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SHORT COMMUNICATIONS

Sentinel Lymph Node Biopsy for Risk-Reducing Mastectomy

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■ **Abstract:** Risk-reducing mastectomy (RRM) confers 90–95% decreased risk of breast cancer, and may reduce mortality, especially in high-risk groups such as BRCA carriers. Risk of occult disease in RRM specimen is ~5%. This demands axillary staging: sentinel lymph node (SLN) biopsy is no longer possible, axillary clearance confers significant risks and may prove negative. Contemporaneous SLN biopsy allows axillary staging with minimal further dissection. Women undergoing RRM and SLN biopsy between June 2005 and July 2010 were reviewed retrospectively from our prospectively maintained database of 1,522 SLN procedures in 1,498 patients. SLN(s) localized using routine tracer methods. SLNs and mastectomy specimens underwent routine histologic examination. Eighty-three RRMs with SLN biopsy were performed in 71 patients (12 bilateral). Indications for RRM: contralateral invasive (55), in situ (5) disease, BRCA 1/2 mutation (12), and strong family history (10). Mean number of SLNs: 1.35. Occult disease was detected in four cases (4.8%), with one case of occult invasive lobular carcinoma (1.2%). Remaining occult disease was lobular in situ neoplasia (LISN). SLNs were negative in all cases. Our findings are comparable to those in the literature: 4.8% rate of occult disease overall, 1.2% invasive. The significant risk with SLN biopsy is lymphoedema, quoted around 7%. We have had no reports of symptomatic lymphoedema in patients undergoing RRM and SLN biopsy. We propose that SLN at the time of mastectomy requires only limited further dissection, and confers minimal risk compared with secondary axillary surgery. ■

Key Words: Occult breast carcinoma, Prophylactic mastectomy, Risk-reducing mastectomy, Sentinel lymph node biopsy

Risk-reducing mastectomy (RRM) confers a 90–95% decreased risk of developing breast cancer (1–4), and, in groups such as BRCA 1 mutation carriers, may reduce breast cancer-associated mortality (2,5,6) if used as a bilateral prophylactic approach. Figures regarding mortality benefit are largely based on simulation models: long-term studies are required to confirm such outcomes. Other methods of managing high-risk groups such as yearly mammograms or MRI cannot reduce breast cancer incidence: although early detection aims to facilitate treatment of early-stage disease and infer improved prognosis, screening is not as effective in these high-risk patient groups, especially in BRCA 1 carriers (7).

The second group of patients undergoing RRM comprises patients who have been treated, either contemporaneously or previously, for a contralateral breast cancer. With the possible exception of patients treated for orthopoxvirus (DCIS), the patients' survival risk lies predominantly with their index cancer in the first few years after surgery, after which the risk of contralateral breast cancer slowly increases (8). Patients with unilateral breast cancer have a two- to sixfold increased risk of contralateral cancer compared with background risk (9): this may be a source of anxiety to patients, who therefore desire an RRM. Recent evidence has illustrated that contralateral RRM may confer an advantage, especially in patients with hormone receptor negative disease, in terms of disease-free and overall survival (10). This benefit may be even higher in patients with breast cancer who are BRCA1/BRCA2 mutation carriers (11). Patients with an index lobular carcinoma or LISN are of higher risk for contralateral disease, and mark out a subset of patients especially suited for RRM.

The evidence that RRM confers a reduction in risk of primary or contralateral breast cancer means that more patients are choosing to undertake this

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procedure. In addition, increased availability of genetic testing, reconstructive options, and patient awareness contribute to rising interest in RRM. The patients undergoing RRM are high risk, with an identified gene mutation, strong family history, or contralateral breast cancer. Their risk, therefore, of occult disease in the contralateral breast is higher than background population risk. The literature provides figures between 2.8% and 10% for occult disease incidence (1,12), with most centers quoting ~5% occult disease pick-up. This includes in situ disease: the rate of occult invasive disease is 1.4–2.5% (12,13).

Post-mastectomy identification of occult invasive disease would necessitate a further operation for axillary staging. Surgery may be complicated by the fact that many patients will have already had reconstructive surgery. Significantly, as mastectomy had been performed, a sentinel lymph node (SLN) biopsy would no longer be possible, and patients would be subjected to formal axillary dissection. A departmental decision was made to introduce SLN biopsy at the time of RRM (±reconstruction). Should occult disease be detected, the axilla would already have been staged, and a negative SLN biopsy would obviate the requirement for further surgery.

Performing SLN biopsy is not risk-free, hence the benefits must be justified against possible side effects. This is particularly pertinent when performing a staging procedure alongside a breast with no known disease. The incidence of lymphoedema after SLN biopsy for patients with a known cancer is quoted at 3–7% (14,15). It was felt that in the case of RRM, however, all patients are undergoing mastectomy, with routine excision of axillary tail: in the majority of cases, the SLN is located at or near the axillary tail (16), with very limited further exploration necessary.

METHODS

Sentinel lymph node biopsy is established for axillary staging of clinically and radiologically node-negative patients with invasive breast cancer (or patients with DCIS meeting the required criteria[1]). SLN biopsy was introduced as per the New Start program (17). Women undergoing RRM from June 2005 had SLN biopsy at the time of surgery. Skin sparing mastectomy was performed as appropriate for the disease and the type of reconstruction, if employed, ensuring full excision of the breast parenchyma, including the axillary tail. Effort was made to reduce dissection in the axilla as much as possible.

It is standard practice in our department to employ touch imprint cytology (TIC) for intra-operative analysis of SLNs during surgery for invasive disease. This was employed on occasion during risk-reducing surgery. Mastectomy specimens and SLNs were then sent off for routine histologic examination.

RESULTS

Data were retrospectively reviewed for patients who underwent RRM with concurrent SLN biopsy during the period June 2005–July 2010. These data were extracted from a larger data base of all patients undergoing SLN during this period (i.e. for early breast cancer). From this data base, a total of 1,522 SLN procedures were performed in 1,498 patients.

Risk-reducing mastectomy with SLN biopsy was performed on 83 breasts in 71 patients (i.e. 12 bilateral cases). The age range of patients undergoing the procedure was 28–66 years: mean 48 years.

The indications for RRMs are illustrated in Table 1.

The mean number of SLNs sent was 1.35, with the modal number being 1, range 1–4. Intraoperative analysis of the SLN was performed using TIC in 35 cases. TIC was negative in all cases.

Occult disease was detected in the mastectomy specimen in four cases. Three cases showed LISN, and one case showed ILC. Therefore, the total rate of occult disease detection was 4.8%, and the rate of invasive cancer detection, 1.2%.

In the case of occult ILC, the 56-year-old patient underwent bilateral RRM for strong family history.

Table 1. Indications for RRM

Indication for RRM	*n*
Previous contralateral mastectomy for DCIS	4
Previous contralateral mastectomy for IDC	44
Previous contralateral mastectomy for ILC	9
Previous contralateral mastectomy for mixed invasive tumor	1
Bilateral RRM following previous unilateral WLE for DCIS	1
Bilateral RRM following previous unilateral WLE for IDC	2
Bilateral RRM for strong family history	3
Bilateral RRM for BRCA 1/2	6
Not stated	1
Total	71

IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; WLE, wide local excision; RRM, risk-reducing mastectomy.

[1]Staging SLN biopsy performed in patients with DCIS undergoing mastectomy, mass forming DCIS.

Table 2. Indications and pathology outcomes with RRM

Occult disease side pathology	Indication for RRM	Contralateral side pathology
LISN	Previous contralateral cancer	Previous mixed invasive carcinoma
LISN	Bilateral RRM for strong family history	Benign
LISN	Previous contralateral cancer	Previous Grade 3 invasive ductal carcinoma
3.5 mm grade 2 invasive lobular carcinoma	Bilateral RRM for strong family history	Benign

A 3.5-mm, Grade 2, ER-positive lobular carcinoma was detected, which was undetected by preoperative imaging investigations. On this occult cancer side, two SLNs had been sent: both were negative on final histology. Intraoperative analysis was not performed. There was no disease in the contralateral breast and the corresponding SLN was also negative.

The cases of occult disease pathology, indication for RRM and contralateral pathology (which may refer to previous surgery, or concurrent surgery in the case of bilateral RRM), are summarized in Table 2.

DISCUSSION

Opinion is divided regarding the use of routine SLN biopsy with RRM, and critics quote the ~7% rate of arm lymphoedema as illustration of potential risk. However, the literature also quotes an ~5% rate of occult cancer detection, which, in cases of invasive disease, would require a potentially debilitating axillary exploration. In women with inherited cancer syndromes, the rate of occult disease incidence may be even higher (18,19).

Our figures are comparable to those in the general literature, with an overall occult detection rate of 4.8%, and invasive disease detection rate of 1.2%. Also in line with the literature is the finding that all occult disease comprised lobular in situ and invasive disease (20). Boughey *et al.* quote 5% occult detection rate, with 1.8% invasive disease. In their study, patients at higher risk of occult disease were older (>60), postmenopausal and with a history of in situ or invasive lobular disease. The patients in our unit with occult disease were middle aged (48, 56, and 66 years old), but without a history of lobular disease.

Recently, attempts have been made to identify the presence of occult disease prior to RRM using MRI. Although utilized in a number of centers, MRI has not been found to be a reliable predictor of occult disease, missing 75% of cases found on final histology in one series (12). The combination of MRI and SLN is costly and does not add significant information.

Although reliant on self-reporting, we have not had any reports of symptomatic lymphoedema in patients who have undergone RRM with contemporaneous SLN biopsy. We feel that the 7% risk quoted far exceeds the true number in this group of patients who are undergoing mastectomy and very limited dissection low in the axilla to excise usually only one SLN (21). In addition, it is well recognized that lymph nodes may be removed within the axillary tail when performing simple mastectomy without deliberate axillary dissection (22): the addition of SLN biopsy merely permits more accurate identification and therefore more targeted analysis of the known sentinel node.

The use of SLN biopsy at the time of RRM has been adopted as routine within our unit since 2005. It adds no significant time to the operation, especially as RRM is often performed alongside lengthy reconstructive procedures such as deep inferior epigastric perforator (DIEP) flaps. Although not commonplace, the finding of occult disease could be considered to justify the routine use of SLN biopsy: eliminating the need for formal axillary clearance in the 1.2% of cases with invasive disease. It is acknowledged that patients with no occult disease received no additional benefit from the SLN biopsy; however, it is felt that the minimal dissection should not confer significant morbidity to the patient. According to the Memorial Sloan Kettering Nomogram to predict risk of lymph node metastases (23), the patient with occult 3.5 mm ILC had an *18%* probability of spread to the SLN: we feel that establishing negativity of the SLN does confer an oncologic advantage.

Prospective data are required to assess the rate of lymphoedema in patients undergoing RRM with SLN biopsy. The balance of benefit versus possible risks should be discussed with patients on a case-by-case basis. Many studies investigating use of SLN biopsy alongside RRM are small, and a multicenter prospective study of RRM would facilitate identification of patients at high risk of occult disease who may be targeted candidates for SLN biopsy. Until that identification is reliably established, we feel that patients with

occult disease may be staged by contemporaneous SLN biopsy with acceptable benefit/risk ratio.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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