RESEARCH LETTER

Squamous cell carcinoma arising within discoid lupus erythematous lesions: A systematic review

To the Editor: Discoid lupus erythematosus (DLE) is the most common form of chronic cutaneous lupus erythematosus, characterized by erythematous, atrophic plaques with scale.[1] An infrequently reported complication of DLE is the development of squamous cell carcinoma (SCC).[1] The aim of this systematic review was to summarize the characteristics and outcomes of SCC arising within DLE lesions.

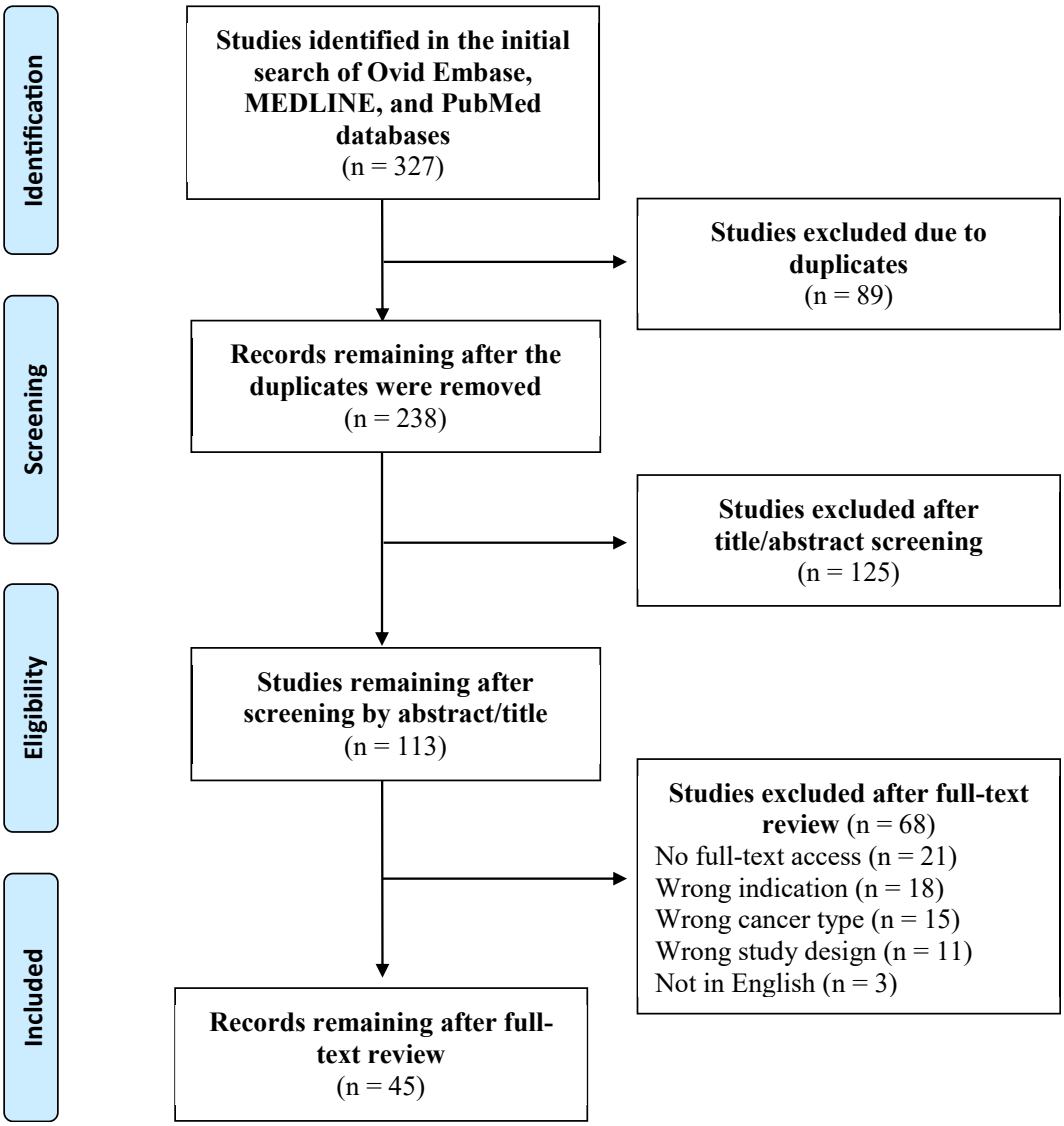

Fig 1. A flow diagram of the literature screened using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The figure is adapted from http://prisma-statement.org.

Table I. Characteristics and outcomes of patients with squamous cell carcinoma arising within discoid lupus erythematosus lesions

Characteristics and outcomes	No. (%)
Age	
Mean age ± SD	50.4 ± 11.4
Range	24-85
Sex	
Female	49 (42.6)
Male	66 (57.4)
Unknown	3
Race	
Black or African American	16 (18.6)
White	6 (7.0)
Asian	64 (74.4)
NR	32
Prior smoking history	
Yes	17 (14.4)
No	101 (85.6)
Prior history of squamous cell carcinoma	
Yes	2 (1.7)
No	116 (98.3)
Prior history of BCC	
Yes	2 (1.7)
No	116 (98.3)
Prior immunosuppressant use	
Yes	5 (12.5)
No	35 (87.5)
Unknown	78
Age at DLE onset (years)	
Mean age ± SD	33.2 ± 7.4
Range	7-58
Type of DLE	
Localized	87 (77.7)
Disseminated	25 (22.3)
NR	6
Hypertrophic	
Yes	10 (90.9)
No	1 (9.1)
NR	107
Duration of DLE disease (years)	
Mean duration ± SD	19.0 ± 10.9
Range	2-44
Location of SCC	
Lower lip	51 (41.8)
Upper lip	14 (11.5)
Forearm	14 (11.5)
Scalp	9 (7.4)
Groin	1 (0.8)
Cheek	9 (7.4)
Hand	7 (5.7)
Extremities	2 (1.6)
Ear	2 (1.6)
Neck	2 (1.6)
Nose	3 (2.5)
Face	3 (2.5)
Lower limb	2 (1.6)
Preauricular area	2 (1.6)
Infra-auricular region	1 (0.8)
Total reported SCCs	122
Treatment for SCC	
Surgical excision alone	47 (81.0)
Surgical excision with chemotherapy	1 (1.7)
Surgical excision with radiation	8 (13.8)
Surgical excision with combined chemotherapy and radiation	2 (3.4)
Unknown	60
Biopsy	
Yes	110 (99.1)
No	1 (0.9)
Unknown	7
Period between DLE and initial SCC lesion (years)	
Mean period ± SD	15.0 ± 7.0
Range	0.5-41
SCC metastasis	
Yes	29 (26.9)
No	79 (73.1)
Unknown	10
Recurrent SCC	
Yes	41 (40.2)
No	61 (59.8)
Unknown	16
Mortality	
Yes	23 (25.0)
No	69 (75.0)
Unknown	26

No. = number; % = percentage.
BCC, Basal cell carcinoma; *DLE*, discoid lupus erythematosus; *NR*, not reported; *SCC*, squamous cell carcinoma; *SD*, standard deviation.

Embase and MEDLINE searches were conducted on June 27, 2020, using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Fig 1). A total of 118 patients from 45 studies were included following the screening process (Tables I and II). Of the 118 patients (mean age: 50.4 years) who developed SCC within DLE lesions, the majority were males (55.9%, n = 66/118). Localized DLE was present in 73.7% (n = 87/118) of the patients and generalized DLE (DLE lesions below the neck) in 21.2% (n = 25/118); 5.1% (n = 6/118) did not report DLE distribution. A positive smoking history and prior immunosuppressant use were reported in 14.4% (n = 17/118) and 12.5% (n = 5/40) of the patients, respectively. The most common sites of SCC development were the lip (53.3%, n = 65/122), forearm (11.5%, n = 14/122), and scalp (7.4%, n = 9/122). The lower lip (41.8%,

Table II. Patients with mortality outcome

Outcomes	No. (%)
SCC metastasis	
Yes	10 (90.9)
No	1 (9.1)
Unknown	12
Recurrent SCC	
Yes	11 (100.0)
No	0 (0.0)
Unknown	12
Cause of death	
Metastasis	14 (60.9)
Sepsis secondary to scalp infection	1 (4.3)
Respiratory failure	1 (4.3)
Unknown	7 (30.4)
Time from initial SCC presentation to death (months)	
Mean time ± SD	22.0 ± 16.8
Range	3.4-54

No. = number; % = percentage.
SCC, Squamous cell carcinoma; *SD*, Standard deviation.

n = 51/122) was more affected than the upper lip (11.5%, n = 14/122).

The mean duration between DLE onset and SCC development was 15.0 years (range: 0.5-41). Of 47 patients who reported treatment outcomes for SCC, all had undergone surgical excision. Eight patients had received radiotherapy, 1 had received chemotherapy, and 2 had received combined radiation and chemotherapy. Of those who reported metastasis and recurrences, 26.9% (n = 29/108) experienced SCC metastasis, and 40.2% (n = 41/102) reported SCC recurrences. In addition, 25.0% (n = 23/92) of the patients reported a mortality outcome due to metastasis (60.9%, n = 14/23), sepsis (4.3%, n = 1/23), and respiratory failure (4.3%, n = 1/23) (Table II).

Although the pathogenesis of SCC development within DLE lesions is unknown, 2 hypotheses have been proposed. First, hypopigmented DLE plaques may predispose the lesions to actinic damage, which has been implicated in SCC.[2] Second, the chronic scarring from DLE, in combination with constant local inflammatory stimuli, might be associated with carcinogenesis.[3] We also found that majority of the SCCs occurred on sun-exposed sites, most commonly the lip. This may be due to constant sun exposure, smoking/tobacco use, and irritation from allergens. For instance, 82.3% (n = 14/17) of the patients who reported a smoking history developed an SCC on the lip. SCC with DLE compared with SCC without DLE emphasizes the significance of this association: tumor recurrence (40% vs 20%), metastasis (26.9% vs 6%), and death (26.1% vs 1%).[4] Although limited literature exists to explain the high recurrence, metastasis, and death outcomes, the prolonged duration between DLE onset and SCC diagnosis or prior failed treatments might be implicated. These patients require prompt surgical treatment after diagnostic biopsy, radiological examination, sentinel lymph node biopsy for high-risk tumors, as well as long-term monitoring.

Given that this review relied largely on published case reports, our findings should be interpreted with caution. Case reports have been documented to have an increased risk of bias.[5] Additionally, reporting bias likely contributed to the high reported rates of tumor recurrence, metastasis, and mortality in the DLE-related SCC group. Further studies focusing on SCC arising within DLE lesions might be warranted.

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Conflicts of interest: R. Gary Sibbald is the project leader for Extension for Community Healthcare Outcomes Ontario Skin and Wound and the former co-chair of the Health Quality Ontario Wound Care Guidelines and of the Registered Nurses' Association of Ontario Pressure Injury Guideline. He is a speaker, consultant, or investigator for AbbVie, Galderma, Leo, Novartis, PediaPharm, Pfizer, and Valeant. Dr Mufti, Mr Maliyar, and Ms Sachdeva have no conflicts of interest to declare.

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REFERENCES

1. Shapera EA, Kim PD. Squamous cell cancer arising in an African American male cheek from discoid lupus: a rare case

and review of the literature. *Case Rep Surg*. 2016;2016:9170424.
2. Grossman D, Leffell DJ. Squamous cell carcinoma. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K, eds. *Fitzpatrick's Dermatology in General Medicine*. 8th ed. McGraw Hill; 2012:1283-1294.
3. Cassarino DS, Derienzo DP, Barr RJ. Cutaneous squamous cell carcinoma: a comprehensive clinicopathologic classification. *J Cutan Pathol*. 2006;33(4):191-206.
4. Clayman GL, Lee JJ, Holsinger FC, et al. Mortality risk from squamous cell skin cancer. *J Clin Oncol*. 2005;23(4):759-765.
5. Murad MH, Sultan S, Haffar S, Bazerbachi F. Methodological quality and synthesis of case series and case reports. *BMJ Evid Based Med*. 2018;23(2):60-63.

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