

# Should a completion lymphadenectomy be performed after a positive biopsy of the sentinel node in melanoma? A vote for „yes”

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In melanomas, as in most solid cancers, surgery is the basic method that leads to a permanent cure. The last 2 years have brought a debate and changes in the recommendations for therapeutic management after positive (confirming a metastasis) biopsy of the sentinel node in relation to completion lymph node dissection (CLND).

Results of a prospective multi-center Multicenter Selective Lymphadenectomy Trial1 (MSLT-1) study indicate that the biopsy of a sentinel node in patients with melanoma:

- allows for identifying groups at high risk of cancer spread,
- helps to properly determine the severity of the disease,
- provides excellent regional control,
- enables patients to be qualified for clinical trials according to the same criteria.

The MSLT-1 study showed no improvement in survival time to relapse and in total survival time in the whole analyzed group of patients undergoing sentinel node biopsy compared to the observed group [1].

Results of two published studies: DeCOG-SLT and MSLT-II with random selection of patients [2, 3], one of which, however, did not have sufficient statistical power [3], did not show improvement in total melanoma-specific survival time [2] and disease-free survival time from distant metastases in patients undergoing the CLND [3]. However, the survival time of disease-free patients undergoing the CLND was longer (fewer relapses in the nodal area). A summary of the trial results is presented in Table I. At the same time, the basic prognostic role of sentinel node biopsy was confirmed.

According to Polish and American recommendations (NCCN, ASCO/SSO) [4–6], radical lymphadenectomy should be considered after histopathological examination of melanoma metastases in the node or sentinel nodes (especially at micro-metastases > 1 mm or when the risk of metastases to other nodes is higher). This is important because in other lymph nodes (*non-sentinel lymph node* – NSLN) melanoma metastases are found by routine histopathological methods in about 20–30% of patients [7]. Close observation and ultrasound examination of the lymphatic flow area every 4–6 months may also be acceptable.

Thus, the CLND remains one of the standard methods of management after a positive biopsy of the sentinel node. So what are the arguments in favor of this course of management?

First of all, in both clinical trials a group of patients with very small metastases to the sentinel node (mainly up to 1 mm) was over-represented. It can therefore be considered that, under real conditions, patients with larger metastases in the sentinel node may benefit from the CLND. Secondly, the lack of CLND implementation does not allow some patients to properly qualify for staging, because there is no information about possible metastases in NSLN. And such information has a prognostic value and may affect the qualification for complementary treatment. On the other hand, CLND significantly reduces the risk of melanoma recurrence in regional lymphatic flow (based on Multicenter Selective Lymphadenectomy Trial-II (MSLT-II): this local lymphatic basin control was  $92 \pm 1.0\%$  after CLND vs.  $77 \pm 1.5\%$  without CLND,  $p < 0.001$ ) [2] – which may be

**Table I.** Results of trials comparing the CLND with observation after positive biopsy of the sentinel node

Trial (authors)	Number of patients	Median time of observation	Survivals/relapses
DeCOG-SLT Leiter et al.	483	34 months	Observation vs. CLND: OS HR 1.02 p = 0.95, 10 years' 62.6% vs. 61.9%; RFS HR 0.959 DMFS 1.19 10 years' 55.8% vs. 55.5%
MSLT-II Faries et al.	1755	43 months	Observation vs. CLND: MSS HR 1.08 p = 0.42; DMFS HR 1.1; DFS CLND 68% vs. observation 63%

significant for some patients. Moreover, all the studies – with a systemic complementary treatment currently registered for routine use (anti-PD-1 nivolumab/pembrolizumab immunotherapy or molecularly directed therapy with BRAF/MEK dabrafenib inhibitors with trametinib) [8–11] – were based on the group of patients after CLND and showed an improvement in results after adjuvant treatment. Finally, any patient on whom the CLND is not performed must be subject to strict observation, which includes ultrasound of regional lymphatic flow every 3–4 months, and under clinical conditions this is not always easy for the patient.

To sum up the discussion whether a complementary lymphadenectomy should be performed in melanoma after a positive biopsy of the sentinel node – the answer is yes, but not in every patient. It should be noted that the role of the CLND in the near future will be individualized and decreasing.

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