JOURNAL OF PLASTIC SURGERY AND HAND SURGERY
2026, VOL. 61, 86–90
https://doi.org/10.2340/jphs.v61.45793

SYSTEMATIC REVIEW

Characteristics and prognosis of skin cancer arising from burn scars: a systematic review

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ABSTRACT

Background: Burn scars are recognized risk factors for malignant skin transformation, most notably Marjolin's ulcer (MU). Despite extensive documentation in case reports and series, the epidemiological characteristics and prognosis of burn scar-related skin cancers have lacked large-scale systematic synthesis.

Methods: We conducted a systematic review in line with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, registered with PROSPERO (CRD42024545404), covering literature from PubMed, Scopus, and Web of Science up to 18 January 2024. Eligible studies included case reports, case series, and observational studies reporting any type of skin cancer in burn scars. Data were extracted on demographics, burn and tumor characteristics, treatment, latency, outcomes, and risk of bias using Joanna Briggs Institute tools.

Results: A total of 211 studies reporting 830 cases were included. The mean latency period from burn injury to cancer diagnosis was 21.7 years (SD = 19.6). Males constituted 53% of patients, with third-degree burns predominating (89.37%) and lower limbs being the most affected site (33.59%). Squamous cell carcinoma (SCC) was the most frequent malignancy (67.19%), followed by basal cell carcinoma (BCC, 3.83%) and other cancers (15.33%). Recurrence occurred in 13.2% of cases; mortality was 6.96%. SCC accounted for most deaths (63.8%), while melanoma and sarcoma exhibited high rates of recurrence and mortality. Lymph node metastasis and distant metastasis were found in 7.56 and 4.74% of cases, respectively.

Conclusion: Skin cancers arising from burn scars, especially SCC, demonstrate aggressive clinical behavior with significant morbidity and mortality. Reduced latency periods and high metastatic potential highlight the importance of vigilant, long-term surveillance and radical initial treatment. This review provides a contemporary benchmark for epidemiological understanding and supports calls for international registries, molecular diagnostics, and standardized management protocols for burn scar malignancies.

ARTICLE HISTORY
Received 16 December 2025
Accepted 8 March 2026
Published 23 April 2026

KEYWORDS
Marjolin's ulcer; burn-scar carcinoma; squamous cell carcinoma; basal cell carcinoma

Introduction

Burn scars, especially those that heal by secondary intention, are a risk factor for the development of various skin cancers [1]. This malignant transformation is commonly known as Marjolin's ulcer (MU), with a reported incidence rate of 0.77–2% [2, 3]. Historically, 'MU' referred to the malignant transformation of cells in an old burn scar. However, 'MU' now broadly defines all malignant tumors that occur in chronic body surface ulcers, inflammations, or burn scars [4, 5].

Although the cause of this transformation is not fully understood, several theories exist. This includes chronic irritation to the wound due to repeated incomplete healing attempts, which overtime speed up proliferation and spontaneous mutations. Toxins released from the scarred tissue may irritate cells and cause mutagenetic effects. Additionally, loss of immunity cells in the chronic scar tissue may cause the malignant cells to be undiscovered [6].

This transformation is usually slow with a mean latent period of 28–35 years between burn scar and onset of malignancy [4]. Possible precipitating factors of malignant transformation include repeated low-grade trauma and incomplete wound healing [7]. Some studies reported on abnormal genetic factors such as p53 [8, 9] and Fas genes in cases with burn scar cancer [10].

Squamous cell carcinoma (SCC) is the most frequent histological type of burn scar cancers followed by basal cell carcinoma (BCC) then melanoma [6, 11], with the extremities, the trunk, and the scalp being the most frequently affected areas [12].

Abundant case reports and retrospective studies have described MU, but with great variability regarding the characteristics, prognosis,

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Supplemental data for this article can be accessed online at https://doi.org/10.2340/jphs.v61.45793

as well as treatment options. There is a lack of large-scale synthesis of evidence regarding burn scar cancer. We aim to fill this gap by providing a systematic review of the characteristics and prognosis of skin cancer arising from burn scars.

Methods

This systematic review followed the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [13] (Supplementary File). The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database under registration number CRD42024545404.

Data sources & search strategy

We conducted a systematic literature search across PubMed, Scopus, and Web of Science from their inception to 18 January 2024, covering all records reporting the onset of skin cancer following burn injury.

The search strategy included the following terms: 'basal cell carcinoma' OR 'squamous cell carcinoma' OR 'tumour' AND 'burn', with Medical Subject Headings (MeSH) applied where applicable.

The broad search term 'tumour' was intentionally used to maximize sensitivity, with malignancies subsequently classified during data extraction according to histopathological diagnosis. Details of the search strategy for each database are provided in Supplementary file.

Study selection

All identified references were imported into EndNote. After removing duplicates, two independent reviewers screened the titles and abstracts for eligibility based on predefined criteria.

Eligible studies included primary research, such as case reports, case series, and observational studies, which reported any type of skin cancer occurring on top of various burn scars (flame, trauma/surgery, skin scratch/friction, scald, infection, electric burn).

We excluded studies involving non-human subjects, non-cancerous skin injuries, which are due to burn injuries or chronic skin damage without histologically confirmed malignancy at the time of initial injury, secondary studies, or those not published in English.

Data extraction and outcome

Data extraction was performed independently by two reviewers. Any conflicts were first discussed and resolved between them. If conflict could not be resolved, a senior author made the final decision.

The extracted data included:

- Study details: first author, year of publication
- Patient characteristics: country, ethnicity, age, and gender
- Burn-related information:
  - Etiology of burn: flame (open fire), trauma/surgery (post-injury damage), skin scratch/friction (repetitive rubbing), scald (hot liquids or steam), infection (chronic infection causing tissue damage), electric burn (electrical current)
  - Burn degree: degree of burn (first, second, third, or mixed)
  - Burn location: head, neck, face, trunk, upper limb, lower limb, or other extremities
  - Age at the time of burn
- Tumor-related data:
  - Type of malignancy: SCC, BCC, or other
  - Method of diagnosis: histopathology, immunoassay
  - Age at diagnosis
  - Treatment modality: surgery, radiotherapy, chemotherapy, immunotherapy
  - The latency period was calculated as the time interval between burn injury and the diagnosis of tumor.
  - The time delay was calculated as the time interval between tumor appearance to diagnosis and treatment.
- Outcomes:
  - Follow-up period
  - Presence or absence of complications
  - Clinical outcomes: recurrence with re-excision, recurrence with flap surgery, lymph node metastasis, distant metastasis, death, and other outcomes
  - Survival time from diagnosis to death

Risk of bias assessment

We assessed the risk of bias using **Joanna Briggs Institute (JBI) critical appraisal tools** according to each study design, case reports, case series, cohort studies, and case-control studies [14].

Three cases were used as the threshold to differentiate between case reports (fewer than three cases) and case series (three or more cases).

Results

Screening process

A total of 5415 records were retrieved from the three databases and were screened by two independent reviewers based on titles and abstracts. Of these, 542 records were deemed eligible for full-text screening, including 203 duplicates. After removing duplicates, 339 unique studies underwent full-text screening, resulting in the inclusion of 211 studies in this systematic review. The search terms used in every database are shown in Supplementary Table 1. The PRISMA flow diagram representing the study selection process and number of records is shown in Figure 1.

Characteristics of the included studies

All the studies included were case reports or case series, except for two case-control studies: Xiao et al. [2] and Xiang et al. [4]. The top three countries contributing case reports on cancer lesion detection overlying skin burns were Iran (23.3%), China (22.8%), and Turkey (11.2%). The remaining case reports and series originated from a wide range of countries across the globe. The studies included were published between 1919 and 2023, with 85 cases published during the period from 2011 to 2023.

The total number of patients included was 830, with a nearly equal male-to-female distribution; 440 patients (53%) were male. The mean age at the time of burn injury was 21.03 years (SD = 19.76). Most reported burns were third-degree burns (n = 311; 89.37%), followed by second-degree (n = 26; 7.47%), mixed degree (n = 10; 2.87%), and first-degree burns (n = 1; 0.28%). The most affected site was the lower limb (n = 267; 33.59%), followed by the head, neck, or face (n = 145; 18.24%), upper limb (n = 81; 10.19%), hands and feet (n = 63; 7.93%), trunk (n = 60; 7.55%), and multiple sites (n = 49; 6.16%).

The mean age at the time of cancer diagnosis was 47.16 years (SD = 15.94), with a mean latency period of 21.7 years (SD = 19.6) from the time of burn injury to cancer diagnosis. The most common type of skin cancer was SCC, reported in 561 patients (67.19%). BCC was observed in 32 patients (3.83%), while other cancer types were reported in 128 patients (15.33%). A combination of SCC and BCC occurred in six patients (0.72%).

Following excision, recurrence occurred in 89 patients (13.2% of 675 patients with outcome data). SCC demonstrated the highest recurrence burden (29 cases, 5.2% of all SCC cases while 32.6% of total recurrences). Other recurrent subtypes included histiocytoma ($n = 4$), melanoma ($n = 4$, 100% of reported melanoma cases), sarcoma ($n = 2$, 50% of reported sarcoma cases), verrucous carcinoma ($n = 2$), pyogenic granuloma ($n = 1$), fibroxanthoma ($n = 1$), pseudoepitheliomatous hyperplasia ($n = 1$), and schwannoma ($n = 1$), and BCC ($n = 3$, 9.4% of BCC cases). Histology was unreported for 40 recurrences (44.9%). Postoperative mortality occurred in 47 patients (6.96% of 675 patients with outcome data). SCC accounted for 30 fatalities (63.8% of total deaths; 5.3% of all SCC cases). Other specified subtypes included sarcoma ($n = 3$), melanoma ($n = 3$), schwannoma ($n = 1$), extraskeletal osteosarcoma ($n = 1$), and BCC (BCC, $n = 1$; 3.1% of BCC cases). Histologic classification remained unavailable for 8 deaths (17.0%). Lymph node metastasis was identified in 51 patients (7.56%), and distant metastasis was detected in 32 patients (4.74%). Table 1 presents a summary of the characteristics of the included studies. Detailed data extracted for each individual study are provided in the Supplementary file.

Table 1. Summary of the characteristics of the included studies.

Variable	Subcategory	Mean (SD)	*N* (%)	Total no. of cases reporting it
Age at time of burn		21.0 (19.8)	-	424
Age at time of cancer diagnosis		47.2 (15.9)	-	644
Latency period		21.7 (19.6)	-	788
Top 3 countries				
	Iran	-	268 (32.3)	829
	China	-	189 (22.8)	
	Turkey	-	93 (11.2)	
Gender (Males)		-	440 (53)	830
Degree of burn				
	First	-	1 (0.3)	348
	Second	-	26 (7.5)	
	Third	-	311 (89.4)	
	Combination	-	10 (2.9)	
Site of burn				
	Head, neck, or face	-	145 (18.2)	795
	Trunk	-	60 (7.6)	
	Upper limb	-	81 (10.2)	
	Lower limb	-	267 (33.6)	
	Extremities	-	63 (7.9)	
	Combination	-	49 (6.2)	
Cancer				
	SCC	-	561 (67.2)	835
	BCC	-	32 (3.8)	
	Other	-	128 (15.3)	
	Combination	-	6 (0.7)	
Complications				
	Recurrence + Re-excision	-	58 (8.6)	675
	Recurrence + Flap surgery	-	6 (0.9)	
	Lymph node metastasis	-	51 (7.6)	
	Distant metastasis	-	32 (4.7)	
	Death	-	47 (7.0)	
	Other	-	57 (8.4)	

Quality assessment of the included studies

The JBI critical appraisal tools, tailored to each study design, were used to assess the quality of the included case reports, case series, and case-control studies. Of the 212 studies, 143 were rated as having good quality, while 63 were rated as fair. Five studies – Pelia et al. (1999), Eastman (2004), Kargr (1996), Hayakawa (1986), and Okamoto (2009) – were assessed as having poor quality. The quality assessment score for each individual study is provided in the Supplementary file.

Discussion and conclusions

This systematic review of 211 studies (reporting 830 MU cases) provides the most comprehensive contemporary analysis of skin malignancies arising in burn scars. It establishes critical epidemiological patterns, prognostic factors, and clinical outcomes that redefine current clinical understanding of MU pathogenesis and management.

Our analysis confirms SCC as the predominant malignancy (67.2%), with a mean latency of 21.7 years post-burn. High complication rates, including recurrence (8.6%), lymph node metastasis (7.6%), and mortality (7.0%) underscore the aggressive nature of these malignancies despite intervention.

Pathophysiological and clinical correlates

The predominance of SCC (SCC; 67.19%) over BCC (BCC; 3.83%) aligns with existing literature on scar-related malignancies [12]. This likely reflects SCC's heightened susceptibility to chronic inflammatory microenvironments in unstable scars, where repeated DNA damage accelerates keratinocyte carcinogenesis [15].

Regarding the 15.33% 'other' malignancies (including sarcomas and adnexal tumors) signals broader oncogenic risk than previously documented. This diversity suggests that chronic inflammation triggers pluripotent progenitor cell dysregulation in scars [16].

Our observed mean latency period of 21.7 years (SD 19.6) contrasts sharply with traditional 28–35 year estimates [4]. This acceleration may reflect modern environmental carcinogen exposure (e.g. air pollutants altering scar biology) or earlier diagnosis due to improved surveillance [17].

The anatomical distribution – predominantly lower limbs (33.59%) and head/neck (18.24%) is consistent with a study by Bazalinski et al. [6] and highlights regions susceptible to repetitive microtrauma and UV exposure. Lower limb predominance (33.59%) supports mechanical stress as a catalyst, where friction and recurrent trauma drive genomic instability in scar tissue [18].

The overwhelming representation of third-degree burns (89.37%) further underscores full-thickness injury as a prerequisite for carcinogenesis, likely through sustained cytokine release and fibroblast dysfunction [6].

Also, the male predominance (53%) correlates with occupational burn exposure and delayed healthcare-seeking behavior [12].

The 13.2% recurrence rate and 6.96% mortality observed in our cohort exceed rates for non-scar cutaneous SCCs [19], emphasizing MU's aggressive biology. High metastatic rates (lymphatic: 7.56%; distant: 4.74%) suggest early nodal evaluation is critical, particularly for lesions > 2 cm or with poor differentiation [20]. The high mortality rate – often linked to delayed intervention – underscores its lethal potential when suboptimally managed. These findings validate current guidelines advocating radical excision with ≥ 1 cm margins and sentinel lymph node biopsy for high-risk lesions [19].

Melanoma demonstrated universal recurrence as well (4/4 cases) with 75% mortality (3/4), while sarcoma recurred in 50% (2/4) with 75% mortality (3/4). BCC showed favorable outcomes (9.4% recurrence, 3.1% mortality). Though based on limited cases, this suggests that histologic subtype can predict recurrence risk and mortality. These findings mandate histology-specific resection strategies as these tumor types differ in their surgical management, with variations in the required extent of excision, and generally necessitate wide surgical margins to ensure adequate oncologic control.

While this review aggregates the largest MU data to date, limitations include:

- Heterogeneity in outcome reporting across case series
- Potential publication bias toward aggressive cases
- The predominance of single-case reports reflects the rarity and long latency of burn-associated malignancies but limits generalizability and precludes quantitative synthesis.
- Scarce molecular data limiting mechanistic analysis.

Additionally, data on initial burn management, including secondary healing versus skin grafting, were inconsistently reported in the included studies, precluding formal comparison. Nevertheless, prolonged inflammation and delayed epithelialization associated with secondary healing may theoretically contribute to increased long-term malignant risk.

Nevertheless, adherence to PRISMA 2020 standards, prospective registration, and dual-reviewer extraction enhance methodological rigor. Although the search strategy employed the broad term 'tumour', included cases were categorized post hoc into specific malignancy types (e.g. SCC, melanoma, sarcoma) based on reported histology. This approach reflects the heterogeneity of burn-associated malignancies and is consistent with the exploratory nature of the review.

We clinically recommend a surveillance protocol of annual scar examinations starting 15 years post-burn, with a low threshold for biopsy of non-healing ulcers or verrucous changes. A therapeutic approach of wide local excision (≥ 1 cm margins) with intraoperative margin assessment with considering sentinel lymph node biopsy for tumors > 2 cm or high-grade histology, and adjuvant radiotherapy for positive margins or perineural invasion, along with early grafting of third-degree burns to reduce unstable scarring [21].

Future studies should establish international registries with standardized molecular profiling, validate immune checkpoint inhibitors in metastatic MU, and explore a standard risk stratification incorporating scar location, depth, and patient genetics predicting transformation risk.

This review highlights MU as a serious and aggressive malignancy arising in the context of burn injuries, associated with substantial morbidity and mortality, and characterized by distinct epidemiological and prognostic features. Reduced latency periods, high metastatic potential, and SCC predominance necessitate vigilant long-term surveillance and radical initial treatment. Integrating molecular diagnostics with standardized management protocols may improve outcomes for this historically neglected complication of burn injury.

Acknowledgements

None

Funding

This work was supported and funded by the Deanship of Scientific Research at Imam Mohammad Ibn Saud Islamic University (IMSIU) (grant no. IMSIU-DDRSP2501).

Disclosure statements

None.

Data availability

All data are available in the manuscript and supplementary file.

Ethics declarations & trial registry information

Not Applicable.

Authors' contributions

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