SUMMARY

Sentinel Lymph Node Biopsy in Breast Cancer Treatment: Indications and Contraindications

March 2012

A production of the Institut national d'excellence en santé et en services sociaux

Summary of the report prepared by
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SUMMARY

Introduction

In Québec, roughly 6200 women have been diagnosed with breast cancer in 2011. Today, owing in part to the Québec Breast Cancer Screening Program, this type of cancer is diagnosed more often at an early stage, allowing less invasive surgical procedures, that is, lumpectomy and sentinel lymph node biopsy (SLNB). The latter technique consists in injecting either a radioactive tracer or a blue dye, or both, into the breast in order to surgically detect the primary lymph nodes likely to harbour metastases if the cancer has spread. The anatomical pathology examination of these sentinel lymph nodes (SLN) provides a good indicator of the status of the other axillary lymph nodes. When the sentinel lymph nodes are free of metastases, axillary lymph node dissection (ALND), a surgical technique that involves removing the axillary lymph nodes, is avoided.

Not all patients with breast cancer are eligible for SLNB. The standard indication is operable, early-stage invasive breast cancer, in the absence of clinically detected axillary adenopathy. Several specific medical situations are contraindications for SLNB, in some cases owing to a lack of scientific evidence. Given the technical advances and new publications in this field, some believe that it is time to reconsider some of these contraindications. The Comité de l’évolution des pratiques en oncologie (CEPO) therefore asked us to examine the validity of the available evidence on the indications and contraindications for SLNB. This is the second in a series of three reports. The first, published in 2009, dealt with the technical aspects of SLNB; the third will address the efficacy (survival, recurrence and morbidity) and safety of SLNB.

Research Method

This is an exhaustive review of the feasibility (SLN identification rate) and diagnostic accuracy (risk of false negatives) of SLNB in the following medical situations: (1) after neoadjuvant chemotherapy; (2) presence of large tumours (> 5 cm); (3) after non-oncological breast surgery, such as breast augmentation or reduction mammoplasty; and (4) after prior SLNB, in the case of tumour recurrence. The identification rate is the likelihood of surgically detecting a sentinel lymph node in an attempted SLNB. The risk of false negatives (RFN) is reported in two ways. The first is the probability that a patient has regional lymph node metastasis when the definitive anatomical pathology examination of the sentinel lymph nodes yields a negative result (1- negative predictive value, that is, the number of false negatives over the total number of false and true negatives $[\text{FN} / (\text{FN} + \text{TN})]$ or 1- NPV). The second is the likelihood that the definitive anatomical pathology examination of the sentinel lymph nodes will be negative when the patient has regional lymph node metastasis (1- sensitivity, that is, the number of false negatives over the total number of true positives and false negatives $[\text{FN} / (\text{TP} + \text{FN})]$).

This report also presents the recommendations issued by recognized major international organizations concerning the four medical situations mentioned above in addition to the following specific situations: presence of clinically suspicious palpable axillary nodes, presence of ductal carcinoma in situ (DCIS), pregnant patients, presence of inflammatory breast cancer, presence of a multicentric or multifocal tumour, presence of bilateral cancer, older age, obesity, male breast cancer, and prior excisional or diagnostic breast biopsy. Note that this report is not a clinical practice guideline nor does it issue clinical practice recommendations.
Results

This exhaustive literature review covers 4 systematic reviews and 32 primary studies. It also addresses the recommendations issued in 11 documents (guidelines, clinical practice guidelines, expert consensus statements and service quality assurance standards) published from 2005 to 2010 inclusively. A literature watch for recommendations was conducted until the end of September 2011.

After neoadjuvant chemotherapy

Since the 2005 recommendation issued by the American Society of Clinical Oncology (ASCO) not to perform SLNB after neoadjuvant chemotherapy (NACT), no guideline based on a systematic literature review has clearly gone against it. This issue nevertheless remains controversial in the absence of suspicious lymph node metastasis at initial clinical examination or ultrasound. This situation calls for the surgeon’s clinical judgment.

Neoadjuvant chemotherapy (NACT) seems to have little impact on the SLN identification rate when patients do not present with signs of axillary node involvement at initial clinical examination (cN0 stage). However, in clinically node-positive (cN+) patients prior to NACT, the SLN identification rate was lower.

In general, the risk of a false-negative (RFN) finding on SLNB (1-NPV) seems higher in patients who have had prior NACT than in those who have not. However, the study samples were very small and the differences were often not significant. This difference may also be partly attributed to the regional lymph node stage (cN) prior to chemotherapy.

Overall, in clinically node-positive (cN+) patients who received NACT and presented with no signs of adenopathy after chemotherapy, the RFN of an SLNB performed after chemotherapy was approximately 17.2% or 10.2% respectively, depending on the way in which the risk was calculated (1-NPV or 1-sensitivity). In cN0 patients who had received prior NACT, the RFN of an SLNB was approximately 8.5% or 10.2% respectively, depending on the way in which the risk was calculated (1-NPV or 1-sensitivity). However, the results were heterogeneous and the overall risk assessment must be interpreted with caution, given its lack of precision.

Presence of large tumours

In 2005, the ASCO did not recommend the use of SLNB in the case of T3 tumours (> 5 cm), owing to a lack of evidence. Since then, Australia has issued guidelines, based on a systematic review of randomized controlled trials (RCTs), that limit the use of SLNB to cases of tumours measuring less than 3 cm in diameter. Two expert consensus statements nevertheless recommend SLNB in the case of T3 tumours in the absence of clinically detected adenopathy.

Tumour size appears to have no significant effect on SLN identification rate. This rate is generally high (≥ 95 %) for T3 tumours (> 5 cm).

The effect of the RFN (1-NPV) for SLNB was observed to increase with T-stage progression, but the effect of tumour stage or size was not as clear when the RFN was calculated for all the patients presenting with lymph node involvement (1-sensitivity); the results were not consistent across the studies.

No comparative diagnostic study or case-series study of at least 100 patients has established the RFN in T3N0 patients at initial clinical presentation.
After breast augmentation or reduction mammoplasty

According to the guidelines based on a systematic literature review, there is insufficient evidence to recommend SLNB to patients who have undergone prior non-oncological breast surgery, such as breast augmentation or reduction mammoplasty.

In four case-series studies of a total of 120 patients who had undergone prior breast augmentation, an SLN identification rate of 100% was reported. In three studies, periareolar or inframammary breast augmentation was performed, whereas, in the fourth study, at least three patients had transaxillary augmentation. The only study that reported an RFN (0%) was conducted on a small sample size, that is, nine cases.

Only one study involved patients (n=20) who had had prior breast reduction; the SLN identification rate was 100%. The RFN of SLNB after breast reduction has not been evaluated.

Reoperative sentinel lymph node biopsy in the case of tumour recurrence

No guideline based on a systematic literature review has been published on this issue. An expert consensus statement has established the feasibility of reoperative SLNB.

Most of the patients who had had reoperative SLNB had received adjuvant radiation therapy to treat primary breast cancer. The SLN identification rate on reoperative SLNB varied from 74.1% to 96.9% in three studies. The RFN was not evaluated.

Other specific medical situations

The recommendations of major international organizations concerning other specific medical situations are briefly presented in the conclusions below.

Conclusions

This report addresses the feasibility and diagnostic accuracy of SLNB in certain specific medical situations, especially with respect to some of its controversial contraindications. In light of this assessment, INESSS submits the following conclusions:

After neoadjuvant chemotherapy

- Sentinel lymph node biopsy (SLNB) is technically feasible after neoadjuvant chemotherapy (NACT). However, the SLN identification rate is decreased in the presence of adenopathy at initial clinical examination.

- The risk of false negative (RFN) findings on SLNB performed after NACT is generally higher, especially in the presence of adenopathy at initial clinical examination. In initial node-positive (cN+) patients, a complete clinical axillary response to NACT, combined with a negative SLNB result after chemotherapy, is not enough to warrant exempting them from axillary lymph node dissection (ALND) outside research context.

- In patients presenting without adenopathy at initial clinical examination, the SLNB performed after NACT led to a lower RFN—although greater than 5%—than that in patients presenting with adenopathy at initial clinical examination. However, few large studies have evaluated this point and their results are heterogeneous.
Presence of large tumours

- Sentinel lymph node biopsy (SLNB) is technically feasible in the case of T3 tumours without adenopathy at clinical examination. A small number of multicentre cohort studies, in which T3 tumours were nevertheless under-represented, generally reported a high SLN identification rate.

- The RFN (1- NPV) of SLNB seems to be influenced by tumour stage, although the effect of tumour size alone has not been isolated. As of the T3 stage (tumour > 5 cm), the RFN varied enormously across the studies, and it was systematically and significantly greater than 5%.

After breast augmentation or reduction mammoplasty

- Although some cases of SLNB after periareolar or inframammary breast augmentation have demonstrated the feasibility of this technique, the number of available results is insufficient to confirm its accuracy. Cases of SLNB after transaxillary breast augmentation are virtually absent from the literature.

- The feasibility and diagnostic accuracy of SLNB after breast reduction have not been sufficiently studied.

Reoperative sentinel lymph node biopsy in the case of recurrence

- The feasibility of reoperative SLNB in the case of locally recurring breast cancer has not been clearly demonstrated, and no evidence demonstrates its diagnostic accuracy in the event of a localized sentinel lymph node.

Other specific medical situations

According to the recommendations of major international organizations recognized in oncology, surgery and nuclear medicine, SLNB is contraindicated in the following cases:

- presence of suspicious palpable axillary lymph nodes;
- ductal carcinoma in situ (DCIS) when mastectomy is not planned, therefore not requiring axillary node assessment;
- pregnant patients if blue dye is used in the technique;
- inflammatory breast cancer.

According to the recommendations issued by these organizations, SLNB is not contraindicated in the following cases:

- ductal carcinoma in situ (DCIS) when a mastectomy is planned;
- multicentric tumours;
- bilateral breast cancer;
- patients aged 65 years or older;
- patients with obesity;
- male breast cancer patients.

Lastly, the indication of SLNB seems to remain under study in the following cases:

- pregnant patients when a radioactive tracer is used alone in the technique;
- multifocal tumours;
- after excisional biopsy.