SENTINEL LYMPH NODE BIOPSY IN THE MANAGEMENT OF PATIENTS WITH MALIGNANT MELANOMA

Nguyen Canh Tung[1,*], Nguyen Huu Quang[1], Nguyen Hong Son[1], Nguyen Dinh Quan[1], Vu Nguyen Binh[1], Le Thanh Hien[1], Ta Thi Ha Phuong[1], Vu Dinh Tam[1], Nguyen Huu Sau[1,2]

ABSTRACT

Objectives: To evaluate the efficacy of sentinel lymph node biopsy in the treatment of malignant melanoma.

Materials and methods: Thirty-two melanoma patients without distant or clinical lymph node metastasis underwent preoperative lymphoscintigraphy using Tc99m and a handheld gamma probe to identify sentinel lymph nodes for biopsy. In cases with detected sentinel lymph node metastasis, the patient may require total complete lymph node dissection, combined with optional systemic therapy. Follow-up was performed to evaluate the efficacy of this procedure.

Results: In 32 melanoma patients, the most common site of primary tumors was the extremity, accounting for 90.6%, with a mean Breslow index (thickness of the primary tumor) of 1.84 mm. The incidence of microscopic lymph node metastasis was 34.4%. For cases with no detected sentinel lymph node metastasis, 100% of patients had a stable condition, and no recurrence or metastasis was detected. In 11 cases with occult nodal metastasis: 2 deaths, 4 patients were treated with chemotherapy, and 5 cases without chemotherapy. The mean duration of hospitalization for the group with sentinel lymph node metastasis was greater than that of the group without sentinel lymph node metastasis, 25.1 ± 3.1 days and 13.5 ± 1.3 days, respectively.

Conclusions: Our results suggest that sentinel lymph node biopsy is a less invasive technique for melanoma patients with no clinically detectable lymph node and distant metastases. This procedure has shown initial outcomes, but it is necessary to conduct a study with a larger sample size and a longer follow-up time, as well as comparing it with a control group for accurate evaluation.

Keywords: *Malignant melanoma, sentinel lymph nodes, lymph node metastasis.*

[1] The National Hospital of Dermatology and Venereology
[2] Hanoi Medical University
** Correspondence: nguyencanhtung1301@gmail.com*
Received 23 June 2023
Revised 22 September 2023
Accepted 27 November 2023
DOI: https://doi.org/10.56320/tcdlhvn.42.132

1. INTRODUCTION

Approximately 15 - 20% of cases of malignant melanoma (MM) involve hidden lymph node metastases, a factor significantly influencing prognostic considerations in melanoma.[1] The historical approach to managing nodal metastases, primarily through complete lymph node dissection (CLND), was associated with complications such as lymphedema, seroma, and hematoma.[2] The advent of sentinel lymph node biopsy (SLNB) in 1992 by Morton and Cochran marked a pivotal shift, establishing it as the standard care for early-stage melanoma. SLNB offers a less invasive means to detect occult lymph node metastases, reducing hospitalization time and complications compared to CLND.[3]

Research underscores the poorer prognosis in patients with sentinel node metastasis compared to those without detectable lymph node involvement. Clinicians use the sentinel lymph node status to stratify MM stages, guide imaging investigations, prescribe therapies, and determine prognosis.[4] Despite the widespread adoption of SLNB, there remains a lack of globally accepted protocols for processing sentinel lymph nodes (SLNs). Conventional processing methods, involving a single routine hematoxylin-eosin (HE)-stained section obtained by bivalving the SLN along its long axis, may overlook small metastases. While CLND was traditionally recommended for patients with positive SLNB results, recent studies have questioned the therapeutic value of immediate CLND after positive SLNB, leading to a shift in the traditional strategy.[5]

Despite the increasing use of SLNB facilitated by advances in radiotechnology, its perceived value varies across different reports. Notably, within our literature scope, there is an absence of reports on the value of SLNB for MM patients in Vietnam. Consequently, this study was undertaken to assess the outcomes of sentinel lymph node biopsy in melanoma patients within this geographical context.

2. MATERIALS AND METHODS

Study design

The study was conducted at the National Hospital of Dermatology and Venereology in Vietnam. This study was designed as a descriptive retrospective study.

Subjects

32 melanoma patients at the National Hospital of Dermatology and Venereology from 2019 to 2022 were included in the study. Inclusion criteria were patients diagnosed with malignant melanoma based on histopathological evidence. No lymph node metastasis was detected based on clinical examination and imaging or fine needle aspiration (FNA). Lymphoscintigraphy with Tc99m radiopharmaceuticals and sentinel lymph node biopsy were conducted under the guidance of a handheld gamma probe. Exclusion criteria were patients not allowed to have lymphoscintigraphy and sentinel lymph node biopsy; patients diagnosed with palpable lymph node metastasis, or imaging, or fine needle aspiration; patients who disagreed to participate in the study.

Materials

Research medical record, Tc^{99m} radiopharmaceuticals, handheld gamma probe, histopathological specimen.

Procedures

We enroll patients diagnosed with primary MM without nodal or distant metastasis based on imaging, ultrasound, and fine needle

aspiration. The patients consented to join this study. Lymphoscintigraphy was conducted using Tc99m radiopharmaceuticals. During the surgery for the excision of primary MM, we used a handheld gamma probe to identify and biopsy the activation nodes. These lymph nodes were analyzed by a histopathologist for the presence of cancer cells. We recorded information about the characteristics of the primary tumor, involvement of sentinel lymph nodes, follow-up, and the outcome of treatment.

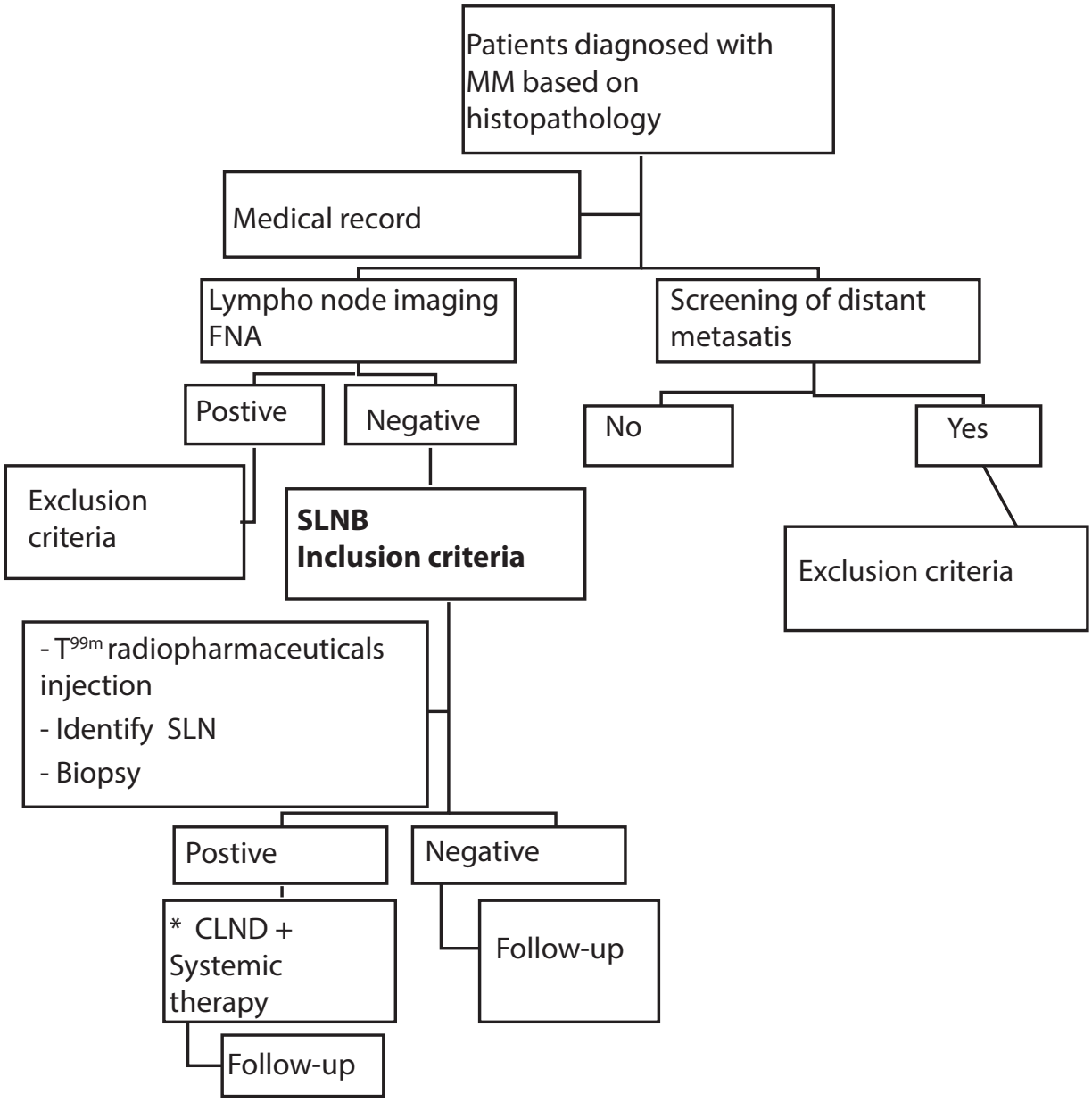

Figure 1. Diagram of the study

Statistical analysis

The data were encrypted and analyzed using the statistical algorithm with SPSS 20.0. The T-test and the Chi-square test were employed to compare the difference between means and prevalence. The difference was considered statistically significant at $p < 0.05$.

Ethical approval

The study was approved by the Ethical Review Board of the National Hospital of Dermatology and Venereology, Vietnam, and written informed consent was obtained from all subjects before their enrollment in the study.

3. RESULTS

3.1. The prevalence of occult nodal metastasis in MM patients

32 patients with a mean age of 60.2 ± 13.1; the youngest patient was 34 years old, and the oldest was 85 years old. Gender distribution showed 13 cases being male (40.6%) and 19 cases being female (59.4%).

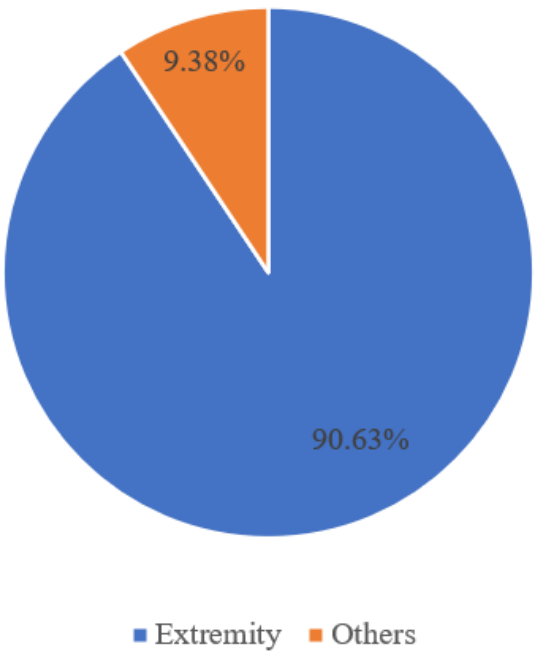

Figure 2. Characteristic of primary tumor site

The most common site of primary tumors was the extremity (foot, hands); 3 out of 32 patients had primary lesions on the thigh, lumbar region, and hypogastrium (as shown in Figure 2).

The thickness of the primary tumor (measured from the granular layer of the epidermis to the deepest position of the cancer tissue) was, on average, 1.8 ± 1.5 mm, in the range from 0 - 7 mm.

Table 1. Occult nodal metastases and the association with Breslow

	n	%	Breslow (mm)	p
Positive node	11	34.4	2.1 ± 1.4	0.31*
Negative node	221	65.6	1.7 ± 1.6	
Total	32	100	1.8 ± 1.5	
**: Mann-Whitney U test*				

The incidence of occult nodal metastases was 34.4%. There was no difference in the thickness of the primary tumor (Breslow) and sentinel lymph node metastases (as shown in Table 2).

3.2. The outcome of sentinel lymph node biopsy in treatment of malignant melanoma

Table 3. Duration of hospitalization

	n	Duration of hospitalization (days)	p
Positive node	11	25.1 ± 3.1	0.00*
Negative node	21	13.5 ± 1.3	
Total	32	17.5 ± 5.9	
**: Mann-Whitney U test*			

The patients had a mean hospitalization duration of 17.5 days. For the group with sentinel lymph node metastasis, it was 25.1 days, which was statistically significantly greater than the group without sentinel lymph node metastasis, with 13.5 days of hospitalization (as shown in Table 3)

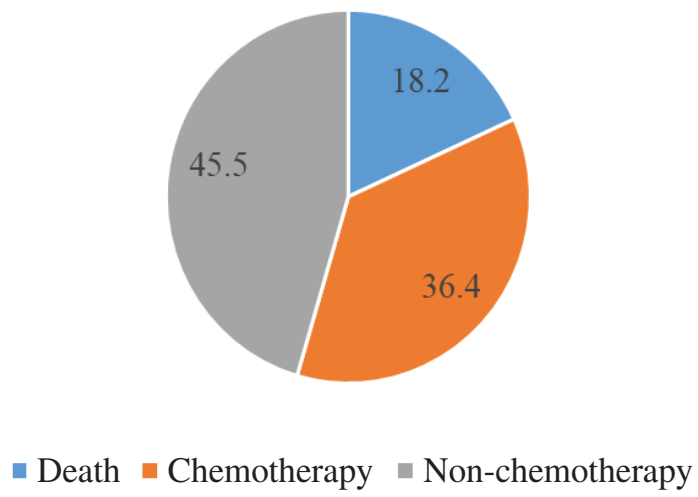

Figure 3. The outcome of patients with occult nodal metastases

In 11 patients with sentinel lymph node metastasis, all patients underwent total lymphadenectomy, with or without chemotherapy. Four patients received systemic chemotherapy, accounting for 36.4%, while five patients were closely monitored (as shown in Figure 3). All cases were stable, and no metastases were detected.

4. DISCUSSION

The role of sentinel lymph node biopsy in the management of nodal metastases in MM has been considered through several comprehensive guidelines. Sentinel lymph node biopsy is recommended for primary lesions with a Breslow thickness of 0.8mm or more or less than 0.8mm with high-risk factors such as patients under 40 years old, invasion of blood vessels, presence of tumor cells in biopsy margins (if close to 0.8mm), and a high rate of mitosis.[3] Our study evaluated the results of sentinel lymph node biopsy in different T (tumor) stages, including cases of in situ melanoma. The classic sentinel lymph node biopsy technique uses a Tc99m radiopharmaceutical injection, followed by a handheld gamma probe and injection of blue dye around the primary lesion to accurately identify the sentinel lymph node for biopsy.

However, some authors suggested that the gamma probe can solely detect high levels of radioactivity without the need for blue dye injection.[4] In our research, sentinel lymph nodes were also identified using a handheld gamma probe.

The rate of lymph node metastasis according to our results was 34.4%, which is higher than that reported by Tejera-Vaquerizo et al. (6.7%) and Kocsis et al. (11.5%) in 2019 and 2020, respectively.[5,6] This may be due to patients in Vietnam seeking medical attention later, resulting in the higher rate of lymph node metastasis. Our study found that if no lymph node metastasis was detected, the 3-year survival rate was 100%, while it was 81.8% in the group with lymph node metastasis. Other authors have also shown a poorer prognosis in patients with occult nodal metastasis.[7,8] In our study, there was no difference in Breslow thickness between the group with and without lymph node metastasis. However, other studies have found a higher rate of sentinel lymph node metastasis in patients with higher Breslow.[9,10] This could be influenced by sample size and errors in Breslow thickness measurement.

When sentinel lymph node metastasis was detected, complete lymph node dissection and adjuvant therapy (chemotherapy) may be indicated.[3] The average hospital stay was 17.5 ± 5.9 days, with longer stays for the group with sentinel lymph node metastasis. In our study, all patients with positive sentinel lymph nodes underwent complete lymph node dissection, and 36.4% received adjuvant chemotherapy. The research also found that the recurrence or metastasis rate in the positive lymph node group was 18.2%, and these patients died quickly thereafter, while there were no cases of recurrence or metastasis in the negative sentinel lymph node group during follow-up. Other studies have reported an average lymph node metastasis rate of 12.5% (ranging from 0 to 34%) in patients with initially negative sentinel lymph nodes during follow-up.[11] Our study may require longer follow-up to evaluate this rate.

5. CONCLUSION

Sentinel lymph node biopsy should be indicated in malignant melanoma cases as

recommended by guidelines, as a method to reduce invasion and improve complications compared to complete lymph node dissection. Although the rate of occult nodal metastases is low, it has prognostic significance for patients. This technique has helped detect many cases of occult lymph node metastasis that were not identified through clinical and imaging diagnoses, and it also helps patients avoid undergoing complete lymph node dissection in early stages, reducing hospitalization time compared to the complete lymph node dissection group. Larger and longer-term research is needed to evaluate the value of this technique as well as factors related to metastasis and prognosis in malignant melanoma patients.

REFERENCE

1. Balch, C. M., Gershenwald, J. E., Soong, S. J., Thompson, J. F., Ding, S., Byrd, D. R., Cascinelli, N., Cochran, A. J., Coit, D. G., Eggermont, A. M., Johnson, T., Kirkwood, J. M., Leong, S. P., McMasters, K. M., Mihm, M. C., Jr, Morton, D. L., Ross, M. I., & Sondak, V. K. (2010). Multivariate analysis of prognostic factors among 2,313 patients with stage III melanoma: comparison of nodal micrometastases versus macrometastases. Journal of clinical oncology: official journal of the American Society of Clinical Oncology, 28(14), 2452 -2459. https://doi.org/10.1200/JCO.2009.27.1627.

2. Durham, A. B., & Wong, S. L. (2014). Sentinel lymph node biopsy in melanoma: final results of MSLT-I. Future oncology (London, England), 10(7), 1121 -1123. https://doi.org/10.2217/fon.14.67.

3. Pathak, S., & Zito, P. M. (2023). Clinical Guidelines for the Staging, Diagnosis, and Management of Cutaneous Malignant Melanoma. In StatPearls. https://pubmed.ncbi.nlm.nih.gov/34283515/

4. Kapteijn, B. A., Nieweg, O. E., Liem, I., Mooi, W. J., Balm, A. J., Muller, S. H., Peterse, J. L., Valdés Olmos, R. A., Hoefnagel, C. A., & Kroon, B. B. (1997). Localizing the sentinel node in cutaneous melanoma: gamma probe detection versus blue dye. Annals of surgical oncology, 4(2), 156 -160. https://doi.org/10.1007/BF02303799.

5. Tejera-Vaquerizo, A., Ribero, S., Puig, S., Boada, A., Paradela, S., Moreno-Ramírez, D., Cañueto, J., de Unamuno, B., Brinca, A., Descalzo-Gallego, M. A., Osella-Abate, S., Cassoni, P., Carrera, C., Vidal-Sicart, S., Bennássar, A., Rull, R., Alos, L., Requena, C., Bolumar, I., Traves, V., … SENTIMEL group (2019). Survival analysis and sentinel lymph node status in thin cutaneous melanoma: A multicenter observational study. Cancer medicine, 8(9), 4235 -4244. https://doi.org/10.1002/cam4.2358.

6. Kocsis, A., Karsko, L., Kurgyis, Z., Besenyi, Z., Pavics, L., Dosa-Racz, E., Kis, E., Baltas, E., Ocsai, H., Varga, E., Bende, B., Varga, A., Mohos, G., Korom, I., Varga, J., Kemeny, L., Nemeth, I. B., & Olah, J. (2020). Is it Necessary to Perform Sentinel Lymph Node Biopsy in Thin Melanoma? A Retrospective Single Center Analysis. Pathology oncology research: POR, 26(3), 1861 -1868. https://doi.org/10.1007/s12253-019-00769-z.

7. Stiegel, E., Xiong, D., Ya, J., Funchain, P., Isakov, R., Gastman, B., & Vij, A. (2018). Prognostic value of sentinel lymph node biopsy according to Breslow thickness for cutaneous melanoma. Journal of the American Academy of Dermatology, 78(5), 942-948. https://doi.org/10.1016/j.jaad.2018.01.030.

8. Hu, Y., Briggs, A., Gennarelli, R. L., Bartlett, E. K., Ariyan, C. E., Coit, D. G., & Brady, M. S. (2020). Sentinel Lymph Node Biopsy for T1b Melanoma: Balancing Prognostic Value and Cost. Annals of

surgical oncology, 27(13), 5248 -5256. https://doi.org/10.1245/s10434-020-08558-8.

9. Venna, S. S., Thummala, S., Nosrati, M., Leong, S. P., Miller, J. R., 3rd, Sagebiel, R. W., & Kashani-Sabet, M. (2013). Analysis of sentinel lymph node positivity in patients with thin primary melanoma. Journal of the American Academy of Dermatology, 68(4), 560 -567. https://doi.org/10.1016/j.jaad.2012.08.045.

10. Chang, J. M., Kosiorek, H. E., Dueck, A. C., Leong, S. P. L., Vetto, J. T., White, R. L., Avisar, E., Sondak, V. K., Messina, J. L., Zager, J. S., Garberoglio, C., Kashani-Sabet, M., & Pockaj, B. A. (2018). Stratifying SLN incidence in intermediate thickness melanoma patients. American journal of surgery, 215(4), 699 -706. https://doi.org/10.1016/j.amjsurg.2017.12.009.

11. Valsecchi, M. E., Silbermins, D., de Rosa, N., Wong, S. L., & Lyman, G. H. (2011). Lymphatic mapping and sentinel lymph node biopsy in patients with melanoma: a meta-analysis. Journal of clinical oncology: official journal of the American Society of Clinical Oncology, 29(11), 1479 -1487. https://doi.org/10.1200/JCO.2010.33.1884.