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The Impact of Sentinel Lymph Node Biopsy and Magnetic Resonance Imaging on Important Outcomes Among Patients With Ductal Carcinoma In Situ

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The objective of this systematic review was to determine the impact of sentinel lymph node (SLN) biopsy and breast magnetic resonance imaging (MRI) on important outcomes for patients with ductal carcinoma in situ. We identified no study that directly evaluated important outcomes for SLN biopsy. So, we determined the incidence of SLN metastases among patients with ductal carcinoma in situ. Using American Joint Committee on Cancer criteria, the incidence of pN1 and pN1(mic) SLN metastases were 0.9% and 1.5%, respectively. Because the incidence of SLN metastasis is very low, SLN biopsy is not likely to affect important outcomes. We identified one study that directly evaluated important outcomes after breast MRI. In this study, the use of MRI did not affect local recurrence rates after breast-conserving surgery and radiation. Although MRI may identify occult multicentric or contralateral breast cancer in some patients, it may also lead to unnecessary biopsies and overtreatment.

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The objective of this systematic review was to determine the impact of sentinel lymph node (SLN) biopsy and breast magnetic resonance imaging (MRI) on important outcomes for patients with ductal carcinoma in situ (DCIS). Important oncological outcomes usually include cancer-specific survival rates, cancer recurrence rates, and health-related quality of life. We found few studies that directly evaluated important outcomes with SLN biopsy or MRI.

Methods

Studies were sought from a wide variety of sources, including MEDLINE via PubMed, Scirus, Cochrane databases, Web sites of the Sloane Project and of the International Breast Cancer Screening Network, and manual searches of reference lists from systematic reviews and consensus conferences. We included articles published from 1965 through January 31, 2009. We searched MESH headings, titles, and abstracts for the terms Ductal Carcinoma In Situ, DCIS, noninfiltrating intraductal carcinoma, carcinoma in situ, intraductal carcinoma, ductal carcinoma in situ of the breast, localized breast cancer, and stage 0 breast cancer. We excluded studies of invasive breast cancer only, non-breast ductal cancers (eg, pancreatic ductal cancer), animal or in vitro experiments, analysis of results from other publications, letters, comments, and case reports. This systematic review included 64 publications for MRI and 50 for SLN biopsy. This article includes an abbreviated reference list.

SLN Biopsy

In the past decade, SLN biopsy has replaced routine axillary lymph node dissection (ALND) for most patients with invasive breast cancer. ALND has not been recommended for patients with DCIS because the preinvasive cells do not metastasize. In 1991, Silverstein et al. (1) reported that less than 1% of patients with DCIS had lymph node metastases detected by ALND. Today, DCIS is usually diagnosed by image-guided core needle biopsy. About 15% of patients with an original diagnosis of DCIS on core needle biopsy will have a final diagnosis of invasive breast cancer after excision or mastectomy (2). The underestimation rates vary considerably among different studies; larger tumor size, presence of a mass, and high nuclear grade are associated with higher underestimation rates. If invasive breast cancer is identified in the excision or mastectomy specimen, axillary staging is recommended to determine prognosis and guide treatment decisions. As a result, some authors recommend SLN biopsy for all or selected patients with DCIS detected with core needle biopsy (3,4).

We identified no study that directly evaluated important outcomes for SLN biopsy among patients with DCIS. Thus, if SLN biopsy indirectly affects important outcomes, a substantial proportion of patients with DCIS should have SLN metastases. We performed several analyses to determine the incidence of SLN metastases in different patient populations.

Because some patients with an original core needle biopsy of DCIS will have invasive breast cancer identified in the excision or mastectomy specimen, we evaluated the incidence of SLN metastases separately for these two groups (5–32). The incidence of SLN metastases was greater for patients with an original diagnosis (9.8%; 95% confidence interval [CI] = 7.6% to 12.7%) as compared with those with a final diagnosis (5.0%; 95% CI = 3.6% to 6.8%) of DCIS. Therefore, studies that include patients with an original diagnosis of DCIS report an increased incidence of SLN metastases.

DCIS with microinvasion (DCISM) is defined by the American Joint Committee on Cancer as microinvasion 0.1 cm or less in

greatest dimension. Some studies evaluating the role of SLN biopsy include DCISM, whereas others include only pure DCIS without microinvasion. Because DCISM may have a higher incidence of SLN metastases, we distinguished DCIS from DCISM in our analysis (5,7–13,15,17,19–25,27–31,33–35). The incidence of SLN metastases was higher for patients with DCISM (9.3%; 95% CI = 6.0% to 14.0%) as compared with those with DCIS (4.8%; 95% CI = 3.4% to 6.7%).

The precise definition of SLN metastases is often not clear or uniform in the published studies. The most widely used definition is the American Joint Committee on Cancer classification, which defines lymph node metastases according to the method of detection (immunohistochemistry [IHC]) and metastasis size: pN0(i−), no regional lymph node metastases, negative IHC; pN0(i+), no lymph node metastases histologically, positive IHC (also known as isolated tumor cells); and pN1(mic), micrometastasis (>0.2 mm, none >2 mm). The clinical significance of pN0(i+) and pN1(mic) has not established for patients with invasive breast cancer or DCIS. We evaluated the incidence of SLN metastases among studies that used American Joint Committee on Cancer definitions (12,15,16,24,25,28,29,36). In our analyses, the incidence of pN1 SLN metastases was 0.9% (95% CI = 0.5% to 1.5%). The incidence of pN1(mic) SLN metastases was 1.5% (95% CI = 0.8% to 2.8%). The incidence of pN0(i+) SLN metastases was 4.2% (95% CI = 2.2% to 7.7%). Thus, the incidence of pN1 metastases was very low for patients with pure DCIS.

Breast MRI

Although DCIS is commonly detected as a small area of microcalcifications on mammography, the disease frequently extends along the ducts and may involve a large portion of the breast with multiple foci. For some patients, mammography can grossly underestimate the extent of DCIS. The treatment of DCIS may be modified by MRI findings, which may lead to wider excisions, unilateral mastectomy, and/or treatment of the contralateral breast. For the purposes of this report, we assume that mammography has been performed and that the diagnosis of DCIS has already been established by either core needle biopsy or excision. So, we analyzed studies that reported the outcomes of breast MRI among patients with established DCIS. For our final analysis, we excluded studies that did not report separate outcomes for patients with DCIS.

We identified one study that directly evaluated important outcomes for patients with DCIS after breast MRI (37). In a study that included 136 patients with DCIS treated with breast-conserving surgery plus radiation therapy, Solin et al. evaluated the local recurrence rates according to the use of breast MRI. Breast MRI was used in 36 patients. The local failure rate was 6% in both the MRI and no MRI groups. This study is limited by the retrospective study design and the exclusion of mastectomy patients who underwent MRI.

We determined whether MRI indirectly affects important outcomes for patients with DCIS. We analyzed the ability of breast MRI to detect occult multicentric disease (either DCIS or invasive breast cancer). Because the presence of multicentric disease is generally considered a contraindication to breast-conserving surgery, MRI can influence treatment recommendations for some patients. Among patients with DCIS, the sensitivity of detecting multicentric disease was generally higher with MRI than with mammography (38–41). In a study that included 51 patients with DCIS, Hwang et al. (38) reported that the sensitivity of detecting multicentric disease was significantly higher for MRI as compared with mammography (MRI, 94%; mammography, 38%; $P < .05$). In another study that included 32 patients with DCIS, Menell et al. (39) also reported that the sensitivity of detecting multicentric disease was higher for MRI (MRI, 80%; mammography, 40%; statistical significance not stated). In another study of 86 patients with DCIS, Santamaría et al. (40) reported that the sensitivity of MRI was not significantly better than mammography (MRI, 42%; mammography, 26%; $P = .453$). Studies by Menell et al. (39) and Hollingsworth and Stough (41) reported that MRI detected occult multicentric disease in 6.3% and 6.3%, of DCIS patients, respectively.

Breast MRI can potentially influence treatment decisions by providing more accurate information on the size and extent of the known DCIS. The results of studies comparing mammography with MRI have not been consistent. In a study of 167 patients with DCIS, Kuhl et al. (42) reported that MRI was not better than mammography in determining size. In another study of 24 patients with DCIS, Uematsu et al. (43) reported that MRI was more accurate than mammography in determining extent of DCIS. Several studies have evaluated the overestimation and underestimation rates of MRI in determining DCIS size (40,44–48). The pooled overall overestimation rate was 25.5% (95% CI = 14.2% to 41.4%); the underestimation rate was 23.0% (95% CI = 16.2% to 31.6%).

Because current breast MRI technology evaluates both breasts, MRI can potentially identify occult contralateral breast cancer. The overall incidence of MRI-detected occult contralateral breast cancer (either DCIS or invasive breast cancer) was about 5% in four different studies (41,49–51). In the largest study that included 196 patients, Lehman et al. (51) reported that MRI detected occult contralateral breast cancer in five patients (2.6%). Importantly, in this study, MRI findings prompted biopsies of the contralateral breast in 18 patients; only five (28%) were positive.

Conclusions

The studies evaluating the role of SLN biopsy for DCIS have multiple limitations including retrospective study design, inclusion of highly selected patients, and unclear definition of SLN "metastasis." Nevertheless, we can conclude that the incidence of pN1(mic) or pN1 SLN metastases is very low for patients with pure DCIS. Therefore, SLN biopsy is not likely to affect important outcomes for most patients with DCIS, especially if excision is planned. The findings of SLN biopsy (isolated "tumor" cells) may lead to overtreatment (ALND, cytotoxic chemotherapy), which may negatively affect patient quality of life. However, SLN should be considered for mastectomy patients because SLN biopsy is not feasible if invasive breast cancer is identified in the mastectomy specimen.

Presently, studies reporting outcomes with MRI use specifically for patients with DCIS are limited. Although breast MRI may detect occult multicentric or contralateral breast disease, it may also lead to unnecessary breast biopsy and overtreatment (mastectomy) in some patients. As a result, scientific data are too limited to provide conclusive recommendations for the use of breast MRI for patients with DCIS.

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