes présentant un risque à vie élevé de développer un cancer du sein se soumettent à un examen annuel d’imagerie par résonance magnétique (IRM) de dépistage à partir de l’âge de 30 ans. Un certain nombre de ces patientes doivent ensuite subir un examen d’IRM de suivi à court terme 6 mois après leur examen de référence. L’objectif de cette étude était de déterminer l’utilité et les résultats de ces examens de suivi à court terme chez cette population. Méthodes : Une analyse rétrospective a été conduite sur 523 patientes ayant subi leur examen d’IRM de référence de dépistage de cancer du sein à haut risque dans notre établissement entre 2013 et 2017. La proportion de patientes ayant bénéficié d’un examen d’IRM de suivi à court terme 6 mois plus tard a été notée. Les résultats obtenus suite à l’IRM de référence et de suivi ont été enregistrés, tout comme l’issue et les résultats des interventions éventuellement effectuées. Résultats : Suite à leur examen de référence de dépistage, 92 patientes (17,6 %) (plage d’âge : 25 à 67 ans; âge moyen : 41 ans) ont bénéficié d’un examen d’IRM de suivi à court terme. Les indications pour un suivi étaient notamment les suivantes : rehaussement parenchymateux de fond marqué, rehaussement sans masse et masse de rehaussement probablement bénigne. Le suivi de 5 (5,4 %) de ces 92 patientes s’est poursuivi par une biopsie dont aucune n’a dévoilé de pathologie maligne. Les autres patientes ont repris le dépistage de routine (91,3 %) ou ont subi un examen d’imagerie complémentaire sous forme d’échographie ou d’IRM de suivi supplémentaire (3,3 %). Conclusion : Il est peu probable que, chez les patientes à haut risque de cancer du sein, un examen d’IRM de suivi à court terme...
Introduction

Breast cancer is a leading cause of morbidity and mortality across the world and represents the most common cause of cancer-related death in women worldwide.1 Given the extensive burden of this disease, multiple screening programs have been implemented to improve detection of breast cancer in its early and potentially treatable stages. The screening protocols differ depending on the lifetime risk of developing breast cancer. In those at high risk of developing breast cancer, the general consensus is for annual mammographic and magnetic resonance imaging (MRI) screening beginning at age 30.2-4

Women at high risk include those with a genetic mutation, such as breast cancer gene (BRCA) 1 or 2, familial predisposition, as well as those who have received prior chest radiation. The lifetime risk of breast cancer among average-risk women is considered to be less than 15%, whereas those considered high risk are over 20% to 25%.5 Several studies have established the superiority of combined mammography and MRI compared with mammography alone in the detection of breast cancer for high-risk individuals.6,7

A proportion of the high-risk patients receiving breast MRI are subsequently required to undergo a short-interval follow-up breast MRI 6 months following their baseline MRI study. This is typically due to various benign-appearing findings that do not otherwise require additional workup with ultrasound or due to excessive enhancement of the background breast parenchyma, which can limit visualization. The underlying intent of short-interval follow-up is to monitor lesions for changes at a shorter interval than the routine annual screening.

In the setting of patients receiving their baseline screening MRI, short-interval follow-up may be recommended for a variety of probable benign findings indicative of the lack of comparison examinations. In fact, previous studies have demonstrated that baseline screening breast MR is associated with a higher likelihood of recommendation for short-interval follow-up than MR imaging with prior comparison studies available.8 However, the utility and benefit of short-interval follow-up breast MRI in this setting has not been well studied, which raises several concerns regarding the value of this recommendation. The purpose of this study was to evaluate the utility and outcome of short-interval follow-up breast MRI 6 months following baseline examination for patients at high risk of developing breast cancer. These studies are categorized as Breast Imaging Reporting and Data System (BI-RADS) 3.2

Methods

High-Risk Screening Population

With institutional research ethics board approval, a retrospective study was performed of all baseline high-risk screening MRI examinations performed at 2 tertiary academic breast imaging centers (SJHH and JH, Hamilton, Canada) from 2013 to 2017. Of these examinations, the baseline MRI studies with recommendation for short-interval follow-up were isolated and further reviewed in detail. The following was recorded: patient age at time of baseline examination, parenchymal tissue composition, degree of background parenchymal enhancement (BPE), reason for short-interval follow-up, and the outcome of the short-interval follow-up. If any biopsies were performed, the histopathology results were also recorded. All patients were followed up for a total of 2 years following their baseline MRI.

The indications for high-risk breast cancer screening followed by our institution and established by Cancer Care Ontario are listed in Table 1. All women regardless of age or menopausal status were included in this study. Those women who had a prior breast MRI examination were excluded.

Breast MRI Technique

Patients were scanned with either a 3 Tesla (Philips Achieva; Amsterdam, Netherlands) or a 1.5 Tesla (GE Signa HDX twin speed; Boston, Massachusetts, United States) magnets. The patients were scanned in a prone position. A specialized breast coil was utilized to obtain images. Intravenous administration of Gadovist contrast (0.1 mmol/kg) was used. The MRI preferably performed during days 5 to 12 of the menstrual cycle to minimize the effect of hormones on the BPE and to reduce the rate of false positives. The field of view was carefully selected to ensure adequate anatomical coverage of the region of interest while maintaining spatial resolution (extending from the clavicles to the inframammary fold, including axilla). Sequences used were localizer, axial T1-weighted fast-field echo 3-dimensional, axial T2-weighted fast-spin echo, axial diffusion-weighted imaging, and axial dynamic postcontrast sequences at 1, 2, 3, 4, 5, and 6 minutes post contrast injection, with each acquisition lasting for 90 seconds.

Magnetic Resonance Imaging Interpretation

All images were interpreted by fellowship-trained breast radiologists. Images were interpreted in conjunction with any
In this retrospective study, a total of 523 patients who received a baseline screening breast MRI between 2013 and 2017 at our institution were reviewed (Table 2). Among these, 92 (17.6%) patients received a short-interval follow-up MRI examination and were included (mean age: 41, age range: 25-67).

In terms of imaging characteristics in this population, the amount of fibroglandular tissue was predominantly categorized as scattered (39.1%) and heterogeneous (33.7%). With regard to BPE, the majority were classified as mild (34.8%) or moderate (33.7%), with several cases demonstrating marked enhancement (22.8%).

In declining frequency, the most common indications for short-interval follow-up were “nonmass enhancement” (NME) and “likely benign enhancing mass” at 34 cases each (36.9%) and other (3.3%). Cases within the “other” category included lesions with peripheral enhancement, which may represent inflamed cysts or those with indeterminate characteristics. These results are summarized in Table 3.

At the time of follow-up, only 5 (5.4%) patients went on to require biopsy. The remainder either returned to routine screening (91.3%) or received further imaging in the form of ultrasound or further follow-up MRI (3.3%). None of these cases were found to have clinically significant findings. Of the 5 biopsies, 4 had benign pathology and 1 case received a diagnosis of atypical lobular hyperplasia (ALH; Table 4). No malignancies were otherwise identified. Collectively, there were no malignancies identified among the 92 cases receiving short-interval follow-up MRI.

**Table 1. Eligibility Criteria for High-Risk Breast Cancer Screening.**

<table>
<thead>
<tr>
<th>High-Risk Breast Cancer Screening Guidelines</th>
<th>Recommendation Population</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Women ages 30-69 years identified as high risk</td>
<td>Meet one of the following risk criteria:</td>
<td>- Known carriers of deleterious gene mutation (eg, BRCA1, BRCA2, TP53, PTEN, CDH1)</td>
</tr>
<tr>
<td>- Are first-degree relatives (parent, brother, sister, or child) of someone who has a gene mutation that increases their risk for breast cancer, have already had genetic counseling, and have chosen not to have genetic testing</td>
<td>- Have been assessed by a genetics clinic as having a 25% or greater lifetime risk of breast cancer based on personal family history</td>
<td></td>
</tr>
<tr>
<td>- Have received radiation therapy to the chest before age 30 and at least 8 years previously</td>
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<td></td>
</tr>
</tbody>
</table>

Abbreviation: MRI, magnetic resonance imaging.

*Adapted from Information from Cancer Care Ontario (Chiarelli et al*).

**Table 2. Total Number of Patients and Average Age of Patients Receiving a Baseline Screening MRI Between 2014 and 2017.**

<table>
<thead>
<tr>
<th>Category</th>
<th>Total Patients</th>
<th>Average Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline screening MRI</td>
<td>523</td>
<td>41.4</td>
</tr>
<tr>
<td>Short-interval follow-up</td>
<td>92 (17.6%)</td>
<td>41.4</td>
</tr>
</tbody>
</table>

Abbreviation: MRI, magnetic resonance imaging.

**Results**

In this retrospective study, a total of 523 patients who received a baseline screening breast MRI between 2013 and 2017 at our institution were reviewed (Table 2). Among these, 92 (17.6%) patients received a short-interval follow-up MRI examination and were included (mean age: 41, age range: 25-67).

In terms of imaging characteristics in this population, the amount of fibroglandular tissue was predominantly categorized as scattered (39.1%) and heterogeneous (33.7%). With regard to BPE, the majority were classified as mild (34.8%) or moderate (33.7%), with several cases demonstrating marked enhancement (22.8%).

In declining frequency, the most common indications for short-interval follow-up were “nonmass enhancement” (NME) and “likely benign enhancing mass” at 34 cases each (36.9%) and other (3.3%). Cases within the “other” category included lesions with peripheral enhancement, which may represent inflamed cysts or those with indeterminate characteristics. These results are summarized in Table 3.

At the time of follow-up, only 5 (5.4%) patients went on to require biopsy. The remainder either returned to routine screening (91.3%) or received further imaging in the form of ultrasound or further follow-up MRI (3.3%). None of these cases were found to have clinically significant findings. Of the 5 biopsies, 4 had benign pathology and 1 case received a diagnosis of atypical lobular hyperplasia (ALH; Table 4). No malignancies were otherwise identified. Collectively, there were no malignancies identified among the 92 cases receiving short-interval follow-up MRI.

**Discussion**

Studies have demonstrated that baseline screening breast MRI is associated with a higher rate of short-interval follow-up compared to MRIs with previous available for comparison. This has been attributed to increased follow-up of probable benign lesions, which are later confirmed to be more definitively benign once they demonstrate stability at follow-up. Consequently, this results in a higher false-positive rate compared to breast MRI studies with a previous available for comparison. This finding raises several issues, particularly pertaining to the risks that patients experience with excessive and potentially unnecessary imaging. These risks include increased patient anxiety, safety concerns with gadolinium contrast exposure, false-positive findings, and higher healthcare costs. Therefore, given the various consequences of repeat imaging, it is necessary to first evaluate the outcomes of patients receiving short-interval follow-up following their baseline screening examination. Specifically, assessment is required on whether or not the increased rate of follow-up among baseline scans is warranted.

In this study, we identified that 17.6% of patients at our institution received a 6-month follow-up breast MRI examination following their initial baseline study. Among the patients receiving short-interval follow-up MRI, NME and likely benign enhancing masses were the most common indications, followed by moderate to marked BPE. Subsequently, 91.3% of patients receiving short-interval follow-up returned to routine screening, with 3.3% receiving additional imaging and 5.4% (5 cases) going on to have a biopsy. None of the 5 biopsies yielded a diagnosis of malignancy. Four biopsies had benign histopathology, and 1 case had a diagnosis of ALH, which is at most a high-risk lesion.

Given that none of the cases in our study demonstrated malignancy following short-interval follow-up, further insight is required into the indications for follow-up to limit unnecessary examinations. The American College of Radiology atlas can be considered a reference in this situation, where a BI-RADS category 3 is assigned to “probably benign findings,” which are considered to have a malignancy rate of less than 2%, but not 0%. This is the case for the 6 month follow-up MRI studies that were evaluated. However, the criteria and indications included in this category are not completely clear at this time and are listed as “intuitive” based on the present finding and radiologist experience. Typically, this category was used in the setting where the interpreting physician hopes to establish stability of the area of concern before returning the patient to routine screening. Unfortunately, this leaves a broad variety of
indications that would qualify for short-interval follow-up, particularly in the setting of a baseline screening examination. The few published studies evaluating the frequency of BI-RADS 3 categorization in breast MRI screening report a rate of 6% to 12%.12-14 Therefore, further research may be directed toward evaluating the indications for follow-up in baseline screening examinations to achieve the 6% to 12% range.

A few studies have been performed evaluating the common indications for short-interval follow-up breast MRI and whether they are appropriate for such a recommendation.12,14-17 DeMartini et al16 studied the impact of BPE on the diagnostic performance of breast MRI and found that increased BPE was associated with a higher abnormal interpretation rate (BI-RADS 0, 3, 4, or 5) and more likely to receive short-interval follow-up compared to other forms of NME. Overall, further research in this area and adherence to accepted guidelines may be of particular benefit in reducing short-interval follow-up rates in the setting of baseline screening MRIs, where comparison examinations are not available to demonstrate stability.

In summary, the findings of this study suggest that short-interval follow-up following a baseline screening breast MRI for a number of nonspecific findings has a very low likelihood of identifying malignancy. However, there are several limitations of this study that must be acknowledged. First, the sample size may not be sufficiently large enough to definitively determine the utility of short-interval follow-up in the setting of baseline screening breast MRI examinations. It is possible that a higher sample size may demonstrate cases of malignancy, which were not found in our patient population. Furthermore, the specific details of each indication for short-interval follow-up were not recorded. There are various subtypes and characteristics of “NME” and “likely benign enhancing masses” that may provide more specific information to better risk stratify patients receiving follow-up examinations. Additionally, the timing of the MRI study with respect to the patient’s cycle was not recorded; this can have an impact on BPE. Nevertheless, this retrospective study can be considered a starting point for additional future work looking at the rate and yield of short-interval follow-up following baseline screening breast MRI studies.

Declaration of Conflicting Interests
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References
4. Chiarelli AM, Prummel MV, Muradali D, et al. Effectiveness of screening with annual magnetic resonance imaging and

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Table 3. Distribution and Characteristics of Patients With Short-Interval Follow-Up MRI Following Baseline MRI Examination for High-Risk Breast Cancer Screening.

<table>
<thead>
<tr>
<th>Category</th>
<th>Parenchymal Tissue (1 = fatty, 2 = scattered, 3 = heterogeneous, 4 = extreme), n (%)</th>
<th>Background Parenchymal Enhancement (BPE: 1 = minimal, 2 = mild, 3 = moderate, 4 = marked), n (%)</th>
<th>Reason for Short-Interval Follow-Up (1 = moderate or marked BPE, 2 = non mass enhancement, 3 = likely benign enhancing mass, 4 = other), n (%)</th>
<th>Outcome of Short-Interval Follow-Up (1 = benign, 2 = additional imaging, 3 = biopsy, 4 = surgery, 5 = false-positive findings, 6 = malignant), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8 (8.7)</td>
<td>8 (8.7)</td>
<td>21 (22.8)</td>
<td>72 (78.3)</td>
</tr>
<tr>
<td>2</td>
<td>36 (39.1)</td>
<td>32 (34.8)</td>
<td>34 (36.9)</td>
<td>3 (3.3)</td>
</tr>
<tr>
<td>3</td>
<td>31 (33.7)</td>
<td>31 (33.7)</td>
<td>31 (36.9)</td>
<td>5 (5.4)</td>
</tr>
<tr>
<td>4</td>
<td>17 (18.5)</td>
<td>21 (22.8)</td>
<td>3 (3.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>5</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>12 (13.0)</td>
</tr>
</tbody>
</table>

Abbreviations: MRI, magnetic resonance imaging; NA, not applicable.

Table 4. Biopsy Results for Patients Who Underwent Biopsy Following the Short-Interval MRI.

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Biopsy Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Benign breast tissue with fibrocystic changes</td>
</tr>
<tr>
<td>2</td>
<td>Atypical lobular hyperplasia (ALH)</td>
</tr>
<tr>
<td>3</td>
<td>Benign fibroglandular tissue</td>
</tr>
<tr>
<td>4</td>
<td>Benign breast tissue with sclerosing adenosis</td>
</tr>
<tr>
<td>5</td>
<td>Benign breast tissue with focal apocrine metaplasia</td>
</tr>
</tbody>
</table>

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