

Staged Excision for Lentigo Maligna and Lentigo Maligna Melanoma

Analysis of Surgical Margins and Long-term Recurrence in 68 Cases from a Single Practice

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ABSTRACT

Introduction: Lentigo maligna is a form of *in situ* melanoma that occurs commonly on sun-exposed skin of middle-aged to elderly adults. Margin-control surgery offers the highest cure rate for lentigo maligna/lentigo maligna melanoma. **Materials and methods:** Charts from the authors' private office from the 20-year period from January 1986 to December 2005 were reviewed to identify patients with histologically confirmed lentigo maligna or lentigo maligna melanoma treated by staged excision. **Results:** Sixty-eight patients (39 men, 29 women; mean age at diagnosis 67.4±10.2 years, range 48–87 years) with 68 tumors were treated in the authors' office for lentigo maligna (58) or lentigo maligna melanoma (10) between January 1986 and December 2005. After excision, patients were followed clinically for a minimum of three years. The mean follow-up duration was 138 months (median 139 months; range 37–330 months). The overall margin for tumor clearance was 7.0±0.55mm with a recurrence rate of 5.9 percent. **Limitations:** The limitations of this study include the retrospective nature of the authors' review, and data collected from a single, private practice setting. **Conclusion:** The authors' findings support staged excision as an effective method of treating lentigo maligna and lentigo maligna melanoma, offering a high cure rate while maximally preserving normal tissue. (*J Clin Aesthet Dermatol.* 2016;9(6):25–30.)

Lentigo maligna (LM) is a form of *in situ* melanoma that occurs commonly on sun-exposed skin of middle-aged to elderly adults.¹ Detection and treatment of this disorder is of paramount importance due to significant risk of progression to lentigo maligna melanoma (LMM).² Margin control surgery offers the highest cure rate for LM/LMM. Reported recurrence rates using standard 5mm margins for LM vary from 8 to 20 percent.³ Limited data are available regarding long-term recurrence after staged excision (SE) of LM/LMM, and to the authors' knowledge this is the largest study to date (n=68) with at least five-year follow-up period. The authors' goal is to add to the body of literature regarding long-term outcomes of staged procedures in the treatment of LM/LMM.

OBJECTIVE

To assess the surgical margins necessary for clearance of

LM/LMM and the long-term recurrence rate of LM/LMM treated by SE with rush permanent sections.

MATERIALS/METHODS

Study design. Charts from the authors' private office from the 20-year period from January 1986 to December 2005 were reviewed to identify patients with histologically confirmed LM or LMM treated by SE. Data recorded included age at diagnosis, gender, site of tumor, histologic subtype of tumor and depth of invasion for LMM, history of previous treatment, clinical tumor dimensions, postoperative defect dimensions, number of stages required to achieve histologically clear margins, and follow-up duration (minimum of 36 months for inclusion). Follow-up was obtained by direct examination by one of the authors. A biopsy was performed if recurrence was suspected clinically.

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TABLE 1. Patient and tumor characteristics of the study population

Number of patients	71
Average age (yrs)	68.3±10.1
Male (%) Female (%)	41 (58) 30 (42)
Tumor type (% of total) LM LMM	71 61 (86) 10 (14)
Primary (%) Recurrent (%)	67 (94) 4 (6)
Sites (% of total) Cheek Arm Nose Forehead/temple Trunk Chin/mandible Neck Ear Scalp Leg Total Head/neck tumors	23 (32) 12 (17) 7 (10) 6 (8) 6 (8) 5 (7) 5 (7) 3 (4) 2 (3) 2 (3) 70 (100) 51 (72)
Left-sided (%) Right-sided (%) Midline (%)	39 (55) 22 (31) 10 (14)
Recurrence (%)	4/71 (5.6)
Follow-up duration (months)	133.2 ± 63.0 (range 12-330)

Patient age and follow-up duration shown as mean values ± standard deviation

Histopathologic definitions. LM was defined as melanoma *in situ* arising in actinically damaged skin, with continuous proliferation of atypical melanocytes, as single confluent cells or in nests, along the basal layer of the epidermis and adnexa, with minimal pagetoid spread. Epidermal atrophy and rete ridge effacement were often present, but were not required for diagnosis. The finding of single scattered atypical melanocytes was not considered sufficient for diagnosis of LM. LMM was defined as LM with the presence of dermal invasion.

SE was performed based on tumor type as we have previously described.¹ Tissue was excised perpendicularly (i.e., at a 90-degree angle), then mapped, dyed, placed in formalin, and sent to the pathology laboratory for rush permanent paraffin-embedded sections. One of the following two procedures was used to prepare the specimens for histologic evaluation. If the specimen was greater than 3 to 4mm wide, the margin was inked by

quadrant with four different colors, sectioned vertically (“breadloafed”) at 3mm intervals and entirely submitted for processing. Each block was step sectioned to ensure thorough sampling. If the specimen was less than 3mm wide, orienting ink was applied and the specimen was submitted en face with the new surgical margin embedded upward. The patient returned the next day for further excision or repair as indicated. When tumor excision was incomplete (defined as nested or confluent single melanocytes with cytologic atypia at or within 2mm of the surgical margin), an additional 2 to 3mm of tissue from the involved margin was excised and processed as described above. SE was continued until clear margins were obtained, at which time the final defect was repaired. Patients returned for routine follow-up at standard clinical intervals (every 3 months for the first year after diagnosis of LM and every 6 months thereafter, and every 3 months after diagnosis of LMM).

Statistical analysis. Continuous variables were analyzed by student’s *t*-test and comparative variables were analyzed with the chi-square test. A *p* value <0.05 was considered statistically significant. Lesion and surgical defect sizes were calculated by averaging the measured length and width and then approximating the area by calculating the area of a circle (πr^2) with diameter equal to this average. To calculate the margin required for tumor clearance, spatially accurate diagrams of the preoperative clinical lesion and the final surgical defect were superimposed. For tumors cleared in one stage, the minimal distance between the clinical lesion and the surgical margin was recorded. For tumors requiring two or more stages for clearance, the minimal distance between the clinical lesion and the defect from the final stage of surgery was recorded. Statistical analysis was performed with SAS software for Windows.

RESULTS

Patient characteristics (Table 1). Sixty-eight patients (39 men, 21 women; mean age at diagnosis 67.4±10.2 years, range 48–87 years) with 68 tumors were treated in the authors’ office for LM (58) or LMM (10) between January 1986 and December 2005. Sixty-four of 68 tumors (94.1%) were primary and 4/68 (5.9%) were recurrent at the time of treatment. Three of the 61 lesions (5%) interpreted as LM on initial biopsy were found to be invasive LMM at the time of SE. Forty-eight tumors (71%) were located on the head and neck. The cheek was the most common tumor site (N=22; 32%), followed by the upper extremity (N=12; 17%). Over half of tumors (N=38; 55%) were left-sided. The mean follow-up duration was 138 months or 11.5 years (median 138 months; range 37–330 months). Throughout follow-up, 14 of 68 patients (20.6%) died, all from unrelated causes. Breslow depth of LMM ranged from 0.26 to 0.65mm for nine cases and was 1.5mm for the tenth.

Surgical features of tumors without recurrence (Table 2). The mean pre-operative lesion size ($1.5\pm 0.2\text{cm}^2$) did not vary by site or tumor type (LM vs.

LMM, primary vs. recurrent). Among the 65 tumors that did not recur, the number of stages required for clear margins (1.8 ± 0.2) did not vary by type of tumor. Clear margins were obtained in one stage in 34 cases (50%), in two stages in 18 cases (26%), in three stages in seven cases (10%), and in four or more stages in five cases (7%). Not surprisingly, the margin required for tumor clearance increased significantly with the stage number. The overall margin for tumor clearance was 7.0 ± 0.5 mm. LM of the cheek required a significantly higher number of stages (2.5 ± 0.4) and a wider margin for clearance (8.7 ± 1.6 mm) than LM at other sites ($p < 0.04$). Comparisons between other sites were not statistically significant.

Recurrence (Table 3). The overall recurrence rate was 4/68 (5.9%). The three recurrences, all local recurrence of LM, were diagnosed at a mean interval of 29 months, including eight months (at the left preauricular cheek), 25 months (at the left lobule), 35 months (at the chin), and 48 months (at the left ala). Each of these three tumors was subsequently treated by SE, with no sign of further recurrence at 18, 4, 15, and 6 months, respectively (data not included). There were no significant differences among these four tumors with regard to preoperative lesion size, surgical defect, or number of stages compared with the 65 tumors that did not recur during the study period.

Adequacy of recommended surgical margins (Table 4). The minimal surgical margin for tumor clearance was measured and compared to the standard recommended clinical margin (5 mm for LM, 10 mm for LMM of Breslow depth < 1 mm). Tumors that recurred were considered to have an inadequate margin. Tumors that were excised in a single stage with initial margins exceeding the recommended margin were not included in this analysis. For LM, 28 of 51 (54%) tumors were cleared with a 5 mm clinical margin, including 18/37 (46%) of LM located on the head and neck. Of LM not cleared with a 5 mm clinical margin (N=23), the average margin for clearance was 10.4 ± 1.0 mm (median 9 mm, range 6–27 mm), requiring an average of 2.9 ± 0.3 stages (range 2–7). For LMM of Breslow depth < 1 mm, 7 of 8 (88%) were cleared with a 10 mm clinical margin

CONCLUSION

In this study, SE of LM/LMM with histologic evaluation of margins on paraffin sections was associated with a recurrence rate of 5.9 percent over a mean follow-up time

exceeding five years. No additional recurrence was seen among the previously reported patients treated by SE during the subsequent follow-up period; one recurrence among 30 new patients was observed. Excision with standard margins (5 mm for LM, 1 cm for LMM with Breslow depth < 1 mm margins) frequently leaves tumor at the surgical margin and may be associated with a recurrence rate of up to 20 percent.³⁻⁶ Thus, various margin control techniques have been advocated including Mohs micrographic surgery (MMS) and SE. Comparative data regarding margin control procedures for treatment of LM/LMM are summarized in Table 5.

MMS is advocated by some surgeons for treatment of LM and LMM.⁷⁻¹³ In the authors' previous report comparing SE with MMS, they found SE to have a significantly lower recurrence rate while being equally tissue-sparing.¹⁴ Of 41 tumors treated with SE in that study, three recurrences (7%) were seen over an average follow-up period of nearly eight years, while 6/18 tumors (33%) treated by MMS recurred over an average follow-up period of nearly 10 years. A recent study by Bricca et al¹⁵ described a low (0.5%) recurrence rate with Mohs excision (MMS) in the

TABLE 2. Surgical features of LM/LMM without recurrence

	PRE-OP LESION AREA (cm ²)	NUMBER OF STAGES	MARGIN FOR TUMOR CLEARANCE (mm)
By tumor type			
LM (N=55)	1.3 ± 0.2	1.8 ± 0.2	6.6 ± 0.6
LMM (N=10)	2.0 ± 0.7	1.7 ± 0.5	9.0 ± 1.5
LM/LMM by stage			
Stage 1 (N=34)	1.5 ± 0.3	1	4.2 ± 0.3
Stage 2 (N=18)	1.3 ± 0.2	2	6.1 ± 0.7*
Stage 3 (N=7)	1.8 ± 0.6	3	6.8 ± 0.8**
Stage 4+ (N=5)	2.2 ± 0.7	5.4 ± 0.5	15.7 ± 2.5***
LM by site			
Cheek (N=17)	1.6 ± 0.3	2.5 ± 0.4 ^y	8.7 ± 1.7 ^y
Scalp/forehead/temple (N=7)	1.9 ± 0.9	1.6 ± 0.2	6.2 ± 1.3
Nose (N=5)	1.1 ± 0.5	2.2 ± 0.7	4.9 ± 1.7
Chin/mandible (N=4)	1.3 ± 0.6	1.5 ± 0.3	7.5 ± 1.3
Neck (N=2)	0.5 ± 0.1	1	2.8 ± 0.2
Ear (N=3)	0.5 ± 0.1	1.3 ± 0.3	7.5 ± 0.5
Extremity (N=11)	1.7 ± 0.6	1.6 ± 0.2	5.5 ± 0.6
Trunk (N=6)	0.9 ± 0.2	1.2 ± 0.2	4.5 ± 0.7
Subtotal, head/neck (N=41)	1.4 ± 0.2	2 ± 0.2	7.1 ± 0.8
Subtotal, trunk/extremity (N=17)	1.4 ± 0.3	1.5 ± 0.2	5.1 ± 0.4
Total (N=55)	1.5 ± 0.2	1.8 ± 0.2	6.6 ± 0.6

Pre-operative lesion area and margin for tumor clearance measured as described in Methods. Results are shown as mean value ± standard error.

* Stage 2 margins significantly greater than stage 1 margin ($p < 0.01$).

** Stage 3 margins significantly greater than stage 1 margin ($p < 0.005$).

*** Stage 4+ margins significantly greater than stage 1 ($p < 0.0001$), stage 2 ($p < 0.001$), and stage 3 ($p < 0.005$).

^yCheek number of stages and margin significantly greater than LM at noncheek sites ($p < 0.04$)

TABLE 3. Recurrences

PATIENT (SEX)	SITE	STAGES	MARGIN (mm)	TIME TO RECURRENCE (MONTHS)
71 (F)	Chin	2	9	35
68 (F)	Left ala (recurrent)	2	4	48
74 (M)	Left preauricular cheek	1	5	8
73 (M)	Left lobe	1	2.5	25

TABLE 4. Adequacy of recommended margins by site

LM	5mm MARGIN ADEQUATE (%)
Cheek	7/17 (41)
Scalp/forehead/temple	4/6 (67)
Nose	4/6 (67)
Chin/mandible	1/4 (25)
Neck	2/2 (100)
Ear	0/2 (0)
Subtotal, head/neck	18/37 (46)
Extremity	5/8 (63)
Trunk	5/6 (83)
Subtotal, trunk/ extremity	10/14 (71)
Total	28/51 (54)
LMM (<1 MM)	10 MM MARGIN ADEQUATE (%)
Head/neck	5/6 (83)
Trunk/extremity	2/2 (100)
Total	7/8 (88)

treatment of melanoma and melanoma *in situ* lesions with a five-year follow up, but did not evaluate LM or LMM lesions specifically.¹⁵ Bene et al¹⁰ reported a three-percent recurrence rate with MMS over a 63-month follow-up period for LM. Hou et al¹⁶ had a 1.9-percent recurrence rate with MMS with a mean follow-up time of 7.9 years. A study in 2006 by the University of Minnesota evaluating MMS with Mel-5 stained sections reported a 0.5-percent recurrence rate with a mean follow-up duration of 38.4 months.⁷ The updated study published in 2013 followed an additional 174 patients at a mean of 34 months. Of those 174 patients, there were five recurrences in four patients.¹⁷

Although MMS is an effective surgical option for treatment of LM, efficacy of this procedure is largely dependent on the quality of frozen sections, the ability of the lab to use immunostains and the experience of the dermatologic surgeon in interpreting melanocytic lesions on frozen sections. This is evident in the wide range of sensitivity and specificity reported of MMS in the literature

(59–100% and 81–90% for sensitivity and specificity, respectively).^{9,18} The use of immunostains may help to increase concordance rates between frozen and permanent sections and has led to more consistent MMS outcomes.^{7,15,19}

To the authors' knowledge, there are no other studies evaluating SE reported in the literature with greater than 10 years of follow-up data. There are only two other studies evaluating SE reported in the literature with at least five years of follow-up data,^{14,20} with the authors' current study containing the largest number of patients (n= 68). A recent study by Abdelmalek et al²¹ reviewing geometric staged excision for LM and LMM of 293 patients reported a recurrence rate of 1.7 percent; however, the mean follow-up time was only 32.3 months. As most recurrences of LM and LMM occur at 3 to 5 years after excision,^{14,20} at least five years of follow-up is needed to reflect true outcome data. While the authors' study has 11.5 years of follow-up data, our percent deceased throughout follow-up was 20.6 percent; however, all deaths were from unrelated causes.

The finding that nearly half of tumors were not cleared with the recommended 5mm surgical margin underscores the importance of margin-control surgery, and is well-supported by other studies in the recent dermatologic literature.^{3,14,20–33} The authors' recurrence rate of 5.9 percent is similar to the previous study by Bub et al²⁰ evaluating staged excision with at least five-year follow-up. The mean time to recurrence for the four recurrent tumors in our study was 24.3 months and underscores the necessity for frequent follow-up visits for these patients.

The authors' findings support SE as an effective method of treating LM and LMM, offering a high cure rate while maximally preserving normal tissue. Their findings show that a standard 5mm clinical margin for LM is often inadequate for tumor resection and thus highlight the advantage of margin-control surgery. The limitations of the authors' study include that their results are from a single institution and may reflect biases inherent in their patient population and the retrospective nature of their study design.

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TABLE 5. Recurrence rates and follow up for SE

REFERENCE	F/U DURATION	RECURRENCE RATE	PATIENT NUMBER	PROGRESSION TO LMM	PRE-OP	POST-OP
Bub et al ¹⁹	57 months	5%	62	5%	2.1 x 1.5	3.3 x 2.5
Walling ¹⁴	95 months	7.3%	41	Not reported	1.5 x 0.2	7.1 x 1.0
Bosbous ²⁴	2.25 years	1.7%	59	10%	1.5 x 1.4	3.4 x 3.1
Current study	138 months	5.9%	68	Not reported	1.5 ± 0.2cm ²	8.1cm ²
Johnson ²⁵	Not reported	0%	35	Not reported	Not reported	Not reported
Hill and Gramp ³¹	25 months	1/66	66	32%	23mm	34mm
Zitelli ⁸	5 years	0.5% (LM data not addressed)	553	Not reported	Not reported*	Not reported*
Bhardwaj ⁷	38.4 months	0%	200	Not reported	6.4cm ²	16.4cm ²
Bene ¹⁰	50 months	1%	116	Not reported	Not reported	Not reported
Temple ²⁹	29.8 months	0	153	Not reported	Not reported	11.8cm ²
Bricca ¹⁵	58 months	0.3% (LM data not addressed)	625	Not reported	N/A*+	N/A*+
Cohen ¹³	58 months	3%	45	none	1.7 x 1.7	4.2 x 4.5
Malhotra ³⁰	32 months	3%	141	None	None	None
Robinson ²⁸	8 years	6%	16	N/A	N/A	N/A
Abdelmalek et al ²⁰	32 months	1.7%	293	Not reported	Not reported	Not reported
Huilgol et al ²⁶	38 months	2%	161	Not reported	Not reported	Not reported
Möller et al ²³	14 months	0%	61		7.2cm ²	
Gaudy-Marquest et al ³²	25.4 months	4.76%	21			27.5cm ²
Hazan et al ²²	Not reported	Not reported	117	Not reported	LM: 11.3mm Lmm: 14.6mm	Not reported
Zalla et al ²⁷	16 months	0%	68	Not reported	Not reported	Not reported

27 included invasive melanoma
 *9mm margin cleared 95% of melanomas
 +did not specifically evaluate LM/LMM

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