Is intraoperative lymphatic mapping and sentinel node biopsy effective and safe in early-stage melanoma?

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Lymphatic mapping and sentinel lymph node biopsy is a safe, accurate, and low-morbidity method for the pathologic staging of the regional nodal basin in primary cutaneous melanoma.

The tumour status of regional lymph nodes is the single most important prognostic factor in patients with cutaneous melanoma.[1] In the early 1990s, complete lymph node dissection (CLND) of the regional basin was the only method available to identify regional nodal metastasis, but this approach had two important drawbacks. First, almost 80% of patients undergoing CLND had no lymph node metastasis, so they would have gained no benefit in terms of staging or survival, but were at increased risk for acute and chronic morbidity as a result of the procedure. Second, the pathologic staging of all regional lymph nodes underestimates the true frequency of nodal metastasis by as much as 14% compared with the focused analysis of one or a few sentinel lymph nodes (SLNs).[2,3] Hence, lymphatic mapping/SLN biopsy (LM/SLNB) has been proposed as a minimally invasive surgical procedure for staging of the regional nodal basin that detects occult metastasis to allow an early therapeutic CLND to be performed.

The results of the international Multicenter Selective Lymphadenectomy Trial MSLT-1 (see opposite) clearly define the feasibility, accuracy and morbidity rate of LM/SLNB within a randomised clinical trial. The overall rate of SLN identification was 95.3%, with the highest rate in the inguinal basin (99.3%), followed by the axillary (96.6%) and the cervical (84.5%) area. The poor rate of SLN identification in the cervical area might be related to the complex lymphatic drainage in the head and neck region. The accuracy of identification was estimated by assessing the incidence of same-basin recurrence in patients who had tumour-negative SLNs. Overall, 59/944 patients (6.3%) with tumour-negative SLNs developed regional nodal metastases, although 11 of these 59 patients had recurrence in a basin that was not sampled. Fifty-two of the 944 patients (5.5%) had local or in-transit recurrence, and in 8 patients this occurred before nodal recurrence, which could have been the source of metastasis to the previously dissected lymph basin ('biological failure'). Notably, the dissected-basin recurrence rate was 10.3% for the first 25 cases of the trial, but this rate decreased to 5.2% after 25 cases, suggesting an increase in the surgeon's proficiency with the procedure following the 'learning phase'. As the MSLT-1 was designed with a mandatory 30-case 'learning phase', and each surgeon had documented at least 15 consecutive cases, surgeons who treat only a few melanoma patients each year do not seem to have the experience required for a high degree of mapping accuracy. LM/SLNB did not influence the incidence of morbidity at the primary site, and only minimally increased regional and systemic complications, whereas complications in the dissected basin were significantly more frequent when LM/SLNB was immediately followed by CLND

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(incidence of complications 10% and 37.2%, respectively; $P<0.0001$).

Certainly, the final results of the survival analysis of the MSLT-1 are awaited with great interest, although preliminary data seem to indicate a survival benefit in the subset of patients with lymph node metastases.[4] The randomisation of a large number of patients has assured an even distribution of prognostic factors between the study arms and, in the observation arm, there were similar incidence rates for tumour-positive SLNs and clinical nodal recurrence. The latter finding suggests that LM/SLNB can provide early identification of patients with occult nodal metastases who would develop clinically appreciable nodal metastases and would be less curable at that far advanced stage of disease.

Details of the references cited in this article can be accessed at www.cancerworld.org/cancerworld

Synopsis

DL Morton, AJ Cochran, JF Thompson, et al. (2005) **Sentinel node biopsy for early-stage melanoma: accuracy and morbidity in MSLT-I, an international multicenter trial.** *Ann Surg* 242:302–311

Background. Studies in breast cancer, melanoma, colon cancer, lung cancer and almost all solid malignancies that spread to lymph nodes have confirmed that metastatic cells move in an orderly manner from the primary site through the lymphatic system to one or two regional sentinel nodes. Lymphatic mapping and sentinel lymph node biopsy (LM/SLNB) is used to identify occult nodal metastases and thus stage the regional nodal basin to target the subset of patients who would benefit from complete lymph node dissection (CLND). LM/SLNB has become an important and well established technique for the staging of melanoma.

Objective. To assess the accuracy and clinical efficacy of LM/SLNB for staging of the regional nodal basin, and to establish its effect on the incidence of morbidity in patients with early-stage melanoma.

Design and intervention. In the international phase III Multicenter Selective Lymphadenectomy Trial (MSLT-1), patients aged 18–75 years with primary cutaneous melanoma (Breslow's thickness* ≥ 1 mm with Clark level** ≥ III, or any Breslow's thickness with Clark level of IV or V) were accrued over 11 years. Sites of melanoma were the trunk, head and neck, extremities, sole of the foot, palm of the hand or a subungual site. In a 'learning phase' of 30 consecutive cases, each of 18 centres in the USA, Europe and Australia were required to demonstrate a sentinel lymph node (SLN) identification rate that was 85% accurate. Patients were randomly assigned to wide excision (WE) plus observation with complete lymphadenectomy if nodal metastases subsequently became clinically evident, or WE plus LM/SLNB with immediate CLND for any sentinel node metastases.

Outcome measures. The accuracy of LM/SLNB and the incidence of early morbidity were assessed.

Results. After a median follow-up of 54 months (range 3 months–10 years), 1,973 patients were eligible for analysis, 800 of whom received WE plus observation and 1,173 of whom received WE plus LM/SLNB. The rate of identification of SLN using LM/SLNB was 95.3% overall, and such rates were higher in the inguinal and axillary regions than in the cervical region (99.3% and 96.6% vs 84.5%). Among the 944 patients with tumour-negative SLNs, regional nodal recurrence occurred in 59 patients (6.3%), and 11 of these patients had recurrence in a basin that had not been sampled. Fifty-two patients had local or in-transit recurrence, which developed in eight patients before nodal recurrence. In 10 centres, which had accrued a total of 918 patients in the study, the dissected-basin recurrence rate was 10.3% for the first 25 cases and 5.2% after 25 further cases. No operative mortalities were reported, surgical complications associated with WE were low, and LM/SLNB did not affect the incidence of surgical morbidity at the primary site. Addition of the CLND procedure in patients undergoing LM/SLNB increased the rate of complications in the dissected basin from 10.1% to 37.2% ($P<0.0001$).

Conclusions. LM/SLNB can accurately identify occult nodal metastases with an associated low morbidity rate; these subclinical lymph node metastases are likely to develop to more advanced, palpable nodal disease if left untreated.

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** Depth of melanoma penetration, measured from the outermost to innermost extent of the tumour; used to estimate survival after tumour excision*

*** Method for measuring the depth of skin penetration of a melanoma according to the anatomic layer (epidermis, dermis, or subcutis) of deepest tumour penetration*