Melanoma Extirpation with Immediate Reconstruction: The Oncologic Safety and Cost Savings of Single-Stage Treatment

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Background: The timing of reconstruction following melanoma extirpation remains controversial, with some advocating definitive reconstruction only when the results of permanent pathologic evaluation are available. The authors evaluated oncologic safety and cost benefit of single-stage neoplasm extirpation with immediate reconstruction.

Methods: The authors reviewed all patients treated with biopsy-proven melanoma followed by immediate reconstruction during a 3-year period (January of 2011 to December of 2013). Patient demographic data, preoperative biopsies, operative details, and postoperative pathology reports were evaluated. Cost analysis was performed using hospital charges for single-stage surgery versus theoretical two-stage surgery.

Results: During the study period, 534 consecutive patients were treated with wide excision and immediate reconstruction, including primary closure in 285 patients (55 percent), local tissue rearrangement in 155 patients (30 percent), and skin grafting in 78 patients (15 percent). The mean patient age was 67 years (range, 19 to 98 years), and the median follow-up time was 1.2 years. Shave biopsy was the most common diagnostic modality, resulting in tumor depth underestimation in 30 patients (6.0 percent). Nine patients (2.7 percent) had positive margins on permanent pathologic evaluation. The only variables associated with positive margins were desmoplastic melanoma ($p = 0.004$) and tumor location on the cheek ($p = 0.0001$). The mean hospital charge for immediate reconstruction was $22,528 compared with the theoretical mean charge of $35,641 for delayed reconstruction, leading to mean savings of 38.5 percent (SD, 7.9 percent).

Conclusion: This large series demonstrates that immediate reconstruction can be safely performed in melanoma patients with an acceptable rate of residual tumor requiring reoperation and significant health care cost savings. (*Plast. Reconstr. Surg.* 138: 256, 2016.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

Cutaneous melanoma is the fifth most common cancer in the United States, with the incidence rising steadily over the past four decades.[1] Although melanoma constitutes a small portion of all skin cancers, it is responsible for the majority of skin cancer–related mortalities, with an estimated 9710 deaths in 2014.[2] Wide local excision is considered the mainstay of treatment for cutaneous melanoma and is dictated by the tumor thickness.[3,4] Current National Comprehensive Cancer Network Clinical Practice Guidelines recommend wide local excision margins of 0.5 cm for in situ lesions, 1 cm for lesions less than or equal to1.0 mm thick, 1 to 2 cm for lesions 1.01 to 2.0 mm thick, and 2 cm for lesions greater than or equal to 2.0 mm thick.[5,6] These wide margins of excision often result in large defects not amenable to primary closure. Reconstruction following

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melanoma extirpation may require skin grafting or adjacent tissue transfer. This depends on the anatomical region involved, and functional and aesthetic considerations.[7–9]

The timing of reconstruction following melanoma extirpation remains controversial. Some centers advocate for definitive reconstruction only when the results of permanent pathologic evaluation are available and the negative margin status is confirmed,[10–12] whereas others argue that immediate reconstruction is oncologically safe.[13] Advantages of single-stage melanoma excision and reconstruction include avoidance of an open wound and a period of disfigurement, potential health care cost savings, and improved patient satisfaction by optimizing immediate aesthetic and functional results.[14] Previous studies have demonstrated that adjacent tissue transfer is a valuable reconstructive option that does not hinder monitoring for recurrence and may actually help prevent local recurrence by allowing larger and more oncologically safe margins to be taken.[15,16] In addition, Parrett et al. discuss potential health care cost savings.[13] However, to the authors' knowledge, no cost analysis has been performed previously evaluating immediate versus delayed reconstruction following melanoma extirpation. The objectives of this study were to (1) determine the incidence of positive margins and local recurrence after wide local excision of cutaneous malignant melanoma with immediate reconstruction, (2) identify patient and tumor characteristics associated with positive margins, and (3) define potential health care cost savings of single-stage versus two-stage melanoma extirpation and reconstruction.

PATIENTS AND METHODS

After receiving approval from the institutional review board, all patients with primary cutaneous melanoma who underwent wide local excision with immediate reconstruction were identified. The study period was 3 years (January of 2011 to December of 2013). All extirpations were performed by a single surgical oncologist (M.B). Patients with metastatic disease, incomplete medical records, or inadequate follow-up were excluded. Data collected from the medical records included patient demographics, melanoma type (i.e., in situ, superficial spreading melanoma, lentigo-maligna melanoma, nodular melanoma, desmoplastic melanoma, not otherwise specified), tumor location, Breslow thickness, mitotic rate, presence of satellitosis and ulceration, reconstruction type (i.e., primary closure, skin graft, or adjacent tissue transfer), cross-sectional area of tumor-related skin defects, sentinel lymph node status, and margin status following wide local excision.

Surgical margins of excision are based on the Breslow thickness and classified by tumor, node, metastasis stage as defined by the American Joint Committee on Cancer (i.e., Tis, in situ; T1, >1.0 mm; T2, 1.01 to 2.0 mm; T3, 2.1 to 4.0 mm; and T4, >4.0 mm).[17] At the time of melanoma extirpation, the specimen is sent for permanent pathologic evaluation. Frozen sections are avoided because of intrinsic technical limitations of the technique. This includes potential loss of critical sampling tissue at the time of sectioning, and lack of fine histologic details compared with the formalin-embedded specimen evaluation. As part of the staging process, lymphatic mapping of the regional lymph node basin is performed with sentinel lymph node biopsy for tumors greater than 1 mm in thickness. If the sentinel lymph node biopsy returns results positive for malignant cells, completion nodal lymphadenectomy is performed at the subsequent operation.[17]

All patients received multidisciplinary evaluation. The treatment plan was coordinated between the surgical oncologist and the plastic surgeon to ensure oncologically safe margins and to provide an appropriate reconstructive plan. Choice of reconstructive modality (i.e., primary closure, skin graft, or adjacent tissue transfer) was based on the location and size of the defect, and surrounding tissue laxity. Results of permanent sections of tumor margins were not available at the time of the immediate reconstruction.

Statistical analysis was performed with a series of univariate analyses using the Fisher's exact test for binary variables, Mann-Whitney *U* test for continuous variables, and logistic regression to identify factors associated with the presence of a positive margin after wide local excision. All calculated *p* values were two-tailed.

Cost analysis was generated by reviewing hospital charges for the single-stage melanoma extirpation and reconstruction and compared to the theoretical costs for two-stage reconstruction. More specifically, 16 patients were randomly selected from our immediate reconstruction cohort to provide a balanced representation of the four main reconstructive modalities: primary closure, split-thickness skin graft, full-thickness skin graft, and local tissue rearrangement. In addition, medical billing and coding experts generated a theoretical cost analysis for the delayed reconstruction group by reviewing hospital charges of

each of those patients as if the reconstruction was performed during a separate procedure. Percentage savings were calculated and averaged.

RESULTS

During the 3-year study period, 534 consecutive patients (280 men and 254 women) were treated with wide local excision of primary cutaneous malignant melanoma and immediate reconstruction. The mean age of the patient population was 67 years (range, 19 to 98 years) and the median follow-up time was 1.2 years. Shave biopsy was the most common diagnostic modality, resulting in tumor depth underestimation in 30 patients (6.0 percent). The majority of patients had invasive melanoma (62 percent), whereas the remaining had melanoma in situ. The most common tumor location was in the back (24 percent), followed by upper extremity and lower extremity (21 percent versus 20 percent, respectively).

In the invasive melanoma cohort (331 patients), median tumor thickness was 1.02 mm, with an average defect size of 25.8 cm^2 (SD, 21.8 cm^2) following tumor extirpation. Methods of skin defect reconstruction included primary closure in 285 patients (55 percent), local tissue rearrangement in 155 patients (30 percent), and skin grafting in 78 patients (15 percent). Table 1 summarizes the patient and tumor characteristics.

Histologically positive margins were found in nine patients (2.7 percent) based on the results of permanent pathologic evaluation. Predominant tumor location was on the cheek for six patients, followed by the scalp, ear, and back (one patient each). The only variables associated with positive margins were presence of desmoplastic melanoma ($p = 0.004$) and tumor location on the cheek ($p = 0.0001$). All patients with positive margins were offered reexcision, typically with 5-mm margins. Eight of the nine patients underwent successful reexcision, and subsequent negative margins were obtained. One patient declined further treatment.

In the positive margins cohort, two of the patients who underwent original reconstruction with full-thickness skin grafting were treated with local tissue rearrangement on reexcision of the positive margins. The tumor location was on the ear and cheek, respectively. In addition, in three of the patients with tumor location on the cheek, narrower margins than that dictated by tumor thickness were taken, secondary to the proximity to the critical anatomical structure such as oral commissure or lower eyelid. This intraoperative decision was made by the surgical oncologist to avoid potential functional deficits in the patients. All patients continued to have close follow-up without reported clinical evidence of recurrent invasive melanoma. Table 2 summarizes the characteristics of the patients with positive margins. Figures 1 and 2 illustrate a case example (patient 1 from Table 2).

Table 1. Patient and Tumor Characteristics

Characteristic	Value (%)
Age, yr	
Mean	67
Range	19–98
Sex	
Female	254 (48)
Male	280 (52)
Melanoma type	
MIS	194
Invasive	332
Breslow thickness (mm)	
Median	1.02
SD	0.46
AJCC tumor classification	
Tis	194 (37)
T1	209 (40)
T2	46 (9)
T3	38 (7)
T4	37 (7)
Mean excision margins, cm	
Tis	0.6
T1	1.0
T2	1.6
T3	1.8
T4	1.8
Mean area of defect, cm^2	25.8
Reconstruction type	
Primary closure	285 (55)
Adjacent tissue transfer	155 (30)
Full-thickness skin graft	61 (12)
Split-thickness skin graft	17 (3)
Median length of follow-up, yr	1.2

MIS, melanoma in situ; AJCC, American Joint Committee on Cancer; T, tumor.

The cost analysis demonstrated a theoretical cost savings for immediate reconstruction. The mean hospital charge for immediate reconstruction was $22,528 compared with the theoretical mean charge of $35,641 for delayed reconstruction, leading to mean savings of 38.5 percent (SD, 7.9 percent).

DISCUSSION

Cutaneous malignant melanoma constitutes less than 10 percent of all skin cancers but is responsible for the majority of skin cancer–related deaths.[10,11] Wide local excision remains the mainstay of treatment, and prompt early diagnosis and surgical intervention can be life saving to many patients. Surgical excision margins are dictated by tumor thickness, and often result in large or

Table 2. Positive Margins Cohort

Patient	Melanoma Type	Location	Tumor Thickness (mm)	Margins (cm)	Initial Reconstruction	Margins at Reoperation (cm)	Reconstruction at Reoperation
1	NOS	Scalp	0.3	1	Local flap	1	Local flap
2	NOS	Ear	0.8	1	FTSG	1	Local flap
3	NOS	Cheek	In situ	0.5	FTSG	0.5	FTSG
4	NOS	Cheek	In situ	0.5	Local flap	0.5	Local flap
5	NOS	Back	In situ	0.5	Primary closure	0.5	Primary closure
6	NOS	Cheek	1.2	1	FTSG	1	Local flap
7	NOS	Cheek	0.5	0.7	Local flap	0.5	Local flap
8	Desmoplastic	Cheek	8.5	1	FTSG	None	None
9	Desmoplastic	Cheek	0.5	1	Local flap	1	Local flap

NOS, not otherwise specified; FTSG, full-thickness skin graft.

Fig. 1. The lesion (from patient 1 in Table 2) has 1-cm margins drawn on all sides of the grossly visible neoplasm.

Fig. 2. Final pathologic evaluation (from patient 1 in Table 2) demonstrated that there was in situ melanoma at the 9-o'clock position of the surgical specimen, which corresponded to the area toward the left ear. A residual local flap with modifications were used to reconstruct the defect.

complex defects requiring reconstructive intervention. Currently, controversy exists over the use of frozen section at the time of primary melanoma excision because of the high rate of false-negative margins. Reported limitations of intraoperative frozen sectioning include lack of fine histologic details, and the risk of missing micrometastatic disease or a small cluster of isolated melanoma cells because of frozen section sampling errors. Therefore, at our institution, we routinely send a formalin-embedded specimen for permanent pathologic evaluation at the time of melanoma extirpation.[18]

Plastic surgeons involved in reconstruction following cutaneous melanoma extirpation frequently deal with a dilemma of when to reconstruct the surgical defects.[19] Some advocate delaying reconstruction until the histologic results of permanent pathologic evaluation become available, whereas others support immediate reconstruction, thus obviating the need for a second operation and a period of disfigurement. According to Sullivan et al., immediate reconstruction can be performed safely with an acceptable low rate of positive margins (6 percent) and local recurrence, with the greatest risk being in locally recurrent, ulcerated, or T4 tumors.[20] Similar results were found in two other recent studies, further supporting the oncologic safety of immediate reconstruction following melanoma extirpation.[13,21]

This study confirms that immediate reconstruction can be safely performed after melanoma extirpation. There is a low rate of positive margins (2.7 percent). Even in those with positive margins, reresection of persistent tumor and reconstruction can be accomplished. Based on the findings presented in this article, the only variables associated with positive margins were desmoplastic melanoma ($p = 0.004$) and tumor location on the cheek ($p = 0.0001$).

Desmoplastic melanoma is a rare, deeply infiltrating subtype of cutaneous melanoma,

characterized by an abundance of fibrous matrix. Diagnosis of desmoplastic melanoma can be challenging from both clinical and histopathologic perspectives, because most cases are amelanotic and may appear similar to other spindle cell lesions of the skin such as dermatofibroma, neurofibroma, and even scar. Desmoplastic melanoma most commonly occurs in the head and neck region.[22–24]

In this study, despite a median thickness of 1.02 mm, the median excision margin was 1.6 cm, which is less than the recommended 2-cm margins. This is most likely attributable to the narrower melanoma excision margins in the cosmetically and functionally sensitive head and neck region. The authors thereby acknowledge that in this specific subset of patients, desmoplastic or cheek melanoma, delayed reconstruction can be considered or the patient counseled preoperatively that a higher likelihood of reoperation exists.

Performing immediate reconstruction in the setting of melanoma extirpation is controversial when considering the use of local flaps. Using primary closure or skin grafts does not pose as much concern. In the case of positive margins with primary closure, very little is altered. The orientation of the tumor can still be discerned and the reexcision performed successfully. Much is the same for skin graft reconstruction, except for the loss of donor-site tissue.

For those patients with local flap reconstruction and positive margins, the surgical oncologist and plastic surgeon worked collaboratively to determine the original tumor location. This was aided by knowledge of the original flap design and use of preoperative photographs. The latter is an important prerequisite when using local flaps in immediate reconstruction of melanoma defects. Flaps were returned to their original location and reoperative margins were drawn at the proposed original site of tumor by the surgical oncologist. In some instances, this does preclude reuse of the flap. Given the low rate of positivity, the authors do not believe that this uncommon scenario should deter the use of local flaps in immediate reconstruction. Instead, in high-risk situations, such as histologically high-risk melanomas or in sensitive tumor locations whereby adequate margins may not be possible, delayed reconstruction, skin grafts, or primary closure may be preferred.

The authors acknowledge certain limitations to this study. Because the number of patients in our series with a positive margin after wide local excision was small, some patient and tumor characteristics associated with a positive margin may not have been found. Prospective trials should be undertaken to identify additional risk factors between tumor characteristics and positive margin after melanoma extirpation.

In addition, our follow-up is shorter than in other similar studies. With longer follow-up, it is possible for the local recurrence rate to increase, but it is encouragingly low at 1.2 years' follow-up. The patients in this study are followed up regularly at the melanoma center, and a future article with 5-year follow-up will be useful to determine long-term recurrence rates. Finally, another limitation of the study design is the absence of the delayed reconstruction group because all of the patients in our patient cohort have undergone immediate reconstruction following melanoma extirpation.

CONCLUSION

To the authors' knowledge, this is the largest series to date demonstrating that immediate reconstruction can be safely performed in melanoma patients, with an acceptable rate of residual tumor requiring reoperation and significant health care cost savings.

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