Mohs micrographic surgery for superficial leiomyosarcoma: a systematic review

Eric C Olsen[1] MD, Steven A Svoboda[2] MD

Affiliations: [1]Department of Dermatology, University of Alabama at Birmingham, Birmingham, Alabama, USA, [2]Department of Dermatology, University of Florida College of Medicine, Gainesville, Florida, USA

Corresponding Author: Eric C Olsen MD, Department of Dermatology FOT 858, University of Alabama Medical Center, 510 20th Street S, Birmingham, AL 35233, Tel: 770-793-5000, Email: eolsenres@gmail.com

Abstract

Superficial leiomyosarcoma is a rare malignancy of muscular origin arising in the skin and soft tissues. Although wide local excision is the standard of care for these tumors, Mohs micrographic surgery is a promising treatment option as it provides for optimal margin control. The object of this systematic review is to examine the efficacy of micrographic surgery in the management of superficial leiomyosarcoma. A literature search was conducted using the PubMed/Medline and Cochrane databases; 14 studies representing 66 patients were included. Analysis demonstrated a notably low rate of recurrence (1.5%) and metastasis (0.0%) in tumors treated with micrographic surgery, contrasting with increased rates of recurrence and metastasis in tumors treated with wide local excision. These data may be influenced by a shortage of subcutaneous leiomyosarcoma in the included patients, as subcutaneous tumors are more likely to recur and metastasize. Further research is warranted to determine the value of Mohs micrographic surgery in treating superficial leiomyosarcoma and specifically, the subcutaneous variant.

Keywords: cutaneous malignancy, dermatologic surgery, leiomyosarcoma, micrographic surgery, Mohs, outcomes

Introduction

Superficial leiomyosarcoma (LMS) is a malignancy of muscular origin that arises in the skin and superficial soft tissues [1,2]. It is a rare tumor, accounting for 2–3% of all cutaneous sarcomas [3]. Superficial LMS can represent either primary or metastatic lesions, whereas primary cases are further subdivided into two distinct histological subtypes based on the site of origin: cutaneous/dermal and subcutaneous/hypodermal [4,5].

Cutaneous LMS arises from the smooth muscle cells associated with arrector pili muscles of hair follicles and sweat glands found in the dermis. These tumors display local recurrence rates following excision that have been estimated at 14%-32%, although they rarely metastasize [2,6-8]. Conversely, subcutaneous LMS originates from smooth muscle cells lining blood vessel walls in the subcutaneous fat. These tumors display a more aggressive phenotype, with reported local recurrence and metastasis rates of 28%-54% and 30%-62%, respectively [7-9].

Standard treatment for superficial LMS consists of wide local excision (WLE) including a 2 to 5 centimeter margin [1,10]. However, Mohs micrographic surgery (MMS), a tissue-sparing and precision-based surgical method traditionally utilized in treatment of cutaneous malignancies including basal cell carcinoma and squamous cell carcinoma, has been suggested as another treatment option to minimize risk of local recurrence and removal of undue amounts of surrounding tissue [11,12].

This review examines the current literature describing the use of MMS for management of superficial LMS. In doing so, we aim to explore the possibility of MMS as an alternative to WLE for the treatment of superficial LMS.

A systematic review adhering to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines was performed using the PubMed/Medline and Cochrane Library databases (**Figure 1**). Key search terms were "Mohs and leiomyosarcoma" and "micrographic and leiomyosarcoma." Additional studies were identified through a manual search of the reference lists from included articles. Studies reporting at least one patient with superficial leiomyosarcoma treated with MMS were included. Two reviewers assessed full-text articles for eligibility for inclusion in the analysis. Exclusion criteria applied included studies in the category of review papers, studies lacking patients with a diagnosis of LMS, studies lacking utilization of MMS, studies lacking follow-up, and studies that aggregated patient data with other cutaneous malignancies. Data extracted included study type, sex, age, tumor diameter, tumor location, histologic subtype (cutaneous or subcutaneous), length of follow-up, and presence of recurrence and metastasis.

Discussion

Our search yielded 41 results, and one additional study was identified by reference list review. Removal of duplicates revealed 27 studies which were assessed for eligibility. After exclusion based on the above criteria, 14 studies were ultimately included in the analysis (**Table 1**). Of these, 7 were case series including multiple patients and 7 were case reports of a single patient, representing a total of 66 patients. Of the 48 patients for whom sex was reported, 30 were male (62.5%). Patient ages ranged between 15 and 84, with an average age of 58.8. Recorded tumor diameters ranged between 0.6cm and 6.2cm. Of cases for which tumor site was reported, 28 (53.8%) presented on the extremities, 12 (23.1%) presented on the trunk, 11 (21.2%) presented on the head/neck, and one (1.9%) presented on the penis. Subtype reporting was inconsistent but of those for which subtype was included, 32 (91.4%) were cutaneous and three (8.6%) were subcutaneous. Recurrence was noted in one (1.6%) patient and no instances of metastasis were recorded.

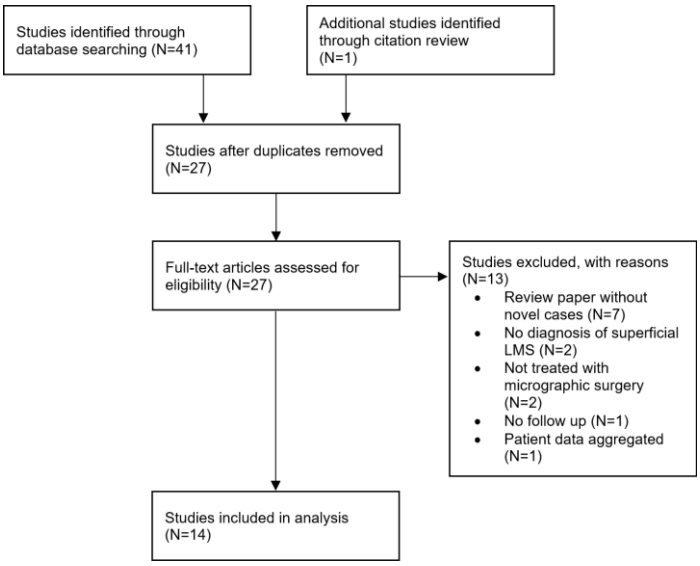

Figure 1. *Flow diagram of the literature search process.*

Superficial LMS is a rare cutaneous malignancy [1,2]. Owing to the uncommon and heterogeneous nature of this tumor, there is no clear consensus on an optimal treatment strategy. Wide local excision is generally accepted as an effective treatment for superficial LMS; however, appropriate margins of excision are unclear, with recommendations between 1cm and 5cm described in the literature [2,13-15].

Appropriate margin control is key in preventing local recurrence [16-18]. Kraft and Fletcher reported that 12 of 18 locally recurrent tumors had positive margins in the primary excision, with margin data unavailable in 5 others [16]. Mohs micrographic surgery facilitates improved margin control by providing complete histopathologic review of all surgical margins [19]. This provides enhanced margin analysis when compared to the "breadloafing" technique utilized in processing WLE specimens, which provides visualization of only 0.1% of the margin [6,20]. The optimal margin control afforded by utilization of MMS in treatment of these tumors may lead to lower rates of local recurrence, as is suggested by the low rate of recurrence demonstrated in the studies included here.

In their report of 15 patients with superficial LMS treated with MMS, Vargas-Mora and colleagues reported no cases of recurrence or metastasis following treatment with a mean follow-up period of

69 months [21]. Winchester and colleagues described no cases of recurrence or metastasis among 14 cases treated with MMS, and Starling and Coldiron reported no recurrence or metastasis in 11 cases treated with MMS [9,11]. Taken together, the data presented here suggest an impressively low rate of recurrence (1.5%) or metastasis (0%) in cases of superficial LMS managed with MMS. The single case of recurrence in the 66 reported cases occurred in a tumor that was already recurrent when treated with MMS, suggesting an intrinsically aggressive tumor biology that may have contributed to additional instances of recurrence [12].

The rarity of superficial leiomyosarcoma makes direct comparison of treatment methods difficult. However, available evidence suggests increased rates of recurrence and metastasis in patients managed with wide local excision as compared to MMS. In a study by Carr and colleagues, 8 of 85 patients (9.4%) with intradermal or subcutaneous LMS experienced recurrence after local excision with margins between.5cm and 2cm [22]. Wellings and colleagues reported a 10% rate of recurrence following wide local excision. However, each of these instances occurred in subcutaneous LMS [23]. Additionally, Winchester and colleagues noted a 9% recurrence rate and 10% metastasis rate among superficial LMS managed with wide local excision, compared to a 0% recurrence rate and 0% metastasis in superficial LMS managed with MMS in the same study [9].

Tumor subtype may play an important role in determining the propensity of the tumor to recur locally or metastasize. In one of the largest studies on leiomyosarcoma, Fields and Helwig documented a 32% rate of local recurrence of cutaneous LMS after excision compared to a 47% rate of recurrence for subcutaneous LMS [2]. Additionally, they described a 33% rate of metastasis for subcutaneous LMS, whereas metastasis of cutaneous LMS is sufficiently rare that later studies have suggested it lacks the capacity to metastasize [16]. Bernstein similarly documented a higher rate of recurrence in subcutaneous LMS compared to cutaneous LMS (54% and 32%, respectively) and reported a similar trend in metastasis as had been previously reported (62% and 5%, respectively), [8]. More recently, Wellings and colleagues reported no recurrences in 35 cases of dermal LMS managed with wide local excision, contrasting with a recurrence rate of 17% in 47 cases of subcutaneous LMS managed with WLE [23].

Of note, only three of the 66 cases were reported as the subcutaneous variant of superficial LMS, although more subcutaneous tumors may have been included but undocumented as such. This may represent selection bias in which cases are treated with MMS, as subcutaneous tumors are more likely to metastasize and clinicians may opt for more aggressive treatment with WLE [9,16]. Of the three subcutaneous LMS managed with MMS reported here, none displayed recurrence or metastasis, suggesting that MMS may hold promise as an effective treatment for these tumors. However, further research is warranted to determine whether MMS is an appropriate treatment modality for subcutaneous LMS.

Our study is limited by the small sample sizes which limit generalizability. Additionally, the lack of uniformity in data reporting, including tumor subtype, across studies hindered a comprehensive comparison and analysis of patient data. The absence of randomized controlled trials or other more robust studies impacts the strength of evidence and short follow-up periods in some studies limits the assessment of long-term outcomes. Finally, selection bias is a concern, as patients may have been selected for treatment with MMS owing to specific patient or tumor characteristics.

Conclusion

Superficial LMS presents a challenge in determining the ideal treatment strategy given its rarity and heterogeneity. Mohs micrographic surgery has long been employed in the management of non-melanoma skin cancers with excellent cosmetic and recurrence outcomes. Mohs micrographic surgery should be considered as an appropriate treatment in superficial LMS as it provides improved margin control, minimizing the risk of recurrence and

metastasis. Additional trials are warranted to investigate the efficacy of MMS in management of superficial LMS.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Table 1. *Reports of superficial leiomyosarcoma managed with Mohs micrographic surgery.*

Author, year	Country	Study type	N (male)	Age (mean)	Tumor diameter, cm (mean, range)	Tumor location	Subtype (cutaneous or subcutaneous)	Mean follow-up (months)	Rate of recurrence	Rate of metastasis
Bernstein, 1996 [8]	USA	CS	2 (1)	48.5	NR	1 Extremity, 1 Trunk	2 Cutaneous	6	0/2	0/2
Brown, 1988 [24]	USA	CR	1 (1)	36	1	1 Penis	NR	24	0/1	NR
Davidson, 1989 [14]	USA	CR	1 (1)	48	1	1 Trunk	1 Cutaneous	30	0/1	0/1
Hall, 2013 [25]	USA	CS	4 (4)	63.5	1.0 (0.6-1.5)	1 Extremity, 3 Head/Neck	4 Cutaneous	35	0/4	0/4
Huether, 2001 [12]	USA	CS	7 (5)	67	3.1 (1.5-6.0)	3 Extremity, 2 Head/Neck, 2 Trunk	NR	52.6	1/7	NR
Humphreys, 2004 [26]	USA	CS	3 (1)	55.3	1.6 (1.5-2)	3 Extremity	2 Cutaneous, 1 Subcutaneous	23.3	0/3	0/3
Iacobucci, 1987 [18]	USA	CR	1 (0)	22	NR	1 Head/Neck	1 Cutaneous	26	0/1	0/1
Murphy-Chutorian, 2019 [27]	USA	CR	1 (1)	76	6.2	1 Extremity	1 Cutaneous	25	0/1	0/1
Spencer and Amonette, 1996 [28]	USA	CR	1 (1)	62	1.5	1 Head/Neck	1 Cutaneous	48	0/1	0/1
Starling and Coldiron, 2011 [11]	USA	CS	11 (7)	54.5	2.3 (1.1-6.0)	6 Extremity, 3 Head/Neck, 2 Trunk	NR	53.6	0/11	0/11
Vargas-Mora, 2022 [21]	Spain	CS	15 (8)	53.7	NR	10 Extremity, 5 Trunk	13 Cutaneous, 2 Subcutaneous	69	0/15	0/15
Vujevich, 2008 [6]	USA	CR	1 (1)	15	1.2	1 Head/Neck	1 Cutaneous	NR	0/1	0/1
Winchester, 2014 [9]	USA	CS	14 (nr)	60.3	2.1 (NR)	NR	6 Cutaneous, 8 NR	67	0/14	0/14
Wollina, 2013 [29]	USA	CS	4 (3)	70.8	NR	3 Extremity, 1 Trunk	NR	23.3	0/4	0/4

CC, complete clearance; CR, case report; CS, case series; DB, double-blinded; MC, molluscum contagiosum; N, sample number; ND, not documented; O, observational; OL, open label; P, prospective; PC, placebo-controlled; R, randomized; Rs, retrospective; TOP, topical.