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The importance of sentinel node biopsy and examination in malignant melanoma of the head and neck

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Summary

Background: Malignant melanoma of the head and neck is a highly aggressive tumor with a significant risk of regional and distant metastases. Due to the complex anatomy and rich lymphatic drainage of this area, accurate and timely diagnosis and staging are essential for optimal treatment planning. The sentinel lymph node plays a key role in assessing tumor spread and staging. **Materials and methods:** A retrospective study was conducted on 26 patients with head and neck melanoma who underwent sentinel lymph node biopsy at our institution between 2017 and 2023. We evaluated the success rate of sentinel node localization, presence of metastases, and subsequent lymphadenectomy. **Results:** Sentinel lymph nodes were successfully identified in 23 patients; 5 had positive findings (3 macrometastases, 1 micrometastasis, 1 isolated tumor cells). Lymphadenectomy was indicated in patients with macrometastases, while follow up monitoring was preferred for micrometastases and isolated tumor cells. One patient experienced a complication after lymphadenectomy. Most patients with negative sentinel nodes remained disease-free during follow-up. **Conclusion:** Sentinel lymph node biopsy is a crucial tool for staging and treatment decision-making in head and neck malignant melanoma. The procedure's success depends on surgical expertise. Lymphadenectomy is indicated in cases of macrometastases, whereas micrometastases and isolated tumor cells warrant regular follow up. An individualized, multidisciplinary approach is essential.

Key words

malignant melanoma of the head and neck – sentinel node – lymphadenectomy

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Introduction

Malignant melanoma is a neoplastic disease arising from a neoplastic proliferation of melanocytes and is classified as neuroectodermal tumors. It primarily affects the skin, accounting for approximately 4% of all skin cancers. However, it may also occur in the eye, ear, gastrointestinal tract, or on the mucous membranes of the oral cavity, nasal cavity, or genital tract. Overall, the global incidence of malignant melanoma is increasing, especially among the white population. Malignant melanoma is responsible for up to 73% of deaths from skin cancers. Worldwide, survival rates are higher in developed countries due to early diagnosis and accessible treatment. Patient survival is primarily determined by the stage at which the disease is diagnosed and the location of the melanoma. It has been shown that malignant melanoma occurring in the head or neck region is associated with a significantly worse prognosis and nearly twice the mortality rate compared to melanomas located on the trunk or limbs [1].

The treatment of patients with malignant melanoma at the University Hospital Hradec Králové (UH HK) is comprehensive and centralized, involving a wide range of clinical specialties under the leadership of an oncologist. Primary diagnosis and treatment of early-stage disease are provided by a dermatologist in collaboration with a pathologist and radiologist. Surgical treatment is mainly performed by a plastic surgeon, while sentinel lymph node biopsy in the neck area is carried out by an otorhinolaryngologist. Systemic and radiation therapy are then provided by an oncologist. Therapeutic approaches are directly dependent on the pathological classification of the primary tumor and disease staging.

In the pathological assessment of the primary lesion, tumor thickness – known as the Breslow classification, measured in millimeters – and the presence or absence of ulceration are the key factors. The radicality of the resection margin (R classification), which is determined based on the Breslow depth

Tab. 1. Determination of resection margin based on Breslow thickness.

Breslow thickness	Resection margin
melanoma *in situ*	5 mm
< 1 mm	at least 10 mm
1–2 mm	at least 10–20 mm
> 2 mm	at least 20 mm

Tab. 2. Indications for sentinel lymph node biopsy.

Breslow thickness
clinically highly suspicious lesion without prior biopsy verification > 1 mm
< 1 mm (0.8–1.0 mm) indicated if: • more than 2 mitoses • ulceration • age < 40 years • lymphovascular invasion

(Tab. 1), is also important. Other significant prognostic factors include the mitotic index, lymphovascular or perineural invasion.

Sentinel lymph node biopsy is indicated for melanomas with a Breslow thickness of 1 mm or more, provided there is no evidence of locoregional or distant metastasis. In melanomas with a Breslow thickness of 0.8–1 mm, the procedure is recommended if risk factors are present, such as ulceration of the tumor, high mitotic activity, younger patient age, or lymphangioinvasion [2]. In cases of clinically highly suspicious melanoma, sentinel lymph node biopsy may be indicated even without prior histopathological examination of the primary tumor (Tab. 2).

Previous excision of the primary tumor is not a contraindication for sentinel lymph node biopsy and can be successfully performed even after wide excision of the melanoma. The rate of false-negative results is negligible [3]. Therefore, when excising a clinically non-suspicious lesion, it is recommended to observe a diagnostic margin of 1–2 mm.

Histopathological evaluation of the sentinel lymph node includes the amount and size of metastatic involvement, localization of the metastasis, and assessment of the degree of tumor cell invasion into the sentinel node (sentinel node invasion level – SNIL). In the case of a positive sentinel lymph node, lymphadenectomy may be considered. While it can improve locoregional recurrence rates, it carries a higher risk of morbidity and postoperative complications. Lymphadenectomy is not indicated when only isolated tumor cells (ITCs) are present in the sentinel lymph node. In cases of micrometastases, lymphadenectomy is considered. The definitions of micrometastasis and ITCs are based on the number and arrangement of tumor cells. Micrometastases are defined as deposits > 0.2 mm and ≤ 2.0 mm in size, while ITCs are ≤ 0.2 mm or ≤ 200 cells per section [2]. Results from large trials (e.g., MSLT-II, DeCOG-SLT) show that immediate lymphadenectomy after detection of micrometastasis in the sentinel lymph node does not improve overall survival compared to careful observation. Therefore, there is a growing trend toward individualized management, and surveillance without immediate lymphadenectomy is increasingly accepted, particularly in patients with a low tumor burden in the node (e.g., micrometastasis ≤ 1 mm) [4]. In other cases of positive sentinel lymph nodes, lymphadenectomy is indicated.

At our institution, sentinel lymph node biopsy is performed according to established indication criteria (Tab. 2). In the case of malignant melanomas of the head and neck, the procedure is carried out in cooperation with otorhinolaryngologists, who perform the biopsy. The sentinel node is routinely preoperatively identified using lymphoscintigraphy after peritumoral or periscar intradermal injection of the radiotracer 99mTc-nanocolloid. Subsequent lymphoscintigraphy consists of several dynamic and static scans, and the projection of the sentinel lymph node is marked on the skin surface with a marker. The radionuclide-labeled nanocolloid accumulates in the sentinel lymph node, and only a small portion of the radiotracer may reach higher-order nodes. This is advantageous compared to blue dye, which gradually stains most of the lymph nodes in the drainage area. The marked sentinel node is then intraoperatively located using a gamma probe that guides the surgeon both visually and acoustically to the node. This method of identifying the sentinel lymph node is technically and materially demanding and requires close collaboration between the surgeon, radiologist, and pathologist. The success of sentinel lymph node excision depends on surgical experience – with approx. 95% success after 50 procedures [5,6].

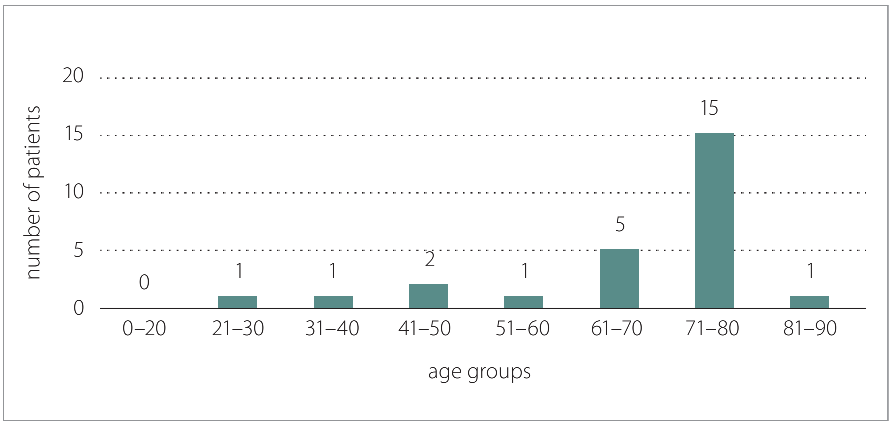
Materials and methods

A retrospective study was conducted at the University Hospital Hradec Králové between 2017 and 2023, including 26 patients diagnosed with malignant melanoma of the head and neck who met the indication criteria for sentinel lymph node biopsy. Most patients were males, with an average age of 66.8 years. Sentinel lymph node biopsy was performed in cooperation with otorhinolaryngologists using preoperative lymphoscintigraphy with peritumoral or periscar intradermal injection of 99mTc-nanocolloid for sentinel node identification. Intraoperative localization was guided by a gamma probe. Histopathological evaluation assessed the presence and extent of metastatic involvement in the sentinel lymph node, including classification into macrometastases, micrometastases, or ITCs. Patients with positive sentinel nodes were considered for lymphadenectomy based on metastasis size and patient factors. Data were analyzed descriptively using counts and percentages. Outcomes analyzed included biopsy success rate, sentinel node positivity, subsequent lymphadenectomy, and postoperative complications.

Results

In our investigation, we conducted a retrospective study in which we monitored our ability to perform sentinel lymph node biopsy, the presence of metastases in the sentinel node, and any subsequent lymphadenectomy in patients with head and neck melanoma.

A total of 26 patients with head and neck melanoma who were indicated for sentinel lymph node biopsy between 2017 and 2023 were included in the study. Most patients were males, with a male-to-female ratio of 19 : 7. The average age of the patients was 66.8 years, with the most represented age group being patients between 71 and 80 years, as shown in Graph 1.



Graph 1. Distribution of patients in age groups.

More than one-third of the patients had a primary malignant melanoma with a Breslow thickness greater than 4.0 mm. One patient had a Breslow thickness of 0.7 mm; however, sentinel lymph node biopsy was still indicated by the oncologist due to ulceration and the patient's young age (Tab. 3).

Tab. 3. Number of patients according to Breslow classification.

Breslow thickness – number of patients	
< 1.0 mm	1
1.01–2.0 mm	9
2.01–4.0 mm	6
> 4.0 mm	10
total	26

Successful excision of the sentinel lymph node was achieved in 23 out of the 26 patients. Of these, the sentinel node was evaluated as negative in 18 patients (Tab. 4). In 2 additional patients, the sentinel lymph node could not be located intraoperatively by the otorhinolaryngologist, despite preoperative marking. In 1 patient, the sentinel lymph node was not visualized at all following radiotracer administration.

Tab. 4. Number of patients according to sentinel node evaluation.

Sentinel node evaluation	
positive	5
negative	18
not found/not displayed	3
total	26

In five cases where the sentinel lymph node was classified as positive, three involved macrometastases of malignant melanoma. In the remaining two patients, micrometastases or ITCs were detected in the sentinel lymph node (Tab. 5).

Tab. 5. Distribution of metastases in positive sentinel lymph nodes

Type of metastasis	
macrometastasis (> 2.0 mm)	3
micrometastasis (> 0.2 mm–2.0 mm)	1
ITCs (≤ 0.2 mm)	1

ITCs – isolated tumor cells

In patients with macrometastases detected in the sentinel lymph node, lymphadenectomy was indicated. One patient, due to advanced age and comorbidities, refused the procedure and was placed under observation. No relapse of the disease was observed during the study period. The remaining two patients underwent lymphadenectomy. In one case, the surgery was complicated by bleeding, which required surgical revision. This patient died within 6 months due to generalization of the underlying disease.

Patients with a positive sentinel lymph node who received adjuvant therapy without lymphadenectomy were free of distant metastases 1 year after the diagnosis.

All 18 patients with a negative sentinel lymph node continued to be followed in routine surveillance. In two of them, lymphadenectomy was performed within 5 years of surgery due to the detection of metastasis in cervical lymph nodes. In one patient with a negative sentinel node, distant pulmonary metastasis was discovered 1 year after the initial diagnosis.

A total of three patients with head and neck melanoma in whom the sentinel lymph node was not visualized or detected were monitored and remained free of metastases during the follow-up period.

Discussion

The obtained data were compared with the DeCOG-SLT (Dermatologic Cooperative Oncology Group – Selective Lymphadenectomy Trial) and MSLT-2 (Multicenter Selective Lymphadenectomy Trial) studies [5]. DeCOG is a multicenter randomized trial involving 483 patients conducted between 2006 and 2014, evaluating distant metastasis-free survival, recurrence-free interval, and overall survival in patients undergoing complete cervical dissection for a positive sentinel lymph node compared to patients with a positive sentinel lymph node who remained under observation without lymphadenectomy. No significant difference was observed across all monitored modalities between the group undergoing lymphadenectomy and the group simply monitored after biopsy of a positive sentinel lymph node. Among patients undergoing lymphadenectomy, a higher incidence of lymphedema and increased morbidity was observed [7].

In the MSLT-II study, the main question was whether lymphadenectomy improves melanoma-specific survival (MSS) in patients with a positive sentinel lymph node, compared to merely monitoring the drainage nodes using ultrasonography. The study was conducted on 1925 patients, who were followed for 9.8 years. No statistically significant difference in MSS was found, and a higher incidence of lymphedema was again observed in patients after lymphadenectomy [7].

The obtained data correlate with our small patient cohort, and although the DeCOG-SLT study primarily excluded patients with head and neck melanoma due to the variability of lymphatic drainage in this area, its conclusions are somewhat applicable to patients with melanoma in this region. The significant variability of lymphatic drainage in the head and neck area should not affect the reliability of sentinel lymph node biopsy, provided we have a high-quality detection method. However, sentinel lymph node biopsy is to some extent dependent on the surgeon's experience, and the success rate is around 95% [5]. In our cohort, the success rate was just under 90%. The variability of lymphatic drainage may, however, influence the extent of lymphadenectomy according to anatomically defined cervical regions when indicated. In some cases, it may be difficult to adhere to the excision margins in anatomically exposed areas such as the eye, nose, or lip. In cases of extensive and unclear suspicious lesions, a diagnostic excision can be accepted.

Another histopathological characteristic of malignant melanoma emerging in recent studies is the vertical growth of the primary tumor. It appears that vertical growth correlates with the aggressive behavior of the tumor in terms of invasion into the lymph nodes. To some extent, the Breslow classification is a quantitative representation of the vertical growth of melanoma, but vertical growth itself is a biological concept that also encompasses other signs of invasiveness. Melanomas with vertical growth do not necessarily have a high Breslow thickness. Several studies are currently underway to examine this factor, but further research is needed before it can be applied in clinical practice [8].

Conclusion

The foundation of treatment for head and neck melanoma is sufficiently radical surgical treatment with sentinel lymph node biopsy when indicated, just as with involvement in any other area. Sentinel lymph node biopsy provides crucial information for staging of the disease, which affects prognosis, is independent of other existing variables, and influences decisions regarding adjuvant therapy. Thus, its importance outweighs the relatively small therapeutic effect.

The successful removal of the sentinel lymph node is, to some extent, dependent on the experience of the surgeon. In the case of histopathological involvement of the sentinel lymph node, the size of the metastasis is crucial, with the assumption that when the metastasis is 2 mm or larger, lymph nodes of a higher order are affected, and lymphadenectomy is indicated to prevent early locoregional recurrence of the disease. In cases of micrometastasis ranging from 0.2 to 1.0 mm, or even up to 2.0 mm, or ITC, regular patient observation is recommended to detect metastatic involvement early, without burdening the patient with a demanding surgical procedure.

Cervical lymphadenectomy is an extensive and demanding procedure. In the treatment of malignant melanoma, it is performed in the case of metastatic involvement of the sentinel lymph node by a macrometastasis or when clinically obvious involvement of lymph nodes is observed. Lymphadenectomy in this location may improve locoregional disease control, but it also increases morbidity and postoperative complications. In our small patient cohort, one complication was recorded after lymphadenectomy, namely bleeding that required surgical revision. Based on our own experiences, we agree with the opinion that immediate lymphadenectomy compared to observation does not provide a significant benefit to patients in terms of discovering distant metastases, disease recurrence, or overall survival.

The results obtained from our cohort show the limited predictive value of both positive and negative sentinel lymph node findings in the head and neck area, possibly due to the anatomical variability of lymphatic drainage. This confirms the need for a more individualized follow-up of patients considering the specifics of this location and supports the modern trend of prioritizing observation over regional lymphadenectomy. Follow-up is recommended using ultrasonography at 3-month intervals.

Sentinel lymph node biopsy in patients with head and neck melanoma continues to be routinely performed at our institution in the indicated cases. However, it cannot be ruled out that, depending on the results of ongoing studies, the indications for sentinel lymph node biopsy may become more selective in the future. Interdisciplinary collaboration between the surgeon, oncologist, and dermatologist remain essential, particularly when caring for patients with head and neck melanoma.

Roles of authors

Jan Jaroš was responsible for the collection of all clinical data and carried out the comprehensive evaluation and analysis of the study results. He also prepared the initial draft of the manuscript. Aleš Fibír provided expert supervision throughout the research process, critically reviewed the manuscript for important intellectual content, and guided the interpretation of the findings. He also contributed to the final editing and approval of the manuscript. Both authors actively participated in discussions regarding the study design and data interpretation and have approved the final version for publication.

Disclosure

The authors have no conflicts of interest to disclose. The authors declare that this study has received no financial support. All procedures performed in this study involving human participants were in accordance with ethical standards of the institutional and/or national research committee and with the Helsinki declaration and its later amendments or comparable ethical standards.

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