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# Squamous cell carcinoma developed on inflammatory dermatoses followed at a tertiary hospital between the years 2000 and 2020

*Incidência de casos de carcinoma epidermoide desenvolvido sobre dermatoses inflamatórias, seguidos em um hospital terciário entre os anos 2000 e 2020*

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**ABSTRACT**

**Introduction:** The advent of squamous cell carcinomas (SCC) from chronic dermatoses is known but little explored. Although rare, tumors originating there have a worse prognosis, in part due to late diagnosis.
**Objectives:** This study aims to survey cases of squamous cell carcinoma developed on previous dermatoses diagnosed between 2000 and 2020 in a tertiary health service.
**Methods:** This is a quantitative and retrospective study through biopsy reports survey and medical records review.
**Results:** From an initial list of 11,249 histological reports compatible with squamous cell carcinoma, we obtained a final list of 10 patients. The study findings corroborate the literature regarding some known risk factors: abundant and chronic sun exposure, older than 50 years, lower skin phototypes, and immunosuppression. We also found a high frequency of smoking and lichenoid dermatoses (5/10 patients) in the studied population, including chronic cutaneous lupus erythematosus and hypertrophic lichen planus.
**Conclusions:** It is not possible to predict the primary risk factors for the development of squamous cell carcinomas regarding previous dermatoses, although there is a tendency for their appearance in lichenoid dermatoses and those with longer evolution.
**Keywords:** Skin diseases; Squamous cell carcinoma; Lupus erythematosus, Cutaneous; Lichen planus

**RESUMO**

***Introdução:*** *o advento de carcinomas epidermoides a partir de dermatoses crônicas é conhecido, porém pouco explorado. Embora raros, os tumores daí originados possuem pior prognóstico, em parte devido ao diagnóstico tardio.*
***Objetivos:*** *realizar o levantamento dos casos de carcinomas epidermoides desenvolvidos sobre dermatoses prévias, diagnosticados entre os anos 2000 e 2020, em um serviço terciário de saúde.*
***Métodos:*** *trata-se de um estudo quantitativo e retrospectivo, obtido a partir do levantamento de laudos de biópsias e revisão de prontuários.*
***Resultados:*** *a partir de uma lista inicial de 11.249 laudos histológicos compatíveis com carcinoma epidermoide, foi obtida uma lista final com 10 pacientes. Os achados do estudo corroboram a literatura quanto a alguns fatores de risco já conhecidos: exposição abundante e crônica ao sol, idade acima dos 50 anos, fototipos mais baixos e imunossupressão. Foi encontrada também uma alta frequência de tabagismo e de dermatoses liquenoides (5/10 pacientes) na população estudada, entre elas o lúpus eritematoso cutâneo crônico e o líquen plano hipertrófico.*
***Conclusões:*** *não é possível predizer os fatores de risco mais importantes para o desenvolvimento de carcinomas epidermoides sobre dermatoses prévias, embora haja uma tendência do seu aparecimento sobre dermatoses liquenoides, assim como naquelas de evolução mais longa.*
***Palavras-chave:*** *Dermatopatias; Carcinoma de células escamosas; Lúpus eritematoso cutâneo; Líquen plano*

## Original Article

**Autores:**
Luana Rampazzo Magalhães[1]
Thais Helena Buffo[2]
Elemir Macedo de Souza[2]
Renata Ferreira Magalhães[2]
Andréa Fernandes Eloy da Costa França[2]
Rafael Fantelli Stelinit[3]

[1] State University of Campinas, Faculty of Medical Sciences – FCM, Campinas (SP), Brazil.
[2] State University of Campinas, Department of Dermatology – FCM, Campinas (SP), Brazil.
[3] State University of Campinas, Department of Pathological Anatomy – FCM, Campinas (SP), Brazil.

**Correspondence:**
Luana Rampazzo Magalhães
E-mail: luanarampazzo@gmail.com /l220565@dac.unicamp.br

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## INTRODUCTION

The advent of squamous cell carcinomas (SCCs) from chronic dermatoses is a known, although little explored, phenomenon. Marjolin's ulcer is the name for the malignant transformation that occurs in chronic ulcers and burn scars. Although rare, SCCs originating there have a worse prognosis, partly due to late diagnosis. Less reported is neoplastic transformation from inflammatory dermatoses. There is a description of the appearance of SCCs in lesions of discoid chronic lupus erythematosus, lichen planus, lichen sclerosus et atrophicus, hidradenitis suppurativa, and dystrophic epidermolysis bullosa.[1-12] The pathogenesis of SCCs arising from these dermatoses differs from the one related to chronic sun exposure, although the mechanism is not completely known. The most accepted theory is that the areas where the neoplasia occurs correspond to an "immunologically compromised skin territory".[12]

Therefore, many chronic inflammatory dermatoses require attention in their diagnosis and follow-up to obtain an early diagnosis if they progress to SCC. Studies of these lesions become extremely important, especially to identify additional factors that may predispose to SCC or clinical characteristics that allow for a faster diagnosis of the neoplasm, considering its worse prognosis. The present work aimed to survey and characterize cases of SCC developed over previous inflammatory dermatoses diagnosed between 2000 and 2020 in a tertiary hospital.

## METHODS

It is a quantitative and retrospective study that reviewed the medical records of patients followed up at a tertiary health service in the city of Campinas (SP, Brazil). To obtain the information, we conducted an initial survey by crossing the terms "squamous cell carcinoma" and "skin" described by the SNOMED system in the institution's database during the period. SNOMED is a standardized global nomenclature system for health terms used by the Department of Pathological Anatomy to classify histological reports. The institution's IT sector uses the SNOMED nomenclature to correlate histological reports with the clinical database, allowing for more reliable research. After applying the inclusion and exclusion criteria, we used successive filters to obtain a final list composed only of patients with histological reports of SCC who also had biopsies of diagnosed inflammatory dermatoses. We reviewed the medical records listed to identify the association between the SCC appearance and a previous dermatosis and collected data for analysis.

Regarding the medical records of patients who presented SCC due to a previous dermatosis, the following data were collected:

a) Epidemiological characteristics of the patient: gender, age at diagnosis of SCC, age at diagnosis of previous dermatosis, skin phototype/color, risk factors for the development of SCC (smoking, sun exposure);

b) SCC characteristics: location of the lesion, degree of differentiation, treatment performed, and evolution;

c) Characteristics of previous dermatosis: diagnosis, time of evolution, treatments with immunosuppressant and response, and post-neoplasia evolution.

The inclusion criteria in the study were: a) individuals with anatomopathological reports compatible with cutaneous SCC, conducted at the institution's Pathological Anatomy Service, who had a follow-up of the neoplasia at the same hospital. There was no minimum or maximum age for inclusion in the study. Patients with a histological diagnosis of mucosal SCC, SCC arising from chronic scars – such as ulcers and burns – and SCC associated with genetic syndromes that predispose to photosensitivity or DNA repair defects, such as xeroderma pigmentosum and epidermodysplasia verruciformis, were not included in the study.

We submitted the study to the Research Ethics Committee before data collection.

Descriptive analyses of the prevalence of SCC related to previous inflammatory dermatoses were conducted.

## RESULTS

The initial search results from crossing the terms "squamous cell carcinoma" and "skin" from the SNOMED system generated a list of 11,249 histological reports recorded between 2000 and 2020.

We applied the inclusion and exclusion criteria to this list, as well as successive filters. Histological reports identified from the following filters remained on the list: hyperplasia, fibrosis, wart, Bowen's disease, papilloma, morphological description only, ulcer, vascularization without evidence of malignancy, and deposition of foreign materials. Histological reports identified from the following filters were removed from the list: lipoma, lentigo, sebaceous adenoma, trichoepithelioma, nevus, cyst, melanosis, metastatic neoplasm, keratoacanthoma, basal cell carcinoma, keratosis, fibrous histiocytoma, and sarcoma. After grouping SCC cases by patient, we found 2,296 eligible individuals diagnosed with SCC between 2000 and 2020 (Table 1).

After excluding patients who only had histological reports compatible with SCC, we applied new filters until we obtained a list of patients with histological reports of SCC and "chronic inflammation" or some dermatological diagnosis. We reviewed these descriptions of the histological reports until we obtained a final list of 10 patients. Table 2 shows the epidemiological characteristics of these patients, in addition to the SCCs features and possible factors related to the development of neoplasms (Table 2).

The data obtained allowed us to classify the SCC cases into two groups based on the type of previous dermatosis: a) SCC from lichenoid dermatoses, which included four cases of chronic lupus erythematosus and one case of hypertrophic lichen planus (Figures 1 and 2); and b) SCC from other inflammatory dermatoses, which included diseases such as hidradenitis suppurativa, psoriasis, etc.

**Table 1: Distribution of cutaneous SCC cases reported at HC Unicamp between 2000 and 2020**

| Distribution of cutaneous SCC cases reported at HC Unicamp between 2000 and 2020 | |
|---|---|
| Parameter N | N = 2296 |
| Age (mean ± DP years) | 69.3 ± 13.85 |
| Sex (F/M) | 1056 (46%) /1240 (54%) |
| Number of SCCs per patient (average) | 2.2 |

**Table 2: Data on patients with cutaneous SCC resulting from a chronic inflammatory lesion, between the years 2000 and 2020**

| Patients with cutaneous SCC resulting from a chronic inflammatory lesion | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **N** | **Sex** | **Prior diagnosis** | **SCC diagnosis (years)** | **Evolution time for SCC (years)** | **Skin color** | **SCC site** | **Evolution** | **Risk factors** |
| 1 | M | Hypertrophic lupus erythematosus | 55 | 20 | White | Head and neck | Favorable | Sun exposure Smoking |
| 2 | M | Hypertrophic lupus erythematosus | 54 | 24 | Brown | ul | Favorable | Sun exposure Smoking |
| 3 | F | Hypertrophic lupus erythematosus | 51 | 2 | White | Head and neck | Unfavorable | Sun exposure Smoking |
| 4 | F | Hypertrophic lupus erythematosus | 55 | 24 | Brown | Head and neck | Favorable | Sun exposure Smoking |
| 5 | M | Hypertrophic lichen planus | 23 | 4 | Brown | ll | Unfavorable | ⋆ |
| 6 | F | Vitiligo | 56 | 38 | White | ul | Unfavorable | Sun exposure |
| 7 | M | Hidradenitis | 56 | 10 | White | Genital | Unfavorable | Immunosuppression Smoking⋆ |
| 8 | M | HIV + HPV | 33 | 12 | White | Genital | Unfavorable | Immunosuppression Sun exposure Smoking |
| 9 | F | Psoriasis | 67 | 54 | White | ul | Favorable | Immunosuppression ⋆ |
| 10 | M | Erythrodermic psoriasis | 49 | 17 | White | ul | Unfavorable | Immunosuppression Smoking⋆ |

*ul: upper limbs. ll: lower limbs; ⋆no information on smoking and/or sun exposure in the medical records*

## DISCUSSION

Based on the results of the present study, we observed the rarity of cases of SCC that result from an injury caused by chronic inflammation. Although it was not the object of the research, we found three patients with Marjolin ulcers, demonstrating that the case series of SCC from inflammatory dermatoses in the studied period was higher.

The data found corroborates the literature regarding some risk factors for SCC: abundant and chronic sun exposure (six patients), age over 50 years (eight patients), lower skin phototypes (seven patients), smoking (seven patients), and immu-

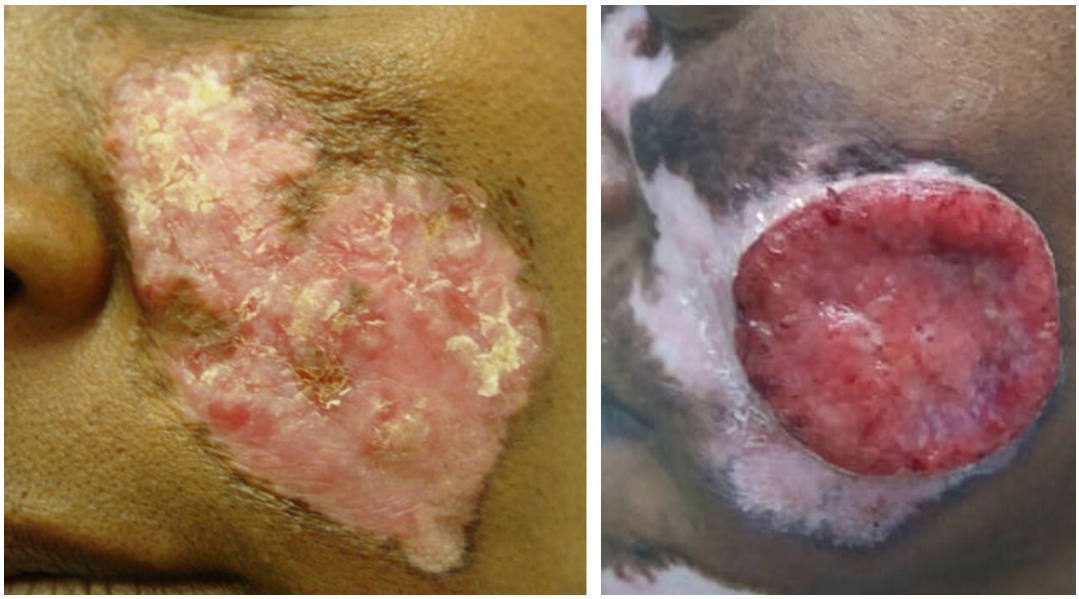

**Figure 1:** Patient with hypertrophic lupus erythematosus (left) with transformation to squamous cell carcinoma (right)

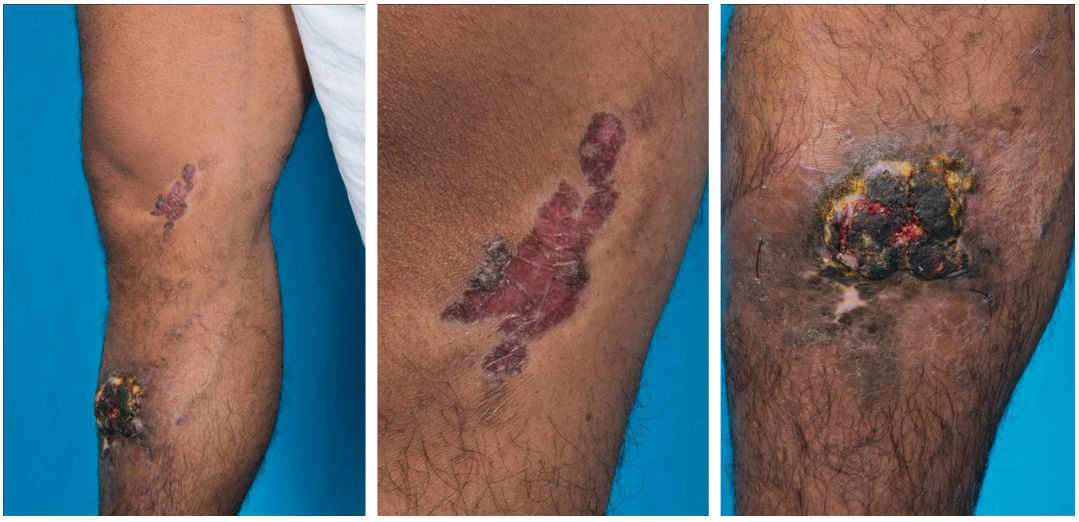

**Figure 2:** Patient with lichen planus with transformation to squamous cell carcinoma (left). Detail of the lichen planus lesion (center). Detail of squamous cell carcinoma (right)

nosuppression (four patients). It is worth mentioning that the immunosuppression found was related to the use of the following medications: methotrexate, cyclosporine, and antiretroviral therapy, involving patients with psoriasis, hidradenitis, and one with HIV infection. On the other hand, although the literature indicates that men are more predisposed to SCC, the present study showed men:women ratio of 3:2, lower than that described in the literature. In addition to the already known risk factors for the development of cutaneous SCC, there was a prevalence of lichenoid dermatoses (five patients) in the studied population concerning all other inflammatory dermatoses.

The SCC occurrence is usually a late event in the evolution of chronic cutaneous lupus erythematosus (CCLE) lesions. Despite this, lupus patients have a 3.6 times higher risk of developing non-melanoma skin cancer. The places most affected by SCC in these patients are those most frequently exposed to sunlight.

Factors predisposing to the transformation of CCLE into SCC include HPV infection, exposure to ultraviolet light, long-term immunosuppressive therapy, scars, and chronic conditions. Such conditions promote the development of keratinocytes with an activated immunophenotype that precedes malignancy.1-5

The relationship between CCLE and SCC is not easy to identify due to the varied clinical presentation. Histological confirmation is essential, although LE may present changes that mimic SCC, especially in its hypertrophic form.

SCC secondary to inflammatory processes such as cutaneous LE has a higher metastasis rate than those that usually develop from sun damage alone. Therefore, early diagnosis is critical to identify suspicious lesions in these patients rapidly, thus avoiding greater involvement of the individual's skin and offering faster and more effective treatment, which involves less morbidity and mortality.

Regarding lichen planus (LP), neoplastic transformation over oral disease lesions has been described, with a rate ranging from 0.3% to 3%, and oral LP is considered pre-neoplastic dermatosis. In its cutaneous form, this occurrence is considered fortuitous with less than 50 reports in the literature and a frequency of less than 0.4%. Nevertheless, hypertrophic LP is the presentation most associated with malignancy.[6-10]

For lichenoid dermatoses, it is believed that the chronic inflammatory state and accelerated cell renewal provide a fertile environment for the development of neoplasms. Cofactors, such as ionizing radiation, treatment with ultraviolet radiation, or immunosuppressant, can interfere with the condition's progression.

Conducting the study in a tertiary health service may overestimate the incidence of SCC in chronic inflammatory dermatoses, which is a limitation of the present study. Furthermore, the association with other dermatoses may be underestimated, such as, for example, SCC resulting from lichen sclerosus, as this pathology occurs preferentially in female genitalia and may be more present in gynecological care centers.

## CONCLUSION

The prevalence of SCC over chronic dermatoses is rare. Although risk factors such as smoking, chronic sun exposure, advanced age, and immunosuppression have been found in our population, it is not possible to state that they are the most important factors for the development of neoplasia. There is a tendency for SCCs to develop in lichenoid dermatoses as well as in longer-lasting dermatoses. ●

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## AUTHORS' CONTRIBUTION:


**Luana Rampazzo Magalhães** ORCID 0009-0001-6556-9877
Study design and planning; preparation and writing of the manuscript; collecting, analyzing and interpreting data; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review.

**Thais Helena Buffo** ORCID 0000-0002-6833-7596
Intellectual participation in propaedeutic and/or therapeutic conduct of studied cases.

**Rafael Fantelli Stelinit** ORCID 0000-0003-0618-1693
Intellectual participation in propaedeutic and/or therapeutic conduct of studied cases.

**Elemir Macedo de Souza** ORCID 0000-0002-3944-0711
Intellectual participation in propaedeutic and/or therapeutic conduct of studied cases.

**Renata Ferreira Magalhães** ORCID 0000-0001-9170-932X
Intellectual participation in propaedeutic and/or therapeutic conduct of studied cases.

**Andréa Fernandes Eloy da Costa França** ORCID 0000-0003-1657-4570
Approval of the final version of the manuscript; study design and planning; effective participation in research orientation; critical review of the manuscript.