



# Burn lesions with progression to neoplasia: Marjolin's ulcer

## *Lesões por queimaduras com evolução para neoplasia: úlceras de Marjolin*

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### ■ ABSTRACT

**Introduction:** Marjolin's ulcer is defined as a malignancy within scars that is usually chronic and results from several lesion types, with burn injuries being the most common. **Methods:** A bibliographic survey was conducted of the Virtual Health Library, PubMed, Scientific Electronic Library Online, and Cochrane databases using the inclusion criteria of studies published in the last 5 years, human studies, and published in English or Portuguese. **Results:** A total of 31 studies were analyzed, of which only 6 were included in the final sample. **Discussion:** Marjolin's ulcer is found in old burn scars and can occur anywhere, but it is more common in the upper and lower limbs. The diagnosis begins with the clinical suspicion based on lesion characteristics: chronic unhealed ulcerative lesions with high and hardened edges, an unpleasant odor, and purulent discharge. However, the diagnosis can only be made histopathologically. The latency period between injury and malignancy is 30–35 years. Although treatment should be individualized since it depends on several factors, surgical excision is considered the gold standard. **Conclusion:** Knowledge about this condition is essential to better patient prognosis and prevent underestimation of possible cases of malignancy, allowing for appropriate therapy to minimize recurrence and enabling prophylactic measures to prevent burn injury and reduce risk factors for malignancy.

**Keywords:** Burns; Skin ulcer; Carcinoma; Healing; Plastic surgery

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## ■ RESUMO

**Introdução:** A Úlcera de Marjolin é definida como a malignização de cicatrizes, geralmente, crônicas, decorrentes de diversos tipos de lesão, sendo mais comum lesões por queimaduras. **Métodos:** Foi realizado levantamento bibliográfico nas plataformas BVS, PubMed, SciELO e Cochrane, tendo como critério de inclusão estudos publicados nos últimos 5 anos, que envolvem a espécie humana, disponíveis na web nos idiomas inglês ou português.

**Resultados:** Analisados um total de 31, dos quais apenas 6 compuseram a amostra final. **Discussão:** As úlceras de Marjolin são encontradas em cicatrizes antigas de queimaduras, podem ocorrer em qualquer local, sendo mais comuns em membros superiores e inferiores. O diagnóstico inicia-se com a suspeita clínica baseada em características das lesões: lesões ulcerativas crônicas que não cicatrizam, com bordas elevadas e endurecidas e odor desagradável, podendo apresentar descarga purulenta. Esse só pode ser efetivado, entretanto, por meio do histopatológico da lesão. O período de latência entre a injúria da lesão e a sua malignização é, em média, de 30 a 35 anos. O tratamento deve ser individualizado, uma vez que depende de diversos fatores. Contudo, considera-se o padrão ouro a excisão cirúrgica.

**Conclusão:** O conhecimento dos profissionais de saúde acerca dessa condição faz-se imprescindível para o melhor prognóstico do paciente. De modo que possíveis casos de malignização não tenham o seu diagnóstico subestimado, permita a terapêutica adequada à minimização das recidivas, e medidas profiláticas sejam efetivadas, no que tange à prevenção da queimadura e à minoração de fatores de risco para a malignização.

**Descritores:** Queimaduras; Úlcera cutânea; Carcinoma; Cicatrização; Cirurgia plástica.

## INTRODUCTION

Worldwide, about 6 million people require medical care because of burns; in Brazil, this number is about 1 million patients per year<sup>1,2</sup>. Such lesions can be caused by thermal, chemical, electrical, biological, or radioactive agents and are divided into three degrees according to their complexity.

In addition to the physical damage, many burn victims suffer from psychological and economic problems due to a prolonged recovery time<sup>3,4</sup>. Given that this pathology requires long and painful treatment, it may, in some cases, be neglected and evolve into a process of lesion malignancy.

Malignant skin lesions are the most frequent form of cancer in Brazil and worldwide, being subdivided into melanoma and non-melanoma, which is the most common, representing 95% of tumors. Exposure to solar radiation is a predisposing factor for squamous cell carcinogenesis and basal cell carcinomas<sup>5,6</sup>.

In 1828, the French surgeon Jean Nicolas Marjolin associated the inadequate treatment of Marjolin's ulcer with burns that were not treated due

to their malignancy. However, the term Marjolin's ulcer was first recognized in 1903 in a description by Da Costa of a malignant process resulting from a burn<sup>8</sup>. The term is currently used more generally for any chronic malignancy in scars, although burns remain the main precursor lesion, with the incidence of burn scar evolving to carcinoma being 0.77–2%<sup>8</sup>.

Although it is possible to identify other malignant neoplasms, such as sarcoma, melanoma, and basal cell carcinoma, the main histopathological sample of the tumor is spinocellular<sup>9</sup>. Thus, 76% of patients with a history of burn scar have squamous cell carcinoma<sup>10</sup>.

Furthermore, this pathology is classified as acute or chronic, lesions that became malignant within or beyond a 12-month period after the injury, respectively<sup>7</sup>.

This study provides knowledge about the above-mentioned problems and the tools used for the effective diagnosis, treatment, and prognosis of Marjolin's ulcer. Thus, it is necessary to use therapeutic tools and medical knowledge to better manage patients, prevent the development of this disease in burn patients, and awaken the interest of clinicians about its early identification.

## OBJECTIVE

The objective of this study is to review the literature on Marjolin's ulcer resulting from burn injuries.

## METHODS

This is an integrative review of burn scar carcinoma, classically known as Marjolin's ulcer. The Virtual Health Library (VHL), PubMed (Publisher Medicine), Scientific Electronic Library Online (SciELO), and Cochrane databases were used. The following controlled keywords were used: "Queimadura/Burn" and "Úlceras de Marjolin/Marjolin's Ulcers." The inclusion criteria established were studies published in the last 5 years of humans and full availability on the web in English or Portuguese.

Moreover, integrative reviews, literature reviews, systematic reviews, and letters to the editor were defined as the exclusion criteria.

## RESULTS

By using the inclusion criteria, we found 31 studies in the databases, of which only six met the inclusion criteria after the analytical reading being included in the final sample of this study (Tables 1 and 2). Of the 11 studies found in the VHL, two letters to the editor, two studies that were not available on the web, and two articles that did not address burns were excluded. Thus, five studies were included in the sample. Eighteen studies were found in PubMed, eight of which were already found in the VHL, three were not available on the web, and six studies were excluded because they did not address burns, one of which addressed trauma-related injuries in general. Thus, only one study of this database was included in the sample. Two studies using the previously determined keywords were found in SciELO, but none of them addressed burns. No study was found in the search of the Cochrane database.

It should be noted that although the last selected study has the term "Literature Review" in its title, a

**Table 1.** Distribution of articles addressing the development of Marjolin's ulcer in burn scars by article title; study type; and publication year, language, and origin. Fortaleza - Ceará, 2019.

Study Title	Study Type	Year	Language	Origin
Úlcera de Marjolin: relato de caso (Marjolin's ulcer: case report)	Case Report	2015	Portuguese	Brazil
Multiple Marjolin's ulcers arising from irradiated post-burn hypertrophic scars: a case report	Case Report	2014	English	Canada
Acute Marjolin's ulcers: a nebulous diagnosis	Case Report Series	2014	English	United States
Incidences of malignancy in chronic burn scar ulcers: experience from Bangladesh	Prospective and Observational Study	2015	English	Bangladesh
Epidemiology and predictors of recurrence of Marjolin's ulcer: experience from Mansoura University	Retrospective Study	2017	English	Egypt
Úlcera de Marjolin: revisão de literatura e relato de caso – (Marjolin's ulcer: literature review and case report)	Case Report	2016	Portuguese	Brazil

**Table 2.** Epidemiological characteristics and treatment reported in case reports. Fortaleza - Ceará, 2019.

Study	Number of cases studied	Age at burn	Age at diagnosis	Sex	Treatment
Úlcera de Marjolin: relato de caso (Marjolin's ulcer: case report)	2	Not reported	Case 1: 59 years Case 2: 82 years	Cases 1 and 2: Male	Cases 1 and 2: Exeresis with wide margin of safety
Multiple Marjolin's ulcers arising from irradiated post-burn hypertrophic scars: a case report	1	4 years	61 years	Male	Exeresis with wide margin of safety Graft for radial artery reconstruction
Acute Marjolin's ulcers: a nebulous diagnosis	3	Not reported	Case 1: 42 years Case 2: 50 years Case 3: 60 years	Case 1: Female Case 2: Male Case 3: Male	Case 1: Exeresis with wide margin (3.5 × 1.8 cm) Case 2: Surgical debridement Case 3: Exeresis with wide margin
Úlcera de Marjolin: revisão de literatura e relato de caso (Marjolin's ulcer: literature review and case report)	1	27 years	52 years	Male	Wide margin exeresis and local graft

type of study that was considered an exclusion criterion, the “Úlcera de Marjolin: Revisão de literatura e relato de caso (Marjolin’s Ulcer: Literature Review and Case Report)” article was actually a case report.

## DISCUSSION

After analyzing the results, we decided to divide the study into the following topics to facilitate understanding.

### Risk Factors and Topography

Although chronic pressure lesions are reported in 2.6% of cases of Marjolin’s ulcer, they are more common in old burn scars, representing 76% of cases, and venous stasis ulcers, representing 6.3% of cases<sup>11</sup>.

A study conducted of 140 patients showed that, on average, 80% of the malignant transformations of burn scars were caused by flames, mainly due to the ability of this etiological agent to deepen the lesion, causing greater stiffness and consequent cracking of the lesion scar<sup>12</sup>.

Moreover, although Marjolin’s ulcers may occur in any location, the upper and lower limbs were the most affected topographies, which is explained by the high incidence of venous stasis burns and ulcers, and the higher propensity to repeated damage in these sites, especially in the joints<sup>12</sup>.

In addition to burn scars with a long healing time, other important risk factors are reported in the literature, such as second intention scars and scars that are easily traumatized, confirming the relevance of topography for assessing lesion malignancy<sup>13</sup>. Skin grafts in deeper burns is mentioned as a protective factor against malignancy<sup>14</sup>.

A study conducted in China demonstrated that easily traumatized scars are a risk factor for the development of Marjolin’s ulcer. Of the 17 patients with Marjolin’s ulcer (35%) they assessed, six reported recurrent ulcers within the lesion<sup>15</sup>.

### Etiology

Although Marjolin’s ulcer is not carcinogenic, its etiology appears to include several factors that are influenced by the trauma that occurs within the region. This trauma makes the lesion more malignant since it intensifies some carcinogenic factors, such as UV rays, due to the greater sensitivity of traumatized skin<sup>13</sup>. It also causes prolonged cell proliferation due to inefficient healing, which can cause mutations in the DNA of these cells<sup>16</sup>.

Another factor that may contribute to carcinogenesis of these lesions is the reduction in

vascularization in the region where the healing process occurs, making the immune response to these cells with mutated DNA less efficient<sup>16</sup>. It also includes lymphatic obliteration due to healing, impairing the presentation of the antigen and the activation of the defense cells<sup>17</sup>.

At the molecular level, some studies have attributed the malignancy process of Marjolin’s ulcer to mutations in the *p53* and *FAS* genes<sup>17</sup>.

### Diagnosis and Latency

The diagnostic approach begins with clinical suspicion of Marjolin’s ulcer based on the lesion’s characteristics, i.e., chronic ulcerative lesions with unhealed high and hardened edges, an unpleasant odor, a budding appearance, and occasional purulent discharge<sup>18</sup>.

Furthermore, it is important to pay attention to the patient’s history since many reports show that the transformation to carcinoma was associated with poorly healing burns during childhood<sup>19</sup>.

Although the diagnosis can be directed by lesion characteristics and anamnesis, it is only made histopathologically<sup>18</sup>. Ulcers persisting for more than 3 months should be biopsied<sup>20</sup>.

A common problem found in health services is the patient’s delay in seeking care, which makes it difficult to make the early diagnosis that is essential for a favorable prognosis. Another problem eventually reported is underestimation of the patient’s condition, postponement of the therapeutic approach, and possible confusion with an infected ulcer<sup>18,14</sup>.

The latency period between injury and malignancy is 11–75 years, with a mean of 30–35 years. Moreover, the patient’s age when the first lesion occurred, such as the burn injury, is inversely proportional to the latency period, i.e., individuals who developed this lesion at an early age have a longer latency period<sup>21</sup>.

### Treatment and Recurrence

Although treatment should be individualized, since it depends on several factors, such as age, comorbidity, and tumor characteristics, surgical excision is considered the gold standard when the tumor has a margin at least 2 cm<sup>18,22</sup>. However, limb amputation and radiotherapy or chemotherapy may also be indicated.

Amputation is convenient when Marjolin’s ulcer infiltrates more deeply, affecting bones and great vessels, with imaging examinations eventually being useful for detecting the degree of bone involvement<sup>14,20</sup>, infectious processes, and significant hemorrhage, and when excision of the lesion may generate greater functional disability<sup>17</sup>.

Radiotherapy may be indicated in cases of metastasis that cannot be surgically corrected, tumors larger than 10 cm with positive lymph nodes after dissection, and head and neck lesions with positive lymph nodes after dissection<sup>23</sup>.

Although chemotherapy is not always indicated, it may be convenient in situations in which the patient does not consent to surgical treatment, has distant metastasis, or experiences disease recurrence<sup>23</sup>.

A study analyzing 412 cases observed Marjolin's ulcer after surgical excision in 16% of reports. This result may be associated with some factors, such as male sex, cooking oil burn, and treatment neglect during the first injury and recurrence<sup>13,24</sup>.

A study in Egypt analyzing 26 cases of Marjolin's ulcer identified other factors as predictors of recurrence, such as young age at the time of diagnosis, malignancy in the nodal groups of lymphatic drainage, and the use of a flap or graft after wide excision<sup>20</sup>.

## CONCLUSION

This study analyzed the literature on Marjolin's ulcer resulting from malignancy of burn scars and discussed risk factors and topography, etiology, diagnosis and latency, and treatment and recurrence.

From the discussion of this review, it was possible to conclude that Marjolin's ulcer presents as malignant skin neoplasms that appear most frequently after thermal burns that require specific and individualized treatment since several factors influence the therapeutic plan.

Despite the need for histopathological confirmation, clinical suspicion together with anamnesis becomes necessary for an early diagnosis, which is essential due to the highly aggressive nature, metastatic potential, and high recurrence rate of Marjolin's ulcer, which in most cases is treated surgically. In more extreme cases of bone involvement, amputation becomes necessary to avoid worse conditions.

Thus, the knowledge of health professionals about Marjolin's ulcers is essential for a better prognosis so that possible cases of malignancy are not underestimated, appropriate therapy is implemented, recurrence is avoided, and prophylactic measures are implemented to effectively avoid burn and mitigate risk factors for malignancy.

Limitations of the present study include the low number of articles describing an epidemiological analysis with a more considerable sample in the analyzed period and the consideration of only Portuguese and English articles, which may have limited the search. Therefore, clinical studies and trials are needed to gain more comprehensive knowledge of Marjolin's ulcer.

## COLLABORATIONS

<b>TMV</b>	Data Curation, Methodology, Writing - Original Draft Preparation, Writing - Review & Editing
<b>MPFFA</b>	Writing - Original Draft Preparation
<b>BMC</b>	Writing - Original Draft Preparation
<b>SLC</b>	Writing - Original Draft Preparation
<b>MCFA</b>	Writing - Original Draft Preparation
<b>NGSO</b>	Review & Editing

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