CUTANEOUS SQUAMOUS CELL CARCINOMA AT NATIONAL HOSPITAL OF DERMATOLOGY AND VENEREOLOGY: A FOLLOW-UP RETROSPECTIVE STUDY

Nguyen Dinh Quan[1,*], Ta Thi Ha Phuong[1], Le Thanh Hien[1], Nguyen Hong Son[1], Nguyen Huu Quang[1], Vu Dinh Tam[1]

ABSTRACT

Objectives: This study assessed the postoperative follow-up attendance of patients with cutaneous squamous cell carcinoma (cSCC) who underwent management at the National Hospital of Dermatology and Venereology, following the protocol based on the American Academy of Dermatology (AAD) guidelines of care for the management of cutaneous squamous cell carcinoma in 2018 and the classification of low and high-risk cSCC according to the National Comprehensive Cancer Network (NCCN).

Materials and methods: A retrospective study involving 60 cSCC patients was conducted. The monitoring included recurrent cancerous lesions, new cancerous lesions (cSCC, BCC, melanoma, and other types), detection of metastatic lesions (lymph node and distant metastases), late complication monitoring (bad scarring), and mortality monitoring.

Results: Depending on their stage and risk factors, cSCC patients underwent tumor removal by wide local excision (61.7%) or Mohs surgery (38.3%). Regional lymph node screening for metastasis included clinical examination, ultrasound, cytology, or sentinel lymph node biopsy (SLNB). Distant metastases in cSCC were infrequent, accounting for 1.7%, mainly presenting as lymph node metastases (6.7%). Patients were re-examined at least 5 years after treatment, revealing 4 of 56 patients with lymph node metastasis, 1 with bone metastasis, and 4 in the high-risk group who succumbed in the subsequent period.

Conclusions: The management of cSCC, following the AAD guidelines and risk classification by NCCN, is effective, with treatment modifications as needed and strict monitoring being imperative.

Keywords: *Cutaneous squamous cell carcinoma (cSCC), high-risk cSCC, sentinel lymph node biopsy, complete lymph node dissection.*

[1]: The National Hospital of Dermatology and Venereology
** Correspondence: drdinhquan@gmail.com*
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1. INTRODUCTION

Cutaneous squamous cell carcinoma (cSCC) is a prevalent and potentially aggressive form of skin cancer that necessitates meticulous management to ensure optimal patient outcomes. The intricacies of cSCC treatment have been considerably refined over time, guided by comprehensive protocols and guidelines. Among these, the "Guidelines of care for the management of cutaneous squamous cell carcinoma in 2018" issued by the American Academy of Dermatology (AAD) stand as a pivotal resource for clinicians. The recommendations within these guidelines, coupled with the risk stratification system provided by the National Comprehensive Cancer Network (NCCN), offer a standardized and evidence-based approach to cSCC diagnosis, treatment, and follow-up.[1,2,3]

The 2018 AAD guidelines encapsulate a multidimensional approach to cSCC management, addressing risk factors, therapeutic interventions, and the postoperative phase. Crucially, these guidelines prioritize risk-based stratification, acknowledging that the complexity of cSCC necessitates tailoring interventions to the specific characteristics and potential aggressiveness of each case. The NCCN complements these guidelines by providing a systematic classification of cSCC into low and high-risk categories, incorporating factors such as tumor size, depth of invasion, and histological characteristics. This risk stratification enables clinicians to discern the appropriate level of intervention for each patient, striking a delicate balance between efficacy and avoiding unnecessary overtreatment.[1,2,4,5]

While these guidelines have undoubtedly enhanced the standard of care for cSCC patients, there remains a critical need to scrutinize the outcomes of postoperative management rigorously[5]. The trajectory of patients after initial interventions, the recurrence rates, and the long-term implications of adherence to the recommended protocols necessitate a comprehensive and nuanced understanding. This study, therefore, embarks on a dedicated postoperative follow-up investigation, focusing on a cohort of patients who underwent cSCC management strictly aligned with the 2018 AAD guidelines and the NCCN risk classification. The primary objective of this research is to evaluate the effectiveness of the implemented management protocol by assessing postoperative outcomes, recurrence rates of patients with cutaneous squamous cell carcinoma (cSCC) who underwent management at the National Hospital of Dermatology and Venereology following the AAD guidelines and risk classification by NCCN.

2. MATERIALS AND METHODS

Study design

The study was conducted at the National Hospital of Dermatology and Venereology in Vietnam. This study was designed as a descriptive retrospective study.

Subjects

60 patients who were diagnosed, treated, monitored and managed according to the protocol in the Department of Plastic and Rehabilitation Surgery between 2016 and 2023 at National Hospital of Dermatology and Venereology, based on the AAD guidelines of care for the management of cutaneous squamous cell carcinoma in 2018. Patients with cSCC after being diagnosed based on clinical and histopathology will be treated and monitored according to the protocol (Diagram 1).

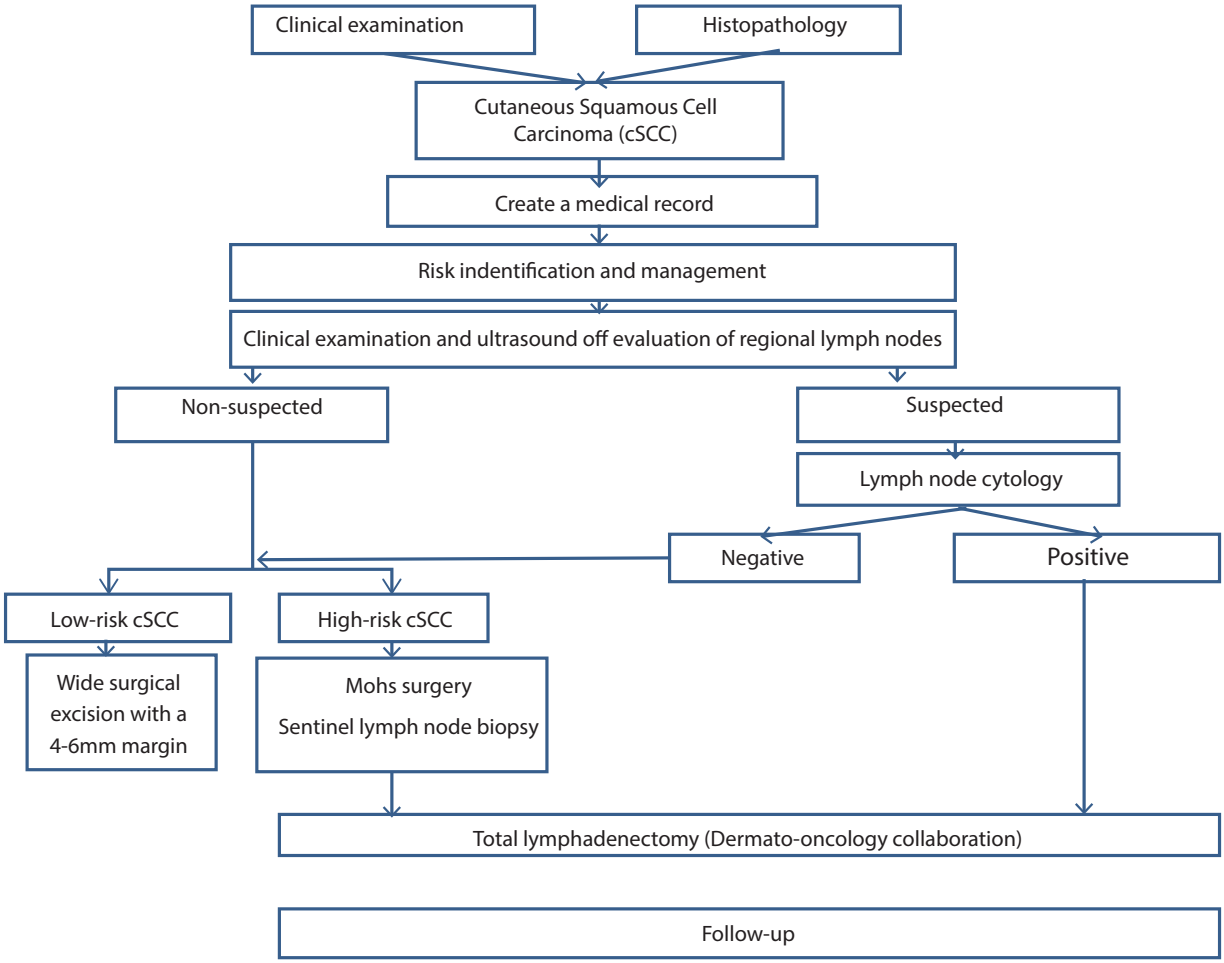

Diagram 1. Recommended protocol for management of cSCC at the National Hospital of Dermatology and Venereology

Based on clinical and histopathological features, cSCC patients are classified into 2 groups of low-risk cSCCs and high-risk cSCCs, according to the National Comprehensive Cancer Network Guidelines (Table 1) and are staged TNM (according to UICC-TNM 8) for treatment selection, monitoring and prognosis[1].

Table 1. National Comprehensive Cancer Network stratification of low versus high risk cSCC[2]

Parameters	Low risk	High risk
Clinical		
Location[*]/size[‡]	Area L <20 mm	Area L ≥20 mm
	Area M[‡] <10 mm	Area M ≥10 mm
		Area H[§]
Borders	Well defined	Poorly defined
Primary vs recurrent	Primary	Recurrent
Immunosuppression	No	Yes
Site of prior radiation therapy or chronic inflammatory process	No	Yes
Rapidly growing tumor	No	Yes
Neurologic symptoms	No	Yes
Pathologic		
Degree of differentiation	Well to moderately differentiated	Poorly differentiated
High-risk histologic subtype[‖]	No	Yes
Depth (thickness or Clark level)[¶]	<2 mm, or I, II, III	≥2 mm or IV, V
Perineural, lymphatic, or vascular involvement	No	Yes

[*]Area L consists of trunk and extremities (excluding hands, feet, nail units, pretibia, and ankles); area M consists of cheeks, forehead, scalp, neck, and pretibia; and area H consists of central face, eyelids, eyebrows, periorbital skin, nose, lips, chin, mandible, preauricular and postauricular skin/sulci, temple, ear, genitalia, hands, and feet.

[†]Greatest tumor diameter, including peripheral rim of erythema.

[‡]Location independent of size may constitute high risk.

§Area H constitutes high-risk on the basis of location, independent of size.

[‖]Adenoid (acantholytic), adenosquamous (showing mucin production), desmoplastic, or metaplastic (carcinosarcomatous) subtypes.

[¶]A modified Breslow measurement should exclude parakeratosis or scale/crust and should be made from base of the ulcer is present. If clinical evaluation of incisional biopsy suggests that microstaging is inadequate, consider narrow-margin excisional biopsy.

Procedures

After treatment, patients were monitored every 3 months for the first 2 years, once every 6 months for the next 2 years and once every 1 year from the 5th year onwards. Patients were monitored for recurrent cancerous lesions, new cancerous lesions (including cSCC, BCC, melanoma, and other types of cancer), detection of metastatic lesions (lymph node metastases and distant metastases), late complication monitoring (bad scarring), mortality monitoring. At follow-up examination, we checked for local recurrence; regional lympho node metastasis by ultrasound and lympho node cytology or biopsy if needed. Moreover, chest x-rays and abdomen ultrasound were ordered also for distant metastatic detection[2,3].

Statistical analysis

The data were encrypted and analyzed using the statistical algorithm with SPSS 20.0.

Ethical approval

The study was approved by the Ethical Review Board of the National Hospital of Dermatology and Venereology, Vietnam, and written informed consent was obtained from all subjects before their enrollment in the study.

3. RESULTS

There are 60 cSCC patients have diagnosed and treated between 2016 and 2023 at National Hospital of Dermatology and Venereology. The median age was 64.2 years (lowest age was 39 years, highest was 95 years), male majority at 51.7%. In our study, up to 66.4% of patients were regularly exposed to direct sunlight for a long time and 21.7% of cases had a previous skin disease (burn scars, chronic skin disease such as pigmentosa, granular epidermal dysplasia, psoriasis, discoid lupus, lichen planus, chronic skin ulcers, radiation dermatitis) which are risk factors for cSCC[4] (Table 2).

Table 2. Characteristics of cSCC patients at NHDV

	n = 60
Age, average	64.2 years
Males	51.7%
Exposure to sunlight	66.4%
Previous skin diseases	21.7%
Immunodeficiency diseases	0

Of the 60 patients, low-risk cSCCs accounted for 8.3% (5/60) and high-risk cSCCs accounted for 91.7% (55/60). There were 5/60 patients needed to be tranfered to other department due to other medical conditions such as tuberculosis, diabetes mellitus, primary breast cancer and cSCC with bone metastases.

About tumor removal, low-risk cSCC patients were treated by wide local excision WLE (4 - 6mm normal skin around). Ideally, high-risk cSCC patients were treated by Mohs surgery. However, WLE was still choosen in some cases depending on the tumor location, tumor size and patient's choice. Mohs surgery was performed in 23/55 patients accounting for 41.8%, all of these patients had lesions in the facial area. WLE was performed in 32 out of 55 patients, accounting for 58.2% (as shown in Table 3).

Table 3. Treatment selection for cSCC patients (n = 60)

	n	**Wide local excision (WLE)**	**Mohs surgery**
Low-risk cSCC	5	5 (100%)	0 (0%)
High-risk cSCC	55	32 (58.2%)	23 (41.8%)

(Low-risk cSCC: Low-risk cutaneous squamous cell carcinoma; High-risk cSCC: High-risk cutaneous squamous cell carcinoma).

About lympho node screening, because cSCC has a low metastasis rate < 5%, imaging diagnosis to find out the metastasis for the whole body are not really necessary.[7,8] Therefore, we conducted a physical examination and ultrasound of regional lymph nodes for all cSCC patients, if there is a suspicious lymph node, we perform a fine-needle aspiration cytology (FNAC). With low-risk cSCCs, if the FNAC is negative with cancer cells, we continue follow-up without further intervention; if the FNAC is positive, we perform a total lymph node removal.[8,9] With high-risk cSCCs, if the FNAC is negative, sentinel lympho node biopsy (SLNB) was offered; if the SLNB is negative, continue follow-up without further intervention; if the FNAC is positive or SLNB is positive with cancer cells, we perform a complete lymph node dissection (CLND).[8,9] 18 out of 55 patients in the high-risk cSCC group underwent SNLB, of which 4 were positive, and these patients were then performed a CLND. We had 11 patients undergo CLND, these were low-risk cSCC patients with postitive FNAC and high-risk cSCC patients with positive FNAC or positive SLNB (as shown in Table 4).

Table 4. Lymph node screening of cSCC patients

	n	Sentinal lymph node biopsy		Complete lymph node dissection
		Positive	Negative	
Low risk cSCC	5	0	0	0
High risk cSCC	55	4	14	11
Total	n = 60			

(Low-risk cSCC: Low-risk cutaneous squamous cell carcinoma; High-risk cSCC: High-risk cutaneous squamous cell carcinoma).

About follow-up, after surgery (tumor removal and reconstructive operation), cSCC patients were monitored for postoperative complications (including early complications and late complications). About early complications, there were 4/56 cases reported including infection, delayed wound dose, and grafted skin necrosis in 4/56 patients (7.1%). About late complications, patients were monitored every 3 months in the first 2 years, every 6 months in the next 2 years and annual examination from the 5th year to find out recurrenences, new cutaneous cancers and metastasis (lymph node metastases, and distant metastases).[8,9,10] After treatment, there were 4 of 56 patients who suffered from lymph node metastasis and 1 patient has bone metastasis. In addition, there were 2 patients who were found out recurrence and 1 patient appeared new cSCC lesion. Unfortunately, 4 patients in high-risk group died including 1 patient who died due to distant metastasis and the remaining 3 patients died due to old (as shown in Table 5).

Table 5. Postoperative follow-up results in low-risk and high-risk cSCC patients

		Before treatment (n)	After treatment (n)
Lymph node metastasis	Low-risk cSCC	0	0
	High-risk cSCC	1	4
Distant metastasis	low-risk cSCC	0	0
	high-risk cSCC	1	1
Recurrence	low-risk cSCC	0	0
	high-risk cSCC	2	2
New lesions appear	low-risk cSCC	0	0
	high-risk cSCC	0	1
Death	low-risk cSCC	0	0
	high-risk cSCC	0	4

(Low-risk cSCC: Low-risk cutaneous squamous cell carcinoma; High-risk cSCC: High-risk cutaneous squamous cell carcinoma).

4. DISCUSSION

In this retrospective study, we followed 60 patients diagnosed with cutaneous squamous cell carcinoma (cSCC) at the National Hospital of Dermatology and Venereology between 2016 and 2023. The management approach was in adherence to the "Guidelines of care for the management of cutaneous squamous cell carcinoma" provided by the American Academy of Dermatology (AAD) and the risk stratification outlined by the National Comprehensive Cancer Network (NCCN).[1,2]

An essential aspect of our approach involved the NCCN risk classification, a framework we found to be suitable and necessary within the context of Vietnam. Unlike the TNM classification, which necessitates more time for patient assessment, the NCCN classification allows for a swifter determination of low or high-risk status, enabling the timely initiation of optimal treatments.[2] The classification into low or high-risk cSCC provided the foundation for consultations between patients and physicians to determine the most appropriate treatment course, aligning with the AAD guidelines.[1]

However, the practicality of adhering strictly to recommended treatments faced challenges, particularly concerning the financial capabilities of patients. In some instances, despite the classification of high-risk cSCC, practical considerations led to the selection of wide local excision (WLE) instead of Mohs surgery, and vice versa. Similarly, in cases of low-risk cSCC, financial constraints occasionally steered the choice toward Mohs surgery instead of WLE. This nuanced decision-making process underscores the complex interplay between clinical guidelines and real-world constraints.

Lymph node screening, a crucial component of postoperative follow-up, encountered difficulties in implementation. The shortage of the radioactive substance used in sentinel lymph node biopsy (SLNB) posed a challenge in executing this recommended screening procedure. Furthermore, patient follow-up presented obstacles due to low awareness and inadequate patient education, contributing to missed follow-up opportunities.[6,7,8]

Despite these challenges, the preliminary evaluation of the treatment and management of cSCC at the National Dermatology Hospital yielded encouraging results. The rates of lymph node metastases, distant metastases, recurrence, new lesions, and mortality due to the disease were 6.7%, 1.7%, 3.3%, 1.7%, and 1.7%, respectively. These outcomes align closely with findings from other relevant studies. However, it is imperative to acknowledge that further monitoring with a larger patient cohort is necessary for a more precise and comprehensive assessment.

In conclusion, while the initial results indicate positive outcomes in the treatment and management of cSCC at the National Dermatology Hospital, the study underscores the need for ongoing refinement and adaptation of clinical guidelines to address real-world challenges. The delicate balance between adhering to established protocols and accommodating practical considerations remains a critical aspect of providing effective and accessible care for cSCC patients. Future studies with expanded patient cohorts will contribute to a more robust understanding of the long-term outcomes and effectiveness of the implemented management protocols.

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