Head and Neck Malignant Melanoma

Margin Status and Immediate Reconstruction

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Abstract: Head and neck melanoma often approaches critical structures. Therefore, excision is often limited, leading to positive margins, and increased local recurrence. Immediate reconstruction carries concern for rearrangement or concealment of cancerous tissues. Therefore, reconstruction is often delayed until confirming negative margins on permanent pathology. Our purpose is to identify variables associated with a positive margin and establish criteria for reconstruction timing. We reviewed 117 consecutive patients who underwent wide local excision of head and neck melanoma. Reconstruction was immediate for 107 and delayed for 10. Six percent of patients had a positive margin after wide local excision with no difference in incidence between immediate and delayed reconstruction ($P = 0.11$). Tumor characteristics associated with a positive margin were locally recurrent, ulcerated, and T4 tumors ($P < 0.05$); and delayed reconstruction should be considered in these circumstances. Immediate reconstruction is safe for the majority of head and neck melanoma and should be based on knowledge of tumor characteristics.

Key Words: melanoma, reconstruction, timing, immediate, margin, head and neck

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Melanoma is the fifth and sixth most common cancer in men and women, respectively.[1] Treatment of cutaneous melanoma is primarily surgical and approximately 20% of all primary cutaneous melanomas occur in the head and neck (HN) region.[2–5] The current recommendations for surgical margins of uninvolved tissue surrounding melanoma are 1 cm for T1 tumors (≤1 mm in thickness),[6,7] 2 cm for T2 (1.01–2 mm), or T3 (2–4 mm) tumors,[8] and 2–3 cm for T4 (>4 mm) tumors.[4,9] These margins are often readily obtained on the trunk and extremity and in many cases the defect can be closed primarily. These same margins often prevent primary closure in the HN and wide margins of extirpation often result in loss of function and disfigurement of critical structures such as the eyelid, ear, nose, or lip. Fear of damage or disfigurement and not obtaining primary closure likely contribute to narrower margins of excision. The result is incomplete excision and the much higher published rate of local recurrence of HN compared with trunk and extremity melanoma (9.4%–13% vs. 0.9%–6.3%).[10]

To achieve both optimal results and low rates of recurrence, the surgical oncologist and the plastic surgeon must work closely together in planning and executing the wide local excision (WLE) and reconstruction. Options for reconstruction include primary closure, secondary closure, skin grafting, or adjacent tissue transfer. The timing of reconstruction of nonmelanoma skin cancer has been debated. Some authors advocate for delayed reconstruction of HN carcinoma, such as squamous cell and basal cell carcinoma, until after review of permanently fixed pathology and confirmation of negative margin status,[11] whereas others argue that immediate tissue transfer reconstruction is safe.[12,13] Immediate frozen section analysis of melanoma margin status is not advised due to the challenging pathologic review of melanoma. Therefore, due to local recurrence concerns, the mainstay of HN cancer defect reconstruction has been delayed skin grafting after review of permanent pathology and immunohistochemistry. This course of treatment is thought to ensure negative margins, enable surveillance of the original site, and not mask a local recurrence at the site of a more complex reconstruction.[11,13–18] However, the often poor esthetic result and patient dissatisfaction with skin grafts due to color mismatch, contour deformity, wound contracture, and disfigurement along with inability to cover exposed cartilage or bone have driven us and others to prefer adjacent tissue transfer for HN reconstruction.[2,13] Adjacent tissue transfer has not been found to hinder monitoring for recurrence and may actually help prevent local recurrence by allowing larger and more oncologically sound margins to be taken.[12,19,20]

The objectives of our study were to (1) determine the overall frequency of a positive margin and patient and tumor characteristics associated with a positive margin after WLE of cutaneous HN malignant melanoma, and (2) establish criteria for performing immediate versus delayed reconstruction.

METHODS

We performed a retrospective review of all patients with HN malignant melanoma who underwent WLE and reconstruction at the University of Washington Medical Center between 1999 and 2004 after receiving approval from the Human Subjects Internal Review Board. Data collected from the medical records included patient demographics, melanoma type (superficial spreading melanoma, lentigo maligna melanoma, nodular melanoma, desmoplastic melanoma, not otherwise specified on pathology reports, in situ [lentigo maligna and all other in situ melanoma], and other [spitzoid, nevoid, amelanotic, and verrucous]), location, primary or recurrent, thickness, satellitosis, mitotic rate (low, intermediate, or high), ulceration, WLE and reconstruction date, reconstruction type (primary closure, skin graft, or adjacent tissue transfer), sentinel and cervical lymph node status, and margin status after WLE. Melanoma thickness was measured in millimeters as defined by Breslow[21] and classified by TNM stage as defined by the American Joint Committee on Cancer (AJCC), 6th Edition, (Tis [in situ], T1 [≤1.0 mm], T2 [1.01–2.0 mm], T3 [2.1–4.0 mm], and T4 [>4.0 mm]).[22]

The oncologic component of the surgery was planned first by the surgical oncologist based on recommended guidelines by tumor depth.[6–8] Reconstruction plan and adjacent tissue transfer design were then coordinated between the surgical oncologist and the plastic surgeon to optimize access to sentinel node(s) without

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compromising flap design. Tumor margins were evaluated by a pathologist using permanent sections and were not available at the time of immediate reconstruction. Reconstruction, immediate or delayed, was performed by a plastic surgeon. The decision to perform immediate or delayed reconstruction was made by the surgical oncologist based on concern for a positive margin after WLE.

Statistical Analysis

We first performed a series of univariate analyses using the Fisher exact test for binary variables, Mann-Whitney *U* test for continuous variables, and logistic regression using indicator variables for categorical variables to compare patients who had immediate or delayed reconstruction and to identify factors associated with the presence of a positive margin after WLE. When a significant association was found among categorical variables and a positive margin, multiple comparisons between categorical variables were performed and adjusted using Bonferroni's method. All calculated *P* values were 2-tailed. Results are presented as odds ratios and 95% confidence intervals (95% CI). All statistical analyses were performed using Stata Version 8 (Stata, College Station, Texas).

RESULTS

Demographic and Clinical Characteristics

One hundred seventeen consecutive patients, 74 men and 43 women, were treated with WLE of HN cutaneous malignant melanoma followed by reconstruction during this 5-year period. Table 1 shows patient and tumor characteristics. Tumors were distributed throughout the HN, with the most common location the cheek, followed by the scalp, and then the forehead (Fig. 1). Of the 117 patients, 107 had primary and 10 had locally recurrent melanoma. The most common type of tumor was nodular, followed by superficial spreading melanoma.

Reconstruction Timing and Type

Reconstruction timing was immediate for 107 and delayed for 10 patients (Table 1). The rationale for delayed reconstruction was determined by the surgical oncologist based on concern for incomplete excision due to a large thin melanoma, indistinct margin, or difficulty in determining adequate WLE. Patients who had immediate and delayed reconstruction were similar with exception to significant differences between tumor thickness and reconstruction type (Table 2). T4 and Tis melanoma were significantly more likely to be delayed than T1, T2, and T3 lesions ($P < 0.05$, Bonferroni corrected).

The most common reconstruction type was adjacent tissue transfer, followed by skin grafting, then primary closure. When primary closure was performed, it was done immediately in all cases and reconstruction by skin graft was performed significantly more often with delayed than immediate reconstruction ($P = 0.01$, Bonferroni corrected). No patient required a free tissue transfer.

Positive Margin, Local Recurrence, and Complications

Overall, a positive margin after WLE occurred in 7 of 117 (6.0%) of patients (Fig. 2). Tumors with a positive margin were located on the cheek for 5 patients, forehead for 1 patient, and neck

TABLE 1. Characteristics of Patients and Tumors by Reconstruction Timing and Margin Status

Characteristic	All Patients (n = 117)	Immediate Reconstruction (n = 107)	Delayed Reconstruction (n = 10)	Margin Negative (n = 110)	Margin Positive (n = 7)
Gender					
Female	43 (36.8%)	38 (35.5%)	5 (50.0%)	40 (36.4%)	3 (42.9%)
Male	74 (63.2%)	69 (64.5%)	5 (50.0%)	70 (63.6%)	4 (57.1%)
Age; y					
Mean ± SD	58.9 ± 18.5	58.9 ± 18.5	58.3 ± 20.4	58.1 ± 18.3	71.4 ± 19.7
Median	61.0	61.0	61.5	60.0	75.0
Tumor status					
Primary	107 (91.5%)	99 (92.5%)	8 (80.0%)	105 (95.5%)	2 (28.6%)
Locally recurrent	10 (8.5%)	8 (7.5%)	2 (20.0%)	5 (4.5%)	5 (71.4%)
Breslow					
Mean ± SD	2.2 ± 2.4 mm	2.3 ± 2.3 mm	1.5 ± 2.8 mm	2.0 ± 2.2 mm	5.0 ± 3.4 mm
Median	1.3 mm	1.4 mm	0 mm	1.2 mm	4.1 mm
AJCC tumor stage, T classification					
Tis	11 (9.4%)	5 (4.7%)	6 (60.0%)	10 (9.1%)	1 (14.3%)
T1	39 (33.3%)	39 (36.4%)	0 (0%)	39 (35.5%)	0 (0%)
T2	21 (17.9%)	20 (18.7%)	1 (10.0%)	21 (19.1%)	0 (0%)
T3	32 (27.4%)	30 (28.0%)	2 (20.0%)	30 (27.3%)	2 (28.6%)
T4	14 (12.0%)	13 (12.1%)	1 (10.0%)	10 (9.1%)	4 (57.1%)
Reconstruction type					
Primary closure	4 (3.4%)	4 (3.7%)	0 (0%)	4 (3.7%)	0 (0%)
Skin graft	14 (12.0%)	10 (9.3%)	4 (40.0%)	11 (10.0%)	3 (42.9%)
Adjacent tissue transfer	99 (84.6%)	93 (86.9%)	6 (60.0%)	95 (86.4%)	4 (57.1%)
Reconstruction timing					
Delayed	10 (85.5%)			8 (7.3%)	2 (28.6%)
Immediate	107 (91.5%)			102 (92.7%)	5 (71.4%)

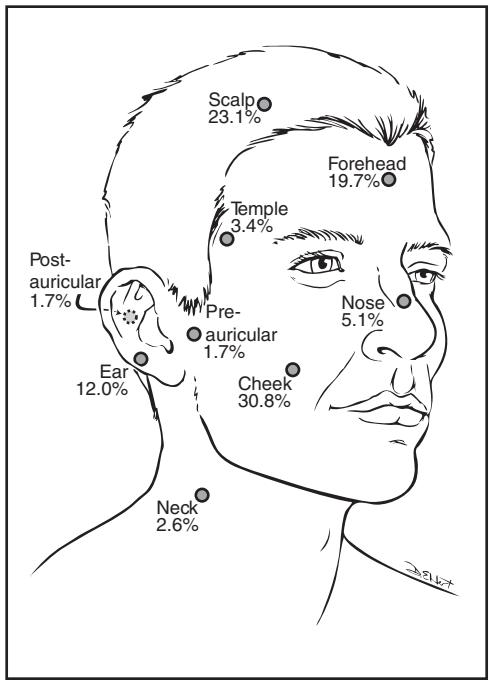

FIGURE 1. Anatomic distribution of melanoma on the head and neck.

TABLE 2. Results of Univariate Analyses Comparing Patient and Tumor Characteristics by Reconstruction Timing and Margin Status

Characteristic	Reconstruction Timing (Immediate vs. Delayed) *P**	Margin Status (Positive vs. Negative) *P**
Gender	0.49	0.71
Age	0.97	0.09
Tumor location	0.13	0.26
Tumor status (primary vs. locally recurrent)	0.20	<0.001
Breslow thickness	0.29	0.01
AJCC T stage	0.005	0.14
Satelitosis	1.0	1.0
Ulceration	0.20	0.03
Regression	0.60	0.62
Angiolymphatic spread	1.0	0.20
Mitotic rate	0.35	0.07
Tumor subtype	0.1	0.19
Reconstruction type	0.04	0.08
Reconstruction timing		0.11

**P* values based on a comparison between patients who underwent immediate and delayed reconstruction and also between patients found to have a positive and negative margin.

AJCC indicates American Joint Committee on Cancer, 6th Edition.

for 1 patient. Variables associated with a positive margin were locally recurrent melanoma, tumor thickness, and ulceration (Table 2). Tumor location, satellitosis, angiolymphatic spread, mitotic rate, tumor type, and sentinel and cervical lymph node status were not found to be associated with a positive margin ($P > 0.05$). A trend toward an association between high mitotic rate and positive margin

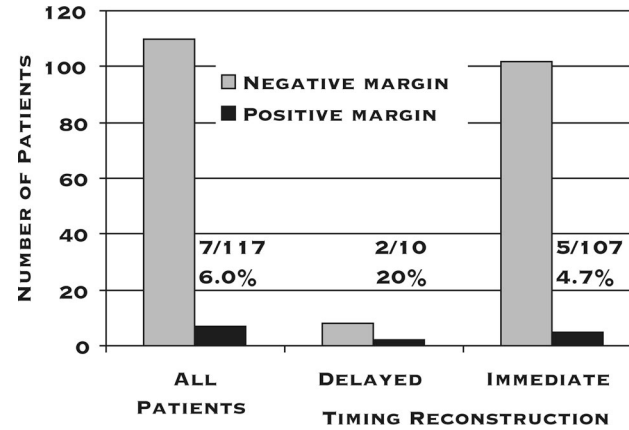

FIGURE 2. Number of patients with negative and positive margin after wide local excision overall and by reconstruction timing.

was seen ($P = 0.07$). A positive margin was found significantly more often with locally recurrent tumors compared with primary tumors ($P < 0.001$). A positive margin after WLE of T1 and T2 lesions was rare as no patients with T1 (0/39 [0%]) nor T2 (0/21 [0%]) had positive margin after WLE. The finding of positive margin after WLE was more common with T3 (2/32 [6.3%]) and most common with T4 tumors (4/14 [28.6%]) (Fig. 3). Tumors with ulceration were significantly associated with a positive margin ($P = 0.03$). Timing of reconstruction was not associated with a positive margin ($P = 0.11$). Despite concern for a positive margin and subsequent delayed reconstruction in 10 patients, only 2 of these patients had a positive margin and both patients had nodular melanoma. A positive margin was found most often with nodular melanoma (Fig. 4) but no significant association between a positive margin and melanoma type was found ($P = 0.19$). No patient with desmoplastic melanoma had a positive margin.

When a histologically positive margin was found, patients were offered reexcision, typically with margins of 5 mm. Two of the 7 patients with a positive margin underwent reexcision, negative margins were obtained, and adjacent tissue was readvanced. Two patients declined a second operation. One of these 2 patients later developed local recurrence of invasive melanoma and underwent repeat WLE. Negative margins were obtained. The remaining 3 of the 7 patients underwent reexcision and readvancement of adjacent

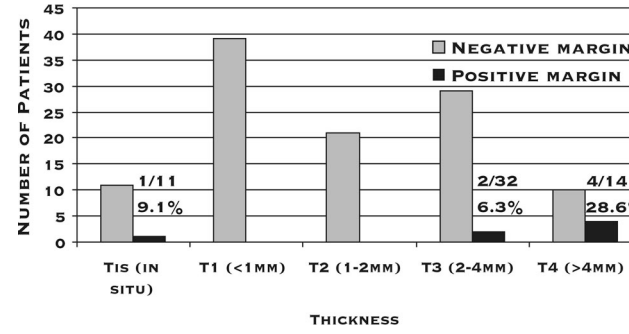

FIGURE 3. Number of patients with negative and positive margin after wide local excision based on melanoma thickness classified by T stage as defined by the American Joint Committee on Cancer, 6th Edition, (Tis [in situ], T1 [≤1.0 mm], T2 [1.01–2.0 mm], T3 [2.1–4.0 mm], and T4 [>4.0 mm]).

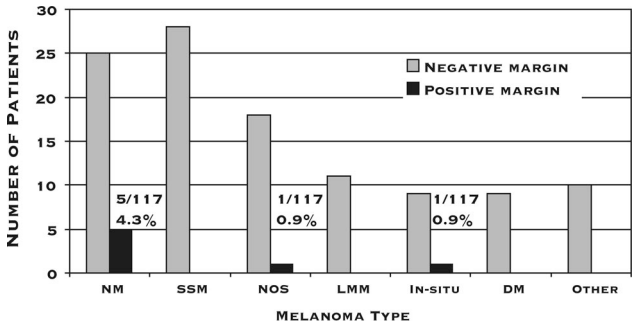

FIGURE 4. Number of patients with negative and positive margin after wide local excision based on melanoma type. NM indicates nodular melanoma; SSM, superficial spreading melanoma; NOS, not otherwise specified on pathology report; LMM, lentigo maligna melanoma; DM, desmoplastic melanoma.

tissue though margins continued to be positive for melanoma in situ despite very wide excision margins due to a diffuse field defect. These 3 patients continue to have close follow-up without reported clinical evidence of recurrent invasive melanoma.

Early complications occurred in 6 patients. One patient developed a hematoma under a cervico-facial flap and required a return to the operating room for evacuation and hemostasis, one patient developed a wound infection that healed with oral antibiotics, 3 patients had partial skin graft loss and all healed secondarily with wound care, and one patient died secondary to postoperative aspiration pneumonia. The 30-day postoperative mortality was 0.9%.

DISCUSSION

We reviewed the clinical and tumor characteristics associated with a histologically positive margin after WLE and the reconstruction timing of 117 consecutive patients; and describe our experience with immediate adjacent tissue transfer after WLE of HN melanoma. Overall, our relatively infrequent (6%) occurrence of positive margin may contribute to reducing previously reported local recurrence rates of 7% to 23% after WLE of HN melanoma.[10,19,23–25] Locally recurrent, ulcerated, and T4 tumors were associated with a positive margin, regardless of reconstructive timing. We believe that immediate adjacent tissue transfer reconstruction is safe in most patients with HN melanoma, unless they have locally recurrent, ulcerated, or T4 disease.

HN melanoma reconstruction has often relied on delayed skin grafting[11,13–18] due to concern for surveillance of subsequent local recurrence. Establishing clinical characteristics associated with positive margins after WLE of HN melanoma is important to determine which surgical cases are suitable for immediate reconstruction. The types of adjacent tissue transfer used for HN reconstruction are beyond the scope of this study and are well described by others.[14,25,26] Several studies have found that adjacent tissue transfer after WLE of melanoma does not adversely affect the ability to treat cancer or delay the detection of local recurrence, and may even decrease local recurrence rates by allowing a more complete resection.[2,12,19,20,25,27] Further, aggressive resection may expose bone, cartilage or other tissues that typically will not accept a skin graft. Compared with skin grafting, adjacent tissue transfer can provide a reliable and superior functional and esthetic result. Cassileth, Lusk, Tenaglia,[28] described psychologic distress after melanoma resection caused by the deep indented scar from skin grafting.

Reconstruction timing can be immediate after WLE or delayed until after review of pathology to ensure negative margins. Some have argued against immediate reconstruction of HN melanoma due to concern for incomplete excision. However, patients prefer a single surgical procedure to a second operation and period of disfigurement.[11] Additionally, with immediate reconstruction, patients require fewer anesthetic episodes, and reduced hospital, and medical costs.[29] Recurrence at the site of a local tissue rearrangement does require reexcision, but typically a simple readvancement of the flap avoids design of a secondary reconstruction.

Immediate reconstruction should be approached with caution in some patients, however. We found patients with locally recurrent melanoma to have a significantly higher risk of having a positive margin after WLE. In other types of locally recurrent HN carcinoma, such as basal cell carcinoma, rates of inadequate excision are high and a cautious approach to immediate reconstruction has also been recommended.[13,30] Therefore, we suggest locally recurrent lesions be treated with the recommended wide excision margins and reconstruction should be delayed until pathology is reviewed and margins are clear of melanoma.

Patients with T4 tumors were associated with an increased risk for a positive margin after WLE when compared with Tis, T1, T2, and T3 tumors. Increasing tumor thickness and Clark's level of HN melanoma are known to be important prognostic factors in local recurrence and survival.[23,24,31–33] Additionally, ulceration is included as the second determinant for the T classification,[34] and has been found to predict node-positive disease and may represent more rapid progression due to increased angiogenesis.[35,36] We found ulceration to be significantly associated with a positive margin after WLE. Given this increased risk for positive margins after WLE, we feel reconstruction should be delayed in patients with T4 tumors and ulcerated tumors.

We acknowledge limitations in the technique of our study. Because the number of patients in our series with a positive margin after WLE was small, some patient and tumor characteristics associated with a positive margin may not have been found. Prospective trials are needed to establish a causal link between tumor characteristics and positive margin after WLE, comparing both immediate and delayed adjacent tissue transfer reconstruction, to best develop a reconstructive algorithm with criteria for reconstruction timing. A larger series with a higher positive margin incidence could help distinguish other variables known to be associated with recurrence, including tumor type and location, angiogenesis and vascular invasion, and microsatellitosis.[23,24,35,36]

CONCLUSION

In summary, we present a series of patients with HN melanoma who had immediate adjacent tissue transfer reconstruction after WLE. We show a low rate of positive margin after WLE, which supports the safety of immediate reconstruction with adjacent tissue transfer. We identified locally recurrent, ulcerated, and increasing tumor thickness to be associated with a positive margin after WLE of HN melanoma. This information will help guide the decision to perform immediate or delayed reconstruction after WLE of HN malignant melanoma.

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