

Biopsy Type and Metastatic Recurrence in Melanoma: A Cohort Study

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ABSTRACT

Background: Melanoma is a dynamic health problem caused by deteriorating melanocytes that generate aberrant melanin that gives color to the skin. It remains the leading cause of death from skin cancer. The incidence and mortality rates of melanoma emphasize the need for a suitable diagnostic biopsy, which is important for the optimal treatment of newly observed melanoma patients.

Objectives: This study aims to evaluate the presence of melanoma metastases, mitotic rate, ulceration, and Breslow thickness, which are the most significant predictors of mortality from melanoma and are important for the diagnosis and optimal treatment of newly diagnosed melanoma patients.

Methods: A cohort of 56 patients diagnosed with melanoma in the upper or lower limbs between 2020 and 2024 was analyzed to investigate whether partial biopsies influence melanoma metastasis. All patients underwent biopsy followed by complete resection and were followed for 3 years. We evaluated clinical characteristics, including Breslow thickness, surgical excision width, CLARK grade, ulcer presence, vascular invasion, and biopsy-excision interval, for their influence on recurrence time. The relationships between these factors and recurrence were assessed using the rank sum test and Spearman correlation analysis.

Results: The results revealed that all patients had metastasis at varying intervals post-surgery, with different patterns observed between upper and lower limb melanomas. However, the correlation between recurrence duration and the analyzed characteristics was not statistically significant.

Conclusion: Thus, our current revelations conclude that complete resection of the tumor lesions is sufficient for patients diagnosed with melanoma after biopsy, and extended resection is unnecessary.

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INTRODUCTION

Melanoma is a serious form of skin cancer caused by deteriorating melanocytes that generate aberrant melanin, the pigment that gives skin its color. It remains the leading cause of death from skin cancer and is expected to rise globally in the upcoming years.^{1,2} Tumor features such as the presence of metastases, mitotic rate, ulceration, and Breslow thickness are the most significant predictors of mortality from melanoma.² The incidence and mortality rates of melanoma emphasize the need for a suitable

diagnostic biopsy, which is important for the optimal treatment of newly observed melanoma patients. In parallel, the tumor characteristics of the initial melanoma provide physicians with crucial prognostic and staging information, as well as guidance for treatment.^{3,4}

The selection of a particular biopsy approach has been found to depend on the size and location of the pigmented lesion, as well as the observations and experience of the physician (Sharma et al). In terms of surgical care, guidelines recommend performing a

diagnostic excision biopsy (DEB) no later than 2 weeks after the patient first presents.^{5,6} When treating clinically suspected melanoma, an excisional biopsy with narrow margins (2 mm) is considered an effective initial treatment. Parallel to this, partial biopsies (punch, shave, curette, and incisional biopsies) are frequently used instead of excisional biopsies.^{3,7,8} However, the impact of an incisional biopsy on the prognosis for the initial diagnosis of melanoma remains debatable. It has been proposed that insufficient removal of the melanoma could cause malignant cells to be dislodged.^{2,9} For this reason, some surgeons prefer complete excisions to prevent tumor cell seeding and to achieve superior histologic results.¹⁰

Nevertheless, shave biopsies, rather than excisional biopsies, are typically used to diagnose melanoma.³ Whether slicing into the tumor causes injury or not remains a major concern that both doctors and patients should discuss.^{10,11} Thus, considering the consequences and queries raised in the literature, our investigations aim to explore whether biopsy affects metastasis and recurrence, as well as the relationship between resection-biopsy interval, tumor mitotic rate, and ulceration.

MATERIALS AND METHODS

Between 2020 and 2024, 56 patients were initially diagnosed via biopsy and subsequently underwent complete resection of melanoma in the upper or lower extremities at our hospital. The cohort included 27 females (48.2%) and 29 males (51.8%) with a median age of 67 years, ranging from 31 to 84 years, and a mean age of 60.24 years. Patients were followed up for 3 years, with follow-up ending upon the appearance of metastases. All patients underwent CT or MRI examinations prior to complete resection.

The patients were analyzed based on Breslow thickness (Group 1. ≤ 1.00 mm, Group 2. 1.01–2.00 mm, Group 3. 2.01–4.00 mm, Group 4. >4.01 mm), Clark level (I–V), vascular invasion, split index, ulceration, surgical excision breadth, and biopsy-excision interval (days) vs transfer interval time (weeks).

The collected data were analyzed statistically to explore the relationships between various characteristics (Thickness, Clark level, vascular invasion, split index, ulceration, surgical excision breadth, biopsy-excision interval, and treatments) and recurrence duration using Spearman correlation analysis and rank sum tests, employing SPSS 11.5 (Statistical Package for the Social Sciences, Windows 2000, Chicago, IL).

RESULTS

Among the 56 patients with malignant melanoma of the upper and lower limbs, 9 cases of melanoma involved the hand, with 2 cases of lung metastasis, 6 cases of simple ipsilateral axillary lymph node metastasis, 1 case of subcutaneous transitional metastasis at the surgical site, and 2 cases of lower extremity

TABLE 1.

Tumor Features of 56 Melanoma Cases		
Recorded Features	Variables	n (%)
Sex	Female	27/56 (48%)
	Male	29/56 (52%)
Age (Years)	Mean	60.24
	Median	67
	Range	31-84
Tumor anatomic site	Hand	9/56 (16%)
	Leg	2/56 (4%)
	Feet	45/56 (80%)
Thickness (mm)	1	5/54 (9.3%)
	2	6/54 (11.1%)
	3	11/54 (20.3%)
	4	32/54 (59.3%)
CLARK rating	1	2/41 (4.9%)
	2	5/41 (12.2%)
	3	11/41 (26.8%)
	4	16/41 (39%)
	5	7/41 (17.1%)
Vessels	-ve	39/44 (88.6%)
	+ve	5/44 (11.4%)
Ulcer	-ve	40/52 (77%)
	+ve	12/52 (23%)
Split index (pieces/mm ²)	Mean	8.08
	Median	6
	Range	1-28
Surgical resection width (cm)	Mean	1.56
	Median	2
	Range	0.4-4
Biopsy-excision interval (days)	Mean	25.76
	Median	18.5
	Range	5-169
Treatments	Interferon	23/53 (43.4%)
	Chemotherapy	13/53 (24.5%)
	No Treatment	17/53 (32.1%)

melanoma with subcutaneous transitional metastasis. Among the 45 patients with melanoma in the foot, 16 had simple ipsilateral inguinal lymph node metastasis, 19 had distant metastasis, 7 had simple subcutaneous metastasis, and 3 had combined ipsilateral inguinal lymph node metastasis and subcutaneous metastasis (Table 1).

TABLE 2.**The Relationship Between Different Characteristics of Patients and the Duration of Recurrence Via Spearman Correlation Analysis**

Characteristics	r _s value	P value
Thickness (mm)	0.224	0.103
CLARK Rating	-0.187	0.242
Vessels	0.123	0.433
Split Index (pieces)	0.119	0.470
Ulcer	0.015	0.915
Surgical Resection Width (cm)	0.089	0.523
Biopsy/Resection Interval (days)	0.024	0.866
Treatments	-0.018	0.900

Spearman Correlation Analysis

Spearman correlation analysis indicated that none of the characteristics (Thickness, Clark level, Vessels, Split Index, Ulcer, Surgical Resection Width, Biopsy-Resection Interval, and Interferon) showed a statistically significant correlation with the duration of recurrence. Negligible or weak relationships were observed between the variables and recurrence duration, as the Spearman correlation coefficients (r_s) for most characteristics were close to zero (Table 2). This analysis expressed Thickness (mm) with a positive correlation to recurrence duration ($r_s=0.224$), but this was not found statistically significant ($P=0.103$). In contrast, Clark level revealed a negative correlation with recurrence duration ($r_s=-0.187$), but statistically, this was not found significant ($P=0.242$). A statistically nonsignificant ($P=0.433$) and weak positive correlation ($r_s=0.123$) was observed in the case of vessels. Split index (pieces) also indicated a weak positive ($r_s=0.119$) and nonsignificant ($P=0.470$) correlation, statistically. Ulcer demonstrated a very weak positive correlation ($r_s=0.015$), with no statistical significance ($P=0.915$). Surgical resection width (cm) was also revealed with a weak positive ($r_s=0.089$) and statistically nonsignificant ($P=0.523$) correlation.

Biopsy to resection interval (days) displayed an extremely weak positive correlation ($r_s=0.024$), with no statistical significance ($P=0.866$). Interferon showed a very weak negative correlation ($r_s=-0.018$), with no statistical significance ($P=0.900$; Table 2).

The findings of Spearman correlation analysis suggest that the analyzed factors may not have a strong influence on recurrence time in the studied population.

Rank Sum Test

According to the rank sum test, none of the characteristics exhibited statistically significant differences in recurrence duration between the groups, despite variability in interquartile ranges and median values across the characteristics. Clark level and Thickness exhibited some variability across categories, but statistical results were revealed as nonsignificant. Similarly, the presence of ulcers and vessels had no significant impact on the median values. Treatments including chemotherapy, interferon, and the control group were also observed to be nonsignificant (Table 3).

DISCUSSION

The use of incisional, punch, or shave biopsies is increasing regardless of guidelines recommending excisional biopsy as the diagnostic procedure for melanoma. Excisional biopsy's frequency (10–86%) for diagnostic objectives varies widely. In addition to risks such as misdiagnosis, staging inaccuracy, and diagnostic uncertainty, the belief that partial biopsy has an adverse effect on prognosis has been disproved in different reports. There has been concern that incomplete excision of melanoma could result in local, regional, or systemic tumor dissemination.¹²⁻¹⁴ According to NCDB reports, incisional biopsies were found to be associated with decreasing overall 5-year survival. The excisional biopsy techniques recommended in the current national guidelines correlate with NCDB reports.¹⁵⁻¹⁷

TABLE 3.**Comparison of Recurrence Duration in Patients With Different Characteristics Via Rank Sum Test**

Characteristics	Categories	M (P_{25}, P_{75})	Z/H value	P value
Thickness (mm)	Group 1	7.77 (5.40, 32.90)	4.072	0.254
	Group 2	21.32 (8.10, 30.52)		
	Group 3	11.30 (2.56, 18.30)		
	Group 4	17.53 (9.07, 36.25)		
CLARK Rating	Group 1	32.60 (7.26, -)	5.259	0.262
	Group 2	15.83 (11.32, 54.22)		
	Group 3	15.60 (7.43, 36.37)		
	Group 4	8.17 (4.08, 19.78)		
	Group 5	15.23 (12.87, 25.30)		
Vessels	Negative	14.39 (6.78, 26.13)	-0.796	0.426
	Positive	19.24 (7.09, 53.75)		
Ulcer	Negative	11.32 (5.81, 37.42)	-0.109	0.914
	Positive	15.22 (7.52, 31.05)		
Treatments	Interferon	15.20 (7.77, 36.70)	0.985	0.611
	Chemotherapy	15.83 (6.22, 23.68)		
	Control	12.87 (4.82, 38.99)		

Therefore, complete excisions are preferred to achieve better outcomes and to avoid the risk of displacing tumor cells to other locations.

A large study found no significant differences between biopsy techniques (complete excision, shave biopsy, and incisional biopsy) regarding the incidence of sentinel lymph node metastases, disease-free survival, locoregional recurrences, overall survival, or distant disease-free survival. Some results revealed that the type of diagnostic biopsy or the tumor cells' presence in the re-excision specimen have no influence on the survival of the melanoma patient.^{15,18} In terms of surgical management, the United States National Comprehensive Cancer Network and British Society of Dermatology recommended diagnostic excision biopsy within 2 weeks of initial presentation. However, there are no guidelines on the optimal time interval between a diagnostic excision biopsy and a wide local excision. Hence, the guidelines of the European Dermatology Forum suggest definitive surgical management within 4 to 6 weeks of the initial diagnosis.^{19,20}

Since the biopsy method does not appear to affect progression-free survival (PFS) or overall survival (OS), we aimed to explore whether different surgical methods promote tumor metastasis and whether strict expansion surgery or even amputation is necessary after an initial local biopsy. Our statistical results suggest that all 56 patients who underwent local biopsy developed metastases after secondary expansion surgery. Only 4 patients (7.5%) had subcutaneous transitional metastases, while the others experienced metastases distant from the surgical site. Based on these findings, we believe that for patients undergoing an initial partial biopsy, expansion surgery may not provide additional benefit during subsequent surgical resection. The tumor may already be adequately removed during re-operation after the biopsy. Our analysis further suggests that melanoma metastasizes away from the surgical site 100% of the time after local excision and pathological examination. This behavior is comparable to a wasp's nest. When undisturbed, the wasps' range of activity remains relatively limited. However, once stimulated, their activity spreads irregularly and rapidly. Similarly, melanoma may already have distant metastases in the early stage, which act as "sentinels" indicating early distant dissemination. The biological behavior of melanoma after being stimulated (eg, through partial biopsy) closely resembles the behavior of wasps when provoked. We refer to this phenomenon as the "wasp effect."

Our study results suggest that expanding the scope of resection in melanoma patients after biopsy does not prevent metastasis, and complete resection of the tumor lesions can help reduce the patient's surgical pain. Future research should focus on exploring whether differences in recurrence and metastasis exist in melanoma patients who undergo extended resection and biopsy at the time of initial diagnosis, providing data to support future treatment principles.

CONCLUSION

The impact of partial biopsy on the recurrence of 56 cases of upper and lower limb melanoma after complete resection was analyzed. The rank sum test and Spearman correlation analysis showed no significant correlation between any factor and the duration of recurrence or metastasis. Although all patients experienced varying degrees of metastasis after surgery, none of the factors studied significantly influenced the duration of recurrence. The study concluded that the analyzed factors did not have a statistically significant impact on melanoma recurrence. Therefore, we believe that expanding the scope of resection after biopsy does not prevent metastasis, and complete resection of the tumor lesion is sufficient.

DISCLOSURES

The authors have no conflicts of interest to disclose.

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