

# Limb amputation for squamous cell carcinoma of the skin - factors involved in this poor evolution

## *Amputação de membros por carcinoma escamocelular da pele - fatores envolvidos nesta evolução desfavorável*

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### A B S T R A C T

**Objective:** To retrospectively analyze a series of cases culminating in amputation for advanced squamous cell carcinoma. **Methods:** We studied eight patients with histologically confirmed squamous cell carcinoma of the skin that had limbs amputated by tumor invasion at our institution between 2005 and 2008. We evaluated the histological factors and the institutional and psychosocial factors that contributed to this unfavorable outcome. **Results:** The mean age at diagnosis was 63 years, 37.5% of patients (three patients) had a history of abusive and continuous exposure to sunlight and six (75%) patients had other risk factors for SCC of the skin. Seven patients were diagnosed when the tumor was already larger than 2cm, and it required a large period of time (6.7 years on average) between the onset of the initial lesion and the correct histopathological diagnosis of locally advanced tumor. **Conclusion:** The unfavorable outcome (amputation) in patients with squamous cell carcinoma may be associated with aggressiveness of cancer and related comorbidities, and may also be influenced by factors such as access to public health, quality of care and patient's relationship with the disease.

**Key words:** Patients. Amputation. Histology. Skin neoplasms. squamous cell carcinoma.

### INTRODUCTION

Squamous cell carcinoma (SCC) is an atypical proliferation of spinous cells of the skin, with invasive character and metastatic potential<sup>1-5</sup>. It Represents approximately 15% of malignant neoplasms of the skin. It is the second most common type of cancer in fair-skinned people and the most common in people with dark skin<sup>6,7</sup>, and is increasing in epidemic proportions frequency<sup>6</sup>. It can occur in normal skin, although it most often originates in previous cutaneous lesions, such as solar keratosis, leukoplakia and radiodermatitis. SCC is more common after 50 years of age in men, usually by a greater exposure to the sun. People with fair skin and immunosuppressed patients are also more susceptible<sup>8-10</sup>. The lesions usually develop in areas exposed to ultraviolet radiation (UVR) as the lower lip, face, upper limbs and neck, or in areas of previous injuries, such as scars and chronic ulcers<sup>8-10</sup>.

In the skin SCC usually begins as an infiltrated, keratotic, indurated or nodular, area, which gradually increases in size and subsequently ulcerates. Metastases

can occur after months or years of illness, being more frequent and precocious in mucosal and hands disease<sup>2,11,12</sup>.

Histologically, the malignant epithelial cells extend deep into the dermis as masses or trabeculae. In SCC of low-grade malignancy cells can be relatively well-differentiated, resembling mature squamous cells and can produce keratin and the typical corneal pearls. In high-grade lesions these epithelial cells can be extremely atypical, with figures of mitoses and abnormal absence of keratinization<sup>1,3-5</sup>.

Most cases have a favorable outcome when followed and treated appropriately. The tumor has idle and not aggressive characteristics in most cases, with a relatively long time for diagnosis and treatment before the member is significantly compromised, requiring amputation. The treatment depends basically on the size of the lesions, since in early ones (<1cm) electrocoagulation is acceptable for locoregional control; in larger lesions resection is desirable with a minimum margin of 0.5 cm, both laterally and deeply. Amputation is not the rule, being used only in advanced cases<sup>13</sup>. Most patients with SCC are successfully

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treated in the clinic, with excellent cosmetic and functional results. The objective of this study was to retrospectively analyze a series of cases culminating in amputation, evaluating the histologic, institutional and psychosocial factors contributing to this unfavorable outcome.

## METHODS

We studied patients with histologically confirmed squamous cell carcinoma of the skin subjected to amputation of one or more limbs by the staff of General Surgery of our institution due to advance of local disease, between the years 2005 and 2008. Data were collected through review of medical records and / or interviews with the patients. The project was approved by the Ethics in Research Committee of Alberto Cavalcanti Hospital (FHEMIG). We collected data on age, sex and origin, and evaluated the following risk factors for squamous cell carcinoma of the skin: history of previous skin lesions, immunosuppression, comorbidities<sup>8-10</sup>, plus information on the tumor itself and its treatment, including resection and postoperative outcome.

## RESULTS

Between 2005 and 2008, eight patients underwent amputation of upper and lower limbs due to locally advanced squamous cell carcinoma. The average age was 63 years (44-83 years) and six patients (75%) were men. Regarding the type of skin, four (50%) were Caucasian and four (50%) Brown. Three (37.5%) patients had continuous exposure to sunlight, and three (37.5%) patients used sunscreen. With regard to other risk factors for SCC, three (37.5%) had exposure to carcinogens (pesticides, hydrocarbons, solvents), two (25%) had a history of sunburn and one (12.5%) was immunocompromised due to a

previous transplant. Regarding lifestyle, four (50%) were smokers or former smokers and three (37.5%) were alcoholics or former alcoholics. Six (75%) patients had previous cutaneous lesions such as keratoses and two (25%) had chronic wounds. As for comorbidities, two (25%) were diabetic and five (62.5%) hypertensive. The characteristics of interest of the patients are grouped in Table 1. The average time between the beginning of the lesion and the histopathologic diagnosis of advanced disease was 6.7 years (81.3 months). The initial diagnosis was correct in seven (87.5%) patients, one having initially received the wrong diagnosis of actinic keratosis; six (75%) patients continued medical care after diagnosis (Table 2). The median time between diagnosis of advanced disease and amputation was 1.01 years (12,14 months). The time from the indication of amputation and the operation in our hospital was less than 20 days in all cases. The lesion was diagnosed early, i.e., less than 2 cm, in only one case (12.5%) and in the seven (87.5%) remaining the primary tumor was greater than 2 cm. The seven patients with more severe injuries had symptoms such as intractable pain, foul smelling and bleeding, having been referred to our tertiary center for evaluation of amputation.

The initial tumor was limited to the skin in three (37.5%) patients, while in five (62.5%) presented with deep invasion (nerves and vessels). Regarding the number of lesions, seven (87.5%) had only one. The upper limb was the initial location of the tumor in six (62.5%) patients and two (25%) had a lesion in the lower limb. The initial tumor size was between 2 cm and 5 cm in two (25%) patients, and greater than 5cm in five (62.5%). In three (37.5%) patients, amputation was the initial therapy, not having been submitted any conservative treatments (resection, cauterization or radiotherapy). Four patients (50%) were subjected to one or more previous operations, and one (12.5%) to radiotherapy. The reconstruction was performed with a grafting one (12.5%) patient and no flap was performed. Of the patients submitted to previous treatments,

**Table 1** – Characteristics of patients.

Characteristics	Number de Patients	%
<b>Gender</b>		
Male	6	75
Female	2	25
<b>Type of Skin</b>		
White	4	50
Black	0	0
Brown	4	50
<b>Smoker or ex-smoker</b>		
Yes	4	50
No	4	50
<b>Alcoholic or ex-alcoholic</b>		
Sim	3	37.5
Não	5	62.5

**Table 2 –** Characteristics related to time interval.

From lesion diagnosis to histopathology	Number of patients	%
<6 months	1	12.5
6 months -1 year	1	12.5
1 to 2 years	0	0
2 to 5 years	2	25
>5 years	3	37.5
Non-specified	1	12.5
<b>From lesion diagnosis to amputation</b>		
1-4 months	4	50
4-6 months	0	0
6 months -1 year	0	0
>1 year	3	37.5
Non-specified	1	12.5

two (25%) displayed early relapse. Six patients (75%) had moderately differentiated tumors and two (25%), well-differentiated. When there was any resection prior to amputation, five patients (62.5%) had free margin at histopathologic examination, one (12.5%) had positive lymph node and one patient had tumor infiltration in the resected margin. There was no report on tumor infiltration in two patients.

Tumor size ranged between 5cm and 10cm in six (75%) patients and in two patients it was greater than 10cm. All patients underwent amputation of the affected limb. Amputation was performed with curative intent in seven (87.5%) patients, and palliative (hygienically) in one (12.5%) (Figure 1). The affected limb's function was normal prior to the procedure in five (62.5%) individuals and significantly limited in three (37.5%) (Figure 2). Disarticulation was performed in seven (87.5%) patients. Fingers or the hand were resected in two (25%) patients, the forearm in two (25%), the arm in two (25%) and two (25%) patients had amputated foot or toes. Seven (87.5%) patients received antibiotic therapy prior to amputation.

## DISCUSSION

The squamous cell skin carcinoma is a malignant tumor of low aggressiveness and moderate metastatic potential<sup>11-15</sup>, allowing it to be healed when early treatment is instituted, which consists of resection of the lesion with clear margins<sup>4,11,15</sup>. Even with the late diagnosis of more advanced lesions, there is still a chance of cure, which, however, requires extended resections, with higher functional sequelae.

It is known that the aggressiveness of cancer and related comorbidities contribute to an unfavorable outcome (amputation) in patients with squamous cell carcinoma, as is well established that the desmoplastic growth and thickness of the lesion are independent risk factors for the occurrence of metastases and relapses<sup>4,11,15</sup>.



**Figure 1 -** Advanced, infiltrative and necrotic neoplasia in the right leg of a patient in an area with a prior burn injury.

An important aspect of this paper is to raise the discussion of other factors associated with limb amputation for locally advanced lesions, such as access to public health, health care quality and patient's relationship with the disease. Because it is a study with a small number of cases, further works and analyzes are needed to establish statistical correlations and quantify the impact of these factors in patients with advanced skin cancer. Histological types that are more aggressive and more prone to greater local spread and metastasis are described in several papers<sup>2,9,12,13</sup>. In this series, most patients had more indolent tumors of long-



**Figure 2** - Vegetating, ulcerated and necrotic lesion (SCC) affecting the left arm of a patient.

term evolution. Only one patient, renal transplant, had a more aggressive tumor behavior, with less than six months. This patient with skin type 1, blond and blue eyes, had a history of multiple malignant and premalignant skin lesions. There was a large deterioration in the number and aggressiveness of skin lesions after the use of immunosuppressive drugs to control rejection after transplantation, suggesting that the rapid spread and aggressiveness of the tumor would be more associated with immunosuppression of the patient, not the biological characteristic of neoplasias.

The remaining patients had differentiated or moderately differentiated tumors, with no cases of undifferentiated or unrated tumors. The undifferentiated tumors, thicker, with desmoplastic growth and recurrent, and the tumors that develop on scars, have more aggressive behavior, a higher propensity for local invasion, recurrence and metastases<sup>4,11,15</sup>.

Many patients have the prognosis aggravated by problems arising from limited resources or access to public health. When the disease is properly diagnosed at an early stage, resection or cauterization are possible, and can be performed at the clinic by a general practitioner, dermatologist or surgeon, with a good prognosis for the patient.

What happens is that in many cases the patient, even with a presumed diagnosis of skin cancer, is awaiting surgery for a long time due to bureaucratic procedures, leading to the development of more advanced lesions, with secondary infection and involvement of deep structures, such as nerves, tendons, vessels and bones. By

that time the patient is usually referred to a tertiary center, which often does not have a surgical oncology service. The orthopedist is more focused on amputations due to bone disease and is not confronted with resections of skin compromising the reconstruction tissue and the covering of the stump. Most of general and plastic surgeons do not routinely perform amputations, sometimes tending to carry out more conservative resections, which do not respect oncological principles. Thus, the patient often loses the chance to receive appropriate treatment with curative proposal, with less morbidity and limitation of consequences.

The psychosocial factors that impacted the treatment of these patients should also be discussed. None of the patients who underwent amputation had family income above five minimum wages or level of education as a high school degree or higher, hampering the understanding of disease severity and importance of early treatment.

In our series of eight cases, most patients (six) had other known risk factors for SCC in addition to sun exposure. The average time from onset of injury to definitive diagnosis (histopathological) was relatively long (almost seven years). Only one patient had diagnosis and treatment performed early, i.e., with lesions smaller than 2cm. Most patients had locally advanced lesions affecting bones, vessels and nerves (stage T4)<sup>15</sup>, with partial loss of limb function (Figure 2).

Patients with advanced lesions (> T2) are at high risk of locoregional and metastatic spread<sup>11,15</sup>, emphasizing the importance of early diagnosis and appropriate surgical approach, avoiding outcomes such as amputation or death in patients with a disease of indolent local behavior in most cases.

Amputation is a procedure of considerable functional, psychological and social impact for the patient. Individuals who have acute illnesses that compromise the member, as sudden vascular insufficiency, trauma and even some aggressive bone tumors, have no options or time to develop complex feelings about the amputation. Patients with chronic diseases, including recurring SCC, on their turn, live with these problems for months, years or even decades. These patients try to deny and delay amputation as long as possible, possibly due to the prolonged evolution of the tumor, even in locally advanced and terminal cases. Thus, patients are often treated in advanced stages, leading to a greater chance of local recurrence and lymph node metastasis, cutaneous or distant<sup>11,15</sup>.

The unfavorable outcome (amputation) in patients with squamous cell carcinoma, in addition to being associated with the aggressiveness of cancer and related comorbidities, may still be influenced by other factors, such as access to public health, quality of care and patient's relationship with the disease.

## R E S U M O

**Objetivo:** Analisar retrospectivamente uma série de casos que culminaram em amputação por carcinoma escamocelular avançado. **Métodos:** Foram estudados oito pacientes com diagnóstico histológico de carcinoma escamocelular de pele que tiveram membros amputados por invasão tumoral, em nossa Instituição entre 2005 e 2008. Foram avaliados: fatores histológicos, institucionais e psicossociais que contribuíram para este desfecho desfavorável. **Resultados:** A média de idade ao diagnóstico foi 63 anos; 37,5% dos pacientes (três pacientes) tinham exposição abusiva e contínua aos raios solares, e seis (75%) pacientes tinham outros fatores de risco para CEC de pele. Sete pacientes foram diagnosticados quando o tumor já era maior que 2cm, e foi necessário um período grande de tempo (6,7 anos em média) entre o aparecimento da lesão inicial e o diagnóstico histopatológico correto do tumor localmente avançado. **Conclusão:** O desfecho desfavorável (amputação) nos pacientes portadores de carcinoma espinocelular pode estar associado à agressividade da neoplasia e às comorbidades relacionadas, podendo ainda sofrer influência de fatores como acesso à saúde pública, qualidade da assistência médica e relação do paciente com a doença.

**Descritores:** Pacientes. Amputação. Histologia. Neoplasias de pele. Carcinoma escamocelular.

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