Lentigo Maligna of the head and neck: A retrospective study assessing surgical excision margins in a South African population

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Background: Lentigo maligna (LM) is a subtype of melanoma in situ that occurs on sun-damaged skin and is associated with significant subclinical extension beyond the clinical margins of the lesion.

Objectives: This study aimed to determine if the standard recommended tumor excision margins for LM are adequate to achieve a 97% clearance rate and if any patient or tumor characteristics warranted wider margins.

Methods: This study is a retrospective chart review of all patients who were diagnosed with LM of the head and neck and treated with staged excision.

Results: The study included 64 patients. With a 6 mm surgical excision margin, only 60.9% of LM were completely excised. A 9 mm margin resulted in complete clearance of 71.9% of LM cases, and a 12 mm margin resulted in complete clearance in 90.6%. A surgical excision margin of 18 mm would have been required to excise 96.7% of tumors completely. Recurrent tumors (P = .01) and tumor size larger than 20 mm were associated with wider surgical excision margins (P = .154).

Conclusion: This study of LM in a South African population corroborates that the standard surgical excision margins recommended by international melanoma guidelines for LM are inadequate to achieve a 97% clearance rate. (JAAD Int 2022;7:169-76.)

Key words: Lentigo maligna; melanoma in situ; staged excision.

BACKGROUND

Lentigo maligna (LM) is a specific subtype of melanoma in situ with a lentiginous growth pattern associated with chronic solar UV exposure.[1,2] LM may progress into invasive LM melanoma, with some studies reporting up to 22% of excised LM cases showing invasive disease.[3,4]

Surgical excision remains the first-line therapy for LM. Surgical options include the traditional wide local excision (WLE) and more advanced techniques

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that offer complete peripheral margin control, such as staged excision (SE) and Mohs Micrographic Surgery (MMS). With WLE, international guidelines recommend excision margins of 5-10 mm. Still, due to the reconstruction challenges of closing a large defect on the head and neck, an excision margin closer to 5 mm is often chosen.[5-7] Multiple studies have shown LM of the head and neck to be associated with significant subclinical extension, often beyond 10 mm of the clinically defined tumor margin.[8] Histological analysis of the peripheral margin of the excised tissue block produced by WLE of the LM comprises random vertical sampling. This technique evaluates less than 1% of the peripheral margin and carries a high risk for missing positive margins.[9,10] Several reports observed 9% to 20% recurrence rates after WLE for LM of the head and neck.[3,8]

CAPSULE SUMMARY

1. The standard recommended surgical excision margins for the treatment of lentigo maligna may not achieve a 97% clearance rate.
2. Surgical excision margins wider than 1-cm should be considered when using standard wide local excision for recurrent neck/head LM or for tumors larger than 20 mm.

Previous studies confirmed that SE with rushed permanent sections is superior in obtaining clearance and reduced recurrence rates when compared to conventional WLE since it allows for complete control of the peripheral excision margins.[3,11-14] Recurrence rates for LM after SE have been reported as 1.8% to 4%.[11,12]

MMS with frozen sections and immunohistochemistry staining has proven to be an effective treatment for melanoma in situ (including LM) as well as early invasive melanoma.[15-19] Recently published work showed MMS for early invasive melanoma to offer moderately improved overall survival compared to WLE.[15] Recurrence rates as low as 0% to 2% have been reported for LM treated with MMS using immunostaining.[15,20]

The American Academy of Dermatology recommends that SE and MMS be considered for LM on the head and neck. These techniques provide complete peripheral histological margin assessment and tissue sparing in cosmetically and functionally sensitive areas.[5]

OBJECTIVES

This study aimed to describe the patient demographics, clinical features, tumor characteristics, and histological findings of LM cases on the head and neck treated with SE. Secondary objectives included: (1) to compare our findings of the required surgical excision margin to clear LM cases to international guidelines on surgical excision margins for LM and (2) to determine if any patient or tumor characteristics predicted the need for wider surgical excision margins.

METHODS

This study included all patients with histologically confirmed LM of the head and neck that were treated with SE at the Skinmatters Mohs Micrographic Surgery and Reconstructive Unit (Pretoria, South Africa) between October 2014 and September 2020.

Case identification was achieved by mining the existing clinical files at Skinmatters Mohs Micrographic Surgery and Reconstructive Unit. Epidemiological, clinical, and histological data were collected, recorded, and analyzed.

A biostatistician assisted with the data analysis using Stata version 14. This study was performed in accordance with ethical principles in the Declaration of Helsinki and Good Clinical Practice. It was approved by the Health Research Ethics Committee of the Faculty of Medicine and Health Sciences, University of Stellenbosch (S20/05/125). All data collected were held under the provisions of the 2013 Protection of Personal Information Act and stored in secure manual and electronic files.

Staged excision technique

Various techniques for SE with rushed frozen sections have been described. At the Skinmatters Mohs Micrographic Surgery and Reconstructive Unit, a variation of the "spaghetti" technique is used (Fig 1).[21-23] This technique evaluates the complete peripheral margin around the LM, but the central block is assessed by vertical sectioning for microstaging. This approach differs from complete circumferential deep and peripheral margin assessment and MMS in that it does not assess the complete deep margin.

In all patients, the diagnosis of LM is confirmed before surgery with a biopsy for histological assessment by a pathologist. After visually delineating the clinical margin of the LM, an inner surgical margin of 3 mm is measured and drawn around the lesion with a surgical marker. An outer surgical margin is then measured and marked 6 mm away from the clinical margin of the tumor and 3 mm away from the inner surgical margin. This approach allows a thin strip of tissue, 3 mm wide, to be excised (the so-called

Abbreviations used:

LM: lentigo maligna
MMS: Mohs Micrographic Surgery
SE: staged excision
WLE: wide local excision

spaghetti) with a total initial margin of 6 mm around the visible tumor. The excised rim of tissue is then divided into anatomically identified segments and the outer margins marked with ink for orientation purposes (Fig 1).

A pathologist evaluates longitudinal haematoxylin and eosin and immunohistochemical stained sections from each segment of the specimen. The presence of a positive margin on any of the inked sections will result in a further excision with a 3 mm margin (if the tumor is on a cosmetic sensitive area of the face such as the nose, eyelids, or ears), or a 5 mm margin (if the tumor is on the cheek, chin, temple, scalp, neck, or forehead) from that specific segment. Margins are determined using a tape measure. Assessment of the wider margin follows the same protocol as used for the first specimen. This procedure is repeated until every segment is confirmed tumor-free using the same process.

At the initial excision, the central block (visible bulk tumor) is excised down into the fat (if possible, to the superficial fascia). The defect is sutured temporarily without undermining the peripheral tissue and is marked with silk sutures for orientation. The central block is submitted for formalin-fixed paraffin-embedded vertical sections and routine microstaging of the LM. Final reconstruction is undertaken after confirmation that all the peripheral margins are tumor-free and following microstaging of the LM in the central block.

RESULTS

A total of 64 patients met the inclusion criteria for this study. Table I summarizes the patient demographics and tumor characteristics. The mean age was 67.71 years (SD, 12.93), and most patients were men (64.06%). Shave biopsy was the preferred method for confirming the initial diagnosis (42.2%). The majority of tumors occurred on the cheeks (34.4%), followed by the nose (25%) and ears (14.1%). The median tumor size was 25 mm (IQR, 38). In 39.06% of cases, patients needed more than 1 stage to achieve complete surgical excision of the tumor.

Complete excision of LM was obtained with 6 mm surgical excision margins in 60.9% of the patients, with 9 mm margins in 71.9% of the patients, and 12 mm margins in 90.6% of the patients. A surgical excision margin of 18 mm resulted in complete excision of 96.7% of tumors, and a margin of 21 mm achieved complete tumor excision in 100% of patients. Of the 19 tumors in the study that needed more than 10 mm surgical margins to clear, 89.5% were larger than 20 mm in size ($P = .154$). Previously treated recurring tumors required a mean surgical excision margin of 14.6 mm, and 80% of these tumors required a surgical excision margin wider than 10 mm to achieve tumor clearance ($P = .01$).

Twenty-five LM cases (39.1%) occurred on cosmetic and functionally important areas such as the eyelids, nose, and ears. Within this subgroup, 13 (52%) needed more than 1 excision stage, with an average surgical excision margin of 8.7 mm for complete clearance. A surgical excision margin of 15 mm was required to completely excise 96% of LM in this subgroup. For LM cases occurring on other areas of the head and neck, the average surgical excision margin for complete clearance was 8.1 mm (Table II).

Microstaging of the central block showed invasive melanoma in 6.78% of cases, with a mean Breslow thickness of 0.24 mm (SD, 0.17 mm). Flap procedures were the preferred method for reconstruction. No recurrences occurred to date, with a mean follow-up time of 23.5 months.

DISCUSSION

Complete surgical excision of LM is considered curative, with current international melanoma guidelines recommending surgical excision margins between 5 and 10 mm.[5-7] Of note is that the South African Melanoma Guidelines of 2004 recommend a surgical excision margin of 5 mm for melanoma in situ.[24] The subclinical extension of LM of the head and neck is well known, and multiple studies have shown an extension beyond 10 mm of the clinical tumor-free margin.[8] Incomplete excision may result in recurrences and invasive melanoma that can ultimately be fatal. SE offers a superior alternative to conventional WLE with complete peripheral margin evaluation resulting in lower recurrence rates.[3,11-14]

The current study is the first study to our knowledge that evaluates SE as the preferred treatment of head and neck LM in South Africa. The results strongly suggest that the existing guidelines for conventional WLE of LM on the head and neck do not recommend a wide enough surgical margin to achieve a 97% clearance rate.

The patient demographics and tumor location in our study were in keeping with published reports showing LM to be more common in men and associated with individuals between 60 and 80 years of age. The cheek area was the most common site for

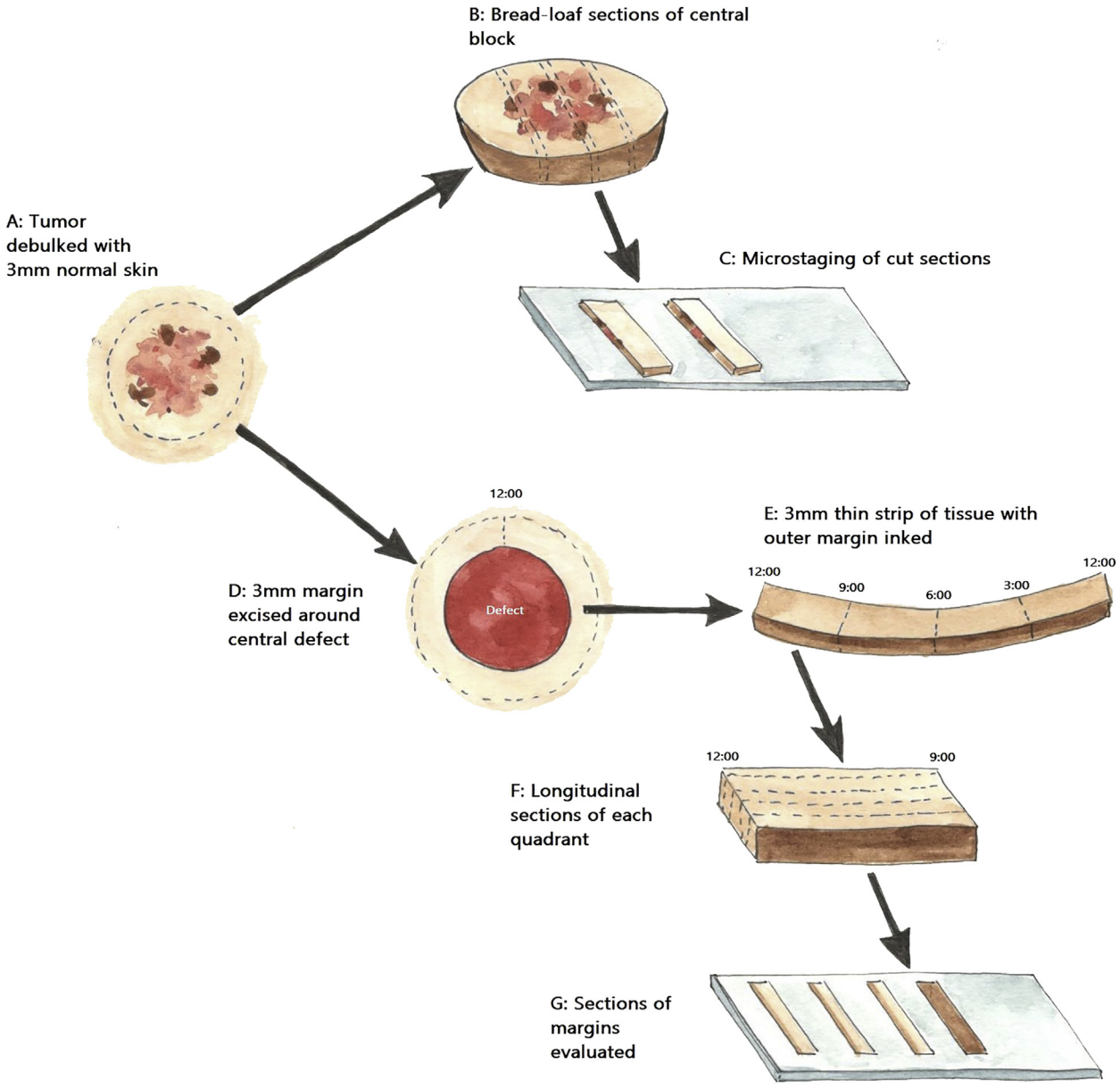

Fig 1. A, A 3 mm inner surgical margin is measured around the visible tumor to identify the central block. **B** and **C**, The central block is sent for permanent vertical (bread-loaf) sectioning and microstaging. **D,** An outer surgical margin measured 3 mm from the central defect is identified. **E**, A 3 mm strip of tissue is excised and divided into segments and marked with ink. **F** and **G**, These sections are submitted for routine processing, paraffin-embedding, and sections and histological assessment. Sections are cut longitudinally and evaluated with the aid of immunohistochemistry by a pathologist. Art: Sarah Boulton.

LM.[3,25] Various studies reported a mean age of 66 years, correlating with the mean age of 67.7 years in this study. However, the current study identified that 31% of patients were younger than 60 years of age.[3,8] A population-based study in the United States showed that the incidence of LM among patients between 45 and 64 years has increased by 52% between 1990 and 2000, therefore supporting other studies suggesting an increase in the incidence of LM in younger age groups.[1,2,26]

Surgical excision margins of 6 mm obtained complete tumor excision in 60.9% of the cases with only 1 surgical stage needed. A recent study by Kunishige et al[8] reported complete tumor excision using 6 mm margins in 79% of 1362 LM cases of the head and neck.[8] This difference between our findings and

Table I. Descriptive statistics

Variable	Frequency	Percentage	Variable	Frequency	Percentage
Gender (n = 64)			Tumor excision stages (n = 64)		
Female	23	35.9	1	39	60.9
Male	41	64.1	2	17	26.6
Age (n = 64)			3	5	7.8
<40	1	1.6	4	2	3.1
40-60	19	29.7	5	1	1.6
61-80	34	53.1	Needed more than 1 stage (n = 64)		
>80	10	15.6	No	39	60.9
			Yes	25	39.1
Type of biopsy (n = 64)			Total margin needed for complete excision in mm (n = 64)		
Punch	21	32.8	6	39	60.9
Shave	27	42.2	6.1 to 9	7	10.9
Excisional	3	4.7	9.1 to 12	12	18.8
Curette	6	9.4	12.1 to 15	2	3.1
Not indicated	7	10.9	15.1 to 18	3	4.7
			18.1 to 21	1	1.6
Recurrence after previous surgery (n = 64)					
No	59	92.2	Central Block (n = 59)		
Yes	5	7.8	No residual LM	26	44.1
Tumor location (n = 64)			LM	29	49.2
Cheek	22	34.4	LM melanoma	4	6.8
Nose	13	20.3			
Temple	3	4.7	CLOSURE TYPE (n = 59)		
Chin	1	1.6	Advancement flap	30	50.85
Scalp	6	9.4	Transposition flap	4	6.78
Eyelid	3	4.7	Medial forehead flap	2	3.39
Neck	4	6.3	STSG	2	3.39
Forehead	3	4.7	Complex linear closure	14	23.73
Ear	9	14.1			
Tumor size group (in mm) (n = 60)			Complex 2 stage closure	1	1.69
<20	13	21.7	Rotational flap	3	5.08
20 to 40	39	65	Temporary Closure	1	1.69
>40	8	13.3	FTSG	2	3.39
Clinical tumor margins (n = 61)					
Well demarcated	29	47.5			
Poorly demarcated	32	52.5			

FTSG, Full-thickness skin grafts; *LM,* lentigo maligna; *STSG,* split-thickness skin graft.

Kunishige's is not apparent but may be due to the subjective nature of clinical assessment of the clinical tumor margins.

Kunishige et al[8] furthermore reported that a margin of at least 12 mm resulted in the complete excision of 97% of LM in their cohort of patients.[8] Multiple previous studies reported that surgical margins between 11 and 25 mm achieved a 97% clearance rate.[8] In our study, an excision margin of 18 mm correlated with the complete excision of 96.7% of tumors. This observation supports existing evidence that WLE with an empirical 10 mm surgical margin is inadequate for a 97% clearance rate of LM of the head and neck.

Our cohort's average surgical excision margin was 8.3 mm, which was congruent with an average excision margin of between 8 and 13 mm reported in other studies.[3,27]

Tissue sparing is of the utmost importance when treating LM on cosmetically and functionally important areas such as the eyelids, nose, and ears. For this reason, LM that needed more than 1 stage in these areas were excised with an additional 3 mm margin as opposed to a 5 mm additional margin for LM occurring on other parts of the head and neck (forehead, temple, chin, cheek, scalp, and neck). Even though tumors on these areas were treated with a narrower (3 mm) additional margin during each

Table II. Comparison between LM on cosmetic and functional important areas and LM on other areas of the head and neck.

	LM (eyelids, nose, ears) (n = 25)		LM other (n = 39)	
Total margin needed for complete excision (mm)	**Frequency**	**Percentage**	**Frequency**	**Percentage**
6	12	48	27	69.2
6.1 to 9	7	28	0	0
9.1 to 12	3	12	9	23.1
12.1 to 15	2	8	0	0
15.1 to 18	1	4	2	5.1
18.1 to 21	0	0	1	2.6
Average surgical excision margin for complete clearance of LM (mm)	8.7		8.1	

LM, Lentigo maligna.

subsequent stage, the average surgical excision margin for this group was 8.7 mm and wider than that of LM on other parts of the head and neck (8.1 mm). This approach of treating LM in cosmetic sensitive areas with an additional margin of less than 5 mm and other areas of the head and neck with an additional 5 mm margin was also used by Moyer et al[14] when they assessed the efficacy of SE for LM of the head and neck. Significant variation exists among published work reporting on additional surgical margins for LM of the head and neck.[4,8,11,14,21] Further research is necessary to determine how different SE techniques affect outcomes and ultimately standardize surgical protocols.

Despite an initial biopsy-proven diagnosis of LM in the current study, subsequent microstaging of the residual tumor in the central block obtained at SE revealed unsuspected LM melanoma in 6.25% of the cases. The mean Breslow thickness for these tumors was 0.24 mm (range, 0.12-0.5 mm). A recent study that specifically investigated the concern of upstaged tumors reported a low risk for upstaging, with most tumors changing to stage T1a with limited implications for further surgical management.[28] Even in cases that may qualify for further surgical management, such as sentinel lymph node biopsy, subsequent surgical intervention is not affected.[28]

Our study reported no recurrences, but not all patients were followed up for a total of 5 years (mean follow-up time, 23.5 months). Recurrence rates for LM of the head and neck treated with SE are reported in other studies to be as low as 1.8%.[12]

LM of special sites such as the head and neck, genitalia, pretibial area, and hands and feet are 10 times more likely to require reconstruction with a flap or graft than melanomas on the trunk and proximal extremities.[29-31] The majority of tumors in our cohort needed tissue rearranging reconstruction, emphasizing the importance of complete margin assessment and certainty of melanoma clearance before undertaking a reconstruction.

Of the 5 recurrent tumors treated with SE in our cohort, 4 (80%) required a surgical excision margin wider than 10 mm to achieve tumor clearance. A previous study by Huilgol et al[31] also reported a correlation between recurrent lesions and increasing surgical margin. The authors reported that 55.9% of recurrent LM required at least 10 mm margins for complete clearance.[31] In our study, 19 (30%) tumors required more than 10 mm surgical margins to excise the LM completely. Of these, 89.5% were larger than 20 mm in size. Other studies also correlated increasing lesion size and the need for wider surgical margins for tumor clearance.[3,6]

Therefore, when considering WLE rather than SE or MMS for a recurrent LM and tumors larger than 20 mm in size, we would recommend a wider margin than would be considered for a primary LM, and ideally exceeding 10 mm.

Limitation

This retrospective study relied on the completeness of clinical and pathology reports. Incomplete records led to tumor size, reconstruction information, and final central block histology unavailable for all patients. Patients were not all followed for a full 5 years to assess for recurrence. Not treating all the tumors requiring a second stage with the same additional margin was another limitation of this study. Considering the variability in LM of the head and neck, it is challenging to draw meaningful conclusions with a small sample size. Since the completion of the study, we have changed our protocol in that all melanomas (including LM) are now treated with complete circumferential deep and peripheral margin assessment to conform with international standards.

Conclusion

This study supports the hypothesis that surgical margins recommended by current guidelines for the treatment of LM of the head and neck are inadequate to achieve a 97% clearance rate and need revision. The study highlights SE as an alternative to conventional WLE for complete peripheral margin assessment, optimal tumor clearance, and tissue sparing in cosmetically and functionally important areas.

Conflicts of interest

None disclosed.

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