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Evaluation of expert criteria for preoperative magnetic resonance imaging of newly diagnosed breast cancer

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ABSTRACT

Despite 2 randomized trials reporting no reduction in operations or local recurrence at 1 year, preoperative magnetic resonance imaging (MRI) is increasingly used in diagnostic workup of breast cancer. We evaluated 5 utilization criteria recently proposed by experts. Of women ($n = 340$) newly diagnosed with unilateral breast cancer who underwent bilateral MRI, most (69.4%) met at least 1 criterion before MRI: mammographic density (44.4%), under consideration for partial breast irradiation (PBI) (19.7%), genetic-familial risk (12.9%), invasive lobular carcinoma (11.8%), and multifocal/multicentric disease (10.6%). MRI detected occult malignant lesion or extension of index lesion in 21.2% of index, 3.3% of contralateral, breasts. No expert criterion was associated with MRI-detected malignant lesion, which associated instead with pre-MRI plan of lumpectomy without PBI (48.2% of subjects): Odds Ratio 3.05, 95% CI 1.57–5.91 (p adjusted for multiple hypothesis testing = 0.007, adjusted for index-vs-contralateral breast and covariates). The expert guidelines were not confirmed by clinical evidence.

1. Introduction

Magnetic resonance imaging (MRI) is increasingly used in the diagnostic workup of breast cancer, both in situ and invasive. Preoperative MRI of the breast is used more often among patients from major metropolitan areas and less often among women who are poor, non-White, or elderly [1,2]. In patients for whom breast cancer treatment is planned, preoperative (MRI) detects additional tumor foci in the ipsilateral breast in 10–30% of cases and clinically and mammographically occult cancer in the contralateral breast in 3–5% [3–5]. Nevertheless, the use of breast MRI to ascertain the extent of disease remains controversial, because of debate regarding longterm clinical benefit from surgical excision of additional tumor detected by MRI of the ipsilateral breast [4,6] and because randomized trials of preoperative MRI have concluded that such imaging does not significantly affect the frequency of avoidable operations (total of initial mastectomies not justified by pathology, re-excisions and mastectomies within 6 months after breast-conserving surgery) [7,8], overall healthcare costs [7], or likelihood of local recurrence at 1 year [7]. Less controversial is the use of preoperative MRI to screen the contralateral breast of patients with proven cancer: for such screening, the American College of Radiology [9] and the European Society of Breast Imaging (EUSOBI) [5] recommend bilateral MRI.

Experts have proposed various guidelines for targeting preoperative MRI to those breast cancer patients with the highest anticipated yield of new malignant findings. For instance, EUSOBI has recommended preoperative MRI especially in the case of dense breasts or invasive lobular carcinoma (ILC) [5]. From expert opinion and a limited number of studies, Sardanelli proposed 6 criteria, any one of which might justify preoperative MRI in breast cancer: extreme or heterogeneous mammographic density, multifocal/multicentric disease, ILC, high genetic-familial risk of breast cancer, “discrepancy >1 cm in size between mammography and ultrasound” in patients under age 60 years, and under consideration for partial breast irradiation (PBI) [10]. Immediately thereafter, a

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working group of the European Society of Breast Cancer Specialists (EUSOMA) endorsed 4 of those criteria, omitting multifocal/multicentric disease and mammographic density; their consensus statement noted intermediate-level evidence for 2 of 4 criteria [11]. To our knowledge, comparable American criteria for preoperative MRI have not been published, but the National Cancer Center Network(NCCN)'s breast cancer guidelines [12] mention that bilateral breast MRI may be appropriate for patients with newly diagnosed breast cancer, to define the extent of disease and detect occult malignant lesions in the index or contralateral breast.

Recently, mammographic density and 3 of the 4 EUSOMA guideline criteria, (ILC, hereditary risk, discrepancy between mammography and ultrasound) were evaluated among 200 breast cancer patients under consideration for breast-conserving surgery [13]. The investigators concluded that none of the criteria they tested distinguished patients in whom preoperative MRI led to switch from breast conservation to mastectomy.

To date, the 6 criteria proposed by Sardanelli [10] (4 of which were endorsed by EUSOMA [11]) have not been formally evaluated for detection of occult malignant lesions among a general sample of breast cancer patients. Therefore, we conducted a retrospective review of consecutive breast cancer patients who underwent preoperative bilateral breast MRI at our institution during a period (2006–2008) when such imaging was routinely performed. Because screening for discrepancy in lesion size between mammography and ultrasound was not part of routine care, we evaluated the other 5 criteria. Our analysis took into account age and other potential confounding factors and adjusted statistical significance to avoid error from multiple hypothesis testing.

2. Methods

2.1. Eligibility criteria

This retrospective study was approved in advance by the City of Hope institutional review board, which granted a waiver of informed consent. Patients newly diagnosed with breast cancer were offered preoperative MRI routinely, without clinical criteria or restrictions. For this study, we reviewed consecutive female patients at least 18 years of age whose diagnosis before any MRI was unilateral breast cancer, who had a contralateral breast, and who underwent bilateral MRI as part of workup for definitive surgery at our center in 2006–2008 without having received neoadjuvant chemotherapy beforehand. Subjects who did not undergo breast cancer surgery as planned were retained in the study.

2.2. MRI technique

MRI examinations were performed on a 1.5 T scanner (Signa Excite; GE Healthcare, Milwaukee, WI) with a dedicated 7 channel in Vivo breast coil. Imaging sequences included bilateral axial STIR, non fat suppressed axial T1, pre- and post-contrast enhanced 1–6 min 3-D dynamic T1 weighted fat saturated sequences. Gadopentetate dimeglumane (MultiHance, Gracco Diagnostics, Princeton NJ) was administered intravenously according to the patient's weight, using the formula 0.1 mmol/kg, maximum at 20 ml. Subtraction images were generated, and a computer-aided display (CAD Stream) was utilized during image interpretation.

Images were viewed on a dedicated workstation by 1 of 6 readers, each with 15–30 years of experience as a breast radiologist. Standardized adjudication of mammographic density and background enhancement was performed retrospectively by the study radiologist (LT, blinded to MMA outcome) per the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) lexicons [14,15].

2.3. Definitions

MRI-detected malignant abnormality (MMA) was a newly identified lesion in either breast (scored 0 or 4 and above per BI-RADS [14] and confirmed to be in situ or invasive cancer by biopsy or pathology) or an extension of the index lesion more than a centimeter greater on MRI than on mammography. Biopsy was guided by ultrasound when the suspect lesion could be thus identified; otherwise, biopsy of suspect lesion was guided by MRI. We defined genetic-familial risk of breast cancer as any BRCA mutation or a first-degree relative diagnosed with premenopausal breast cancer (diagnosed at or before age 50) or with ovarian cancer at any age. Surgeons determined candidacy for PBI prior to MRI according to consensus guidelines [16]. Current HR refers to use of prescription-based hormone within the month before MRI evaluation.

2.4. Statistical analysis

Subject breasts were evaluable as long as any MMA therein had been resolved as malignant or benign before surgery. Associations between the 5 expert criteria [10] and detection of malignant abnormality by preoperative MRI were evaluated using generalized estimating equation modeling, to take into account potential intrapatient correlation between breasts. To maintain the study's overall risk of Type I error below 5%, p values associated with primary risk factors were adjusted for multiple hypothesis testing using the Holm-Bonferroni method [17]. In all, 7 primary "hypotheses" were evaluated: besides ILC, genetic-familial history, and multifocal disease, mammographic density was considered at 2 levels (extreme density and heterogeneous), and surgical plan prior to MRI was considered at 2 levels (lumpectomy with and without consideration of PBI). The preliminary model was adjusted for a single covariate, index versus contralateral breast. No significant interaction was present among the expert criteria. The final model was further adjusted for age at diagnosis, recent use of hormone replacement, and history of smoking (consolidated into never vs ever smoked for better fit to the observed data).

3. Results

3.1. Sample

Subjects ($n = 340$, age 53.4 ± 11.0 years) represented 91.9% of potentially eligible patients. The remaining patients (nonsubjects, $n = 30$) did not undergo routine bilateral MRI at our center for a variety of reasons, none of which appeared to systematically exclude a patient subgroup. Those reasons included: having already undergone preoperative MRI elsewhere, denial of insurance reimbursement, size not accommodated by MRI scanner, patient's refusal of breast conservation, or surgeon's decision to request unilateral or no MRI. Before MRI, most (69.4%) subjects met at least 1 of the 5 criteria being evaluated (Table 1).

3.2. MRI findings

Preoperative MRI detected an abnormality (malignant or otherwise) in 140 (41.2%) subjects, of whom 32 had MRI-detected abnormality in both breasts, for a total of 172 potentially malignant abnormalities. Prior to surgery, 48.3% (83/172) of these abnormalities were confirmed to be malignant, and another 34.9% (60/172) were determined to be benign or atypical cellular hyperplasia (Table 2). The remaining abnormalities (in 28 index, 1 contralateral breast) were not resolved as malignant versus benign