SQUAMOUS CELL CARCINOMA OF THE SKIN – EPIDEMIOLOGICAL DATA

IOANA-ALINA HALIP**, DAN VÂȚĂ*,**, IOANA-ADRIANA POPESCU*, LAURA STĂTESCU*,**, ADRIANA-IONELA PĂTRAȘCU*,**, ALINA STÎNCANU*, PAUL SALAHORU**, DOINIȚA TEMELIE OLINICI*,**, LAURA GHEUCĂ SOLOVĂSTRU*,**

Summary

Cutaneous squamous cell carcinoma is the second most common malignant tumor of the skin. Its development is closely linked to the patient's cumulative exposure to ultraviolet radiation through a mechanism that combines DNA damage with immunosuppression. The retrospective observational study included 38 patients diagnosed with squamous cell carcinomas (SCC) diagnosed histo-pathologically in the period 2015-2019 in the Dermatology Clinic, Emergency County Clinical Hospital "St. Spiridon", Iași. The data obtained indicated when comparing the frequency of cases with histopathologically diagnosed SCC according to the year of hospitalization, that the frequency of in situ SCC / Bowen's disease increased from 0% in 2015 to 14.29% in 2016, then decreased to 0% in 2017 and 2018, after which it increased significantly to 36.36% in 2019. In the age group 10-19 years, the metatypical form appeared significantly more frequently (33.33%) compared to 4.76% of cases with good CCS differentiated (Z = 1.67, p = 0.05) and compared to 0% of cases with moderately differentiated tumors (Z = 1.61, p = 0.047). In the age group 70-79 years, Bowen's disease appeared significantly more frequently (60%) compared to 14.29% with a well-differentiated form and compared to 0% with a metatypical form (Z = 1.70, p = 0, 04). The typical age at presentation for squamous cell carcinoma is about 70 years. However, this varies widely and in certain high-risk groups (eg organ transplant patients, patients with bullous epidermolysis), CCS often manifests at a much younger age.

Key words: *squamous cell carcinoma, epidemiology, histopathological distribution, Bowen's disease, prognosis.*

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Introduction and objectives

Cutaneous squamous cell carcinoma (SCC) represents 20% of the percentage of non-melanoma skin tumors [1, 2]. Its development is closely linked to the patient's cumulative exposure to ultraviolet radiation through a mechanism that combines DNA damage with immunosuppression. More than 1 million cases of CCS are diagnosed in the United States each year [3] and its incidence and prevalence are reported with increasing values [4]. Determining the number of SCCs is difficult because reporting these cases to cancer registries is not necessary and understanding the incidence is essential for planning prevention and treatment strategies and allocating medical resources.

The psychosocial impact on patients with skin tumors such as SCC is marked by emotional reactions such as anxiety, depression or post-traumatic stress [3, 5]. Although mortality from cutaneous CCS is only about 1-3%, the total number of deaths caused by cutaneous CCS has been estimated to be similar to the number of deaths caused by melanoma, because melanoma is uncommon [6, 7, 8, 9]. Forms of advanced cutaneous SCC have a worse prognosis, with 10-year survival rates being less than 20% for

* Dermatology Clinic, 'St. Spiridon' County Emergency Clinical Hospital, 700111 Iași
** 'Grigore T. Popa' University of Medicine and Pharmacy, Faculty of Medicine, 700115 Iași

patients with regional lymph node involvement and less than 10% for patients with distant metastases [10].

The present retrospective observational study aimed to show the profile of SCC skin tumors in the geographical area of Iași County. The main objective was to evaluate the clinical-pathological profile of SCC-type tumors in patients admitted to the Dermatological Clinic, for a period of five years at the County Emergency Clinical Hospital "Saint Spiridon", Iasi. Among the general objectives are the evaluation of the distribution by sex, age groups, environment of origin and the anatomical area of the main types of SCC confirmed histopathologically.

Materials and methods

The retrospective observational study included 38 patients diagnosed histopathologically with SCC between 01.2015-31.12.2019, in the Dermatology Clinic, Emergency County Clinical Hospital "St. Spiridon", Iași. The collection of information from the observation sheets respected both the type of information collected for each patient and the time intervals at which they were obtained.

The inclusion criteria were represented by patients with histopathological diagnosis with SCC, patients whose observation sheets or electronic files contained sufficient information so that their inclusion in the study was relevant. The exclusion criteria targeted patients whose observation sheets or electronic sheets did not contain sufficient information to make their inclusion in the study possible. After applying the selection criteria, a group of 38 patients was created who met all the specified conditions.

The factors studied included:

- non-parametric data of categorical variables: sex (female/male), environment (urban/rural), anatomical region (cephalic and cervical, anterior thorax and abdomen, posterior thorax and lumbosacral region, upper limbs without palmar area, lower limbs without plants, palmoplantar region, anogenital region, oral mucosa, tumor type confirmed by histopathological examination: in situ/Bowen's disease, well differentiated/keratoacanthoma, moderately differentiated, poorly differentiated, metatypical (patients included in the study presented one or two tumors diagnosed clinically and examined and histopathologically);
- parametric data - with patients in the following age groups: 0-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89, 90 -99 to identify tumor frequencies corresponding to these age groups.

Subsequently, we statistically analyzed the data obtained using the software STATISTICA var. 7.0. The research was carried out in accordance with the 1964 Helsinki Declaration and subsequent amendments and was approved by the Ethics Commission of the University of Medicine and Pharmacy "Grigore T. Popa" Iași and by the Ethics Commission of the Emergency County Clinical Hospital "St. Spiridon", Iași, through the ethics opinion in accordance with the Research Law no. 206 of 27 May 2004 on good conduct in scientific research, technological development and innovation, as well as with the European legislation in force (European Regulation 679) on the processing of personal data.

Results

Comparison of the frequency of cases with SCC diagnosed histopathologically according to the year of hospitalization (as shown in Table I and Fig. 1), showed that the frequency of in situ SCC / Bowen's disease increased from 0% in 2015 to 14.29% in 2016, then decreased to 0% in 2017 and 2018, after which it increased significantly to 36.36% in 2019 (compared to 0% in 2015, $Z = 2.02$, $p = 0.02$ and 0% in 2017 , $Z = 2.02$, $p = 0.02$). The frequency of well-differentiated SCC ranged from 44.44% to 71.43%, with no significant differences from one year to another; the frequency of poorly differentiated SCC occurred in only one case in 2017 and 2019, while the metatypic frequency of SCC occurred in only one case in 2016, 2017 and 2019.

The frequency of histopathologically diagnosed forms of SCC did not differ significantly depending on sex or environment of origin. Comparison of the frequency of SCC forms (Table II, Fig. 2) according to age groups highlighted a number of significant differences.

Table I. Distribution of squamous cell carcinomas diagnosed histopathologically during 2015-2019

SCC	Total	Year										Significant differences	
		2015		2016		2017		2018		2019			
		N	%	N	%	N	%	N	%	N	%	Z	p
1	5	0	0↓	1	14,29	0	0↓	0	0	4	36,36	2,02; 2,02	0,02; 0,02
2	21	5	55,56	5	71,43	4	44,44	2	100	5	45,45		
3	7	4	44,44	0	0↓	3	33,33	0	0	0	0↓	2,04, 2,47	0,02; 0,007
4	2	0	0	0	0	1	11,11	0	0	1	9,09		
5	3	0	0	1	14,29	1	11,11	0	0	1	9,09		
Total	38	9	100	7	100	9	100	2	100	11	100		

1: In situ/ Bowen's disease 2: Well differentiated/ keratoacanthoma 3: Moderately differentiated 4: Poorly differentiated 5: Metatypical

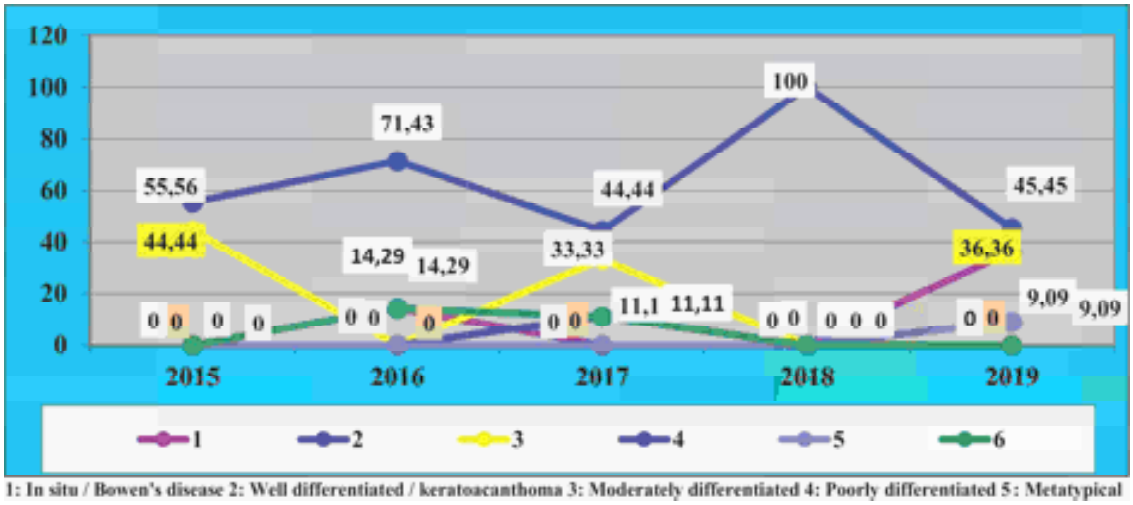


Fig. 1. Evolution of the frequency of SCCs diagnosed histopathologically, during the study

In the age group 10-19 years, metatypical SCC appeared significantly more frequently (one case out of 3 - 33.33%) compared to 4.76% (one case out of 21) in cases with well-differentiated CCS (Z = 1, 67, p = 0.05) and compared to 0% of cases with moderately differentiated SCC (Z = 1.61, p = 0.047); in the age group 30-39 years, metatypical SCC appeared significantly more frequently (2 cases out of 3 - 66.67%) compared to 0% of the cases with well differentiated (Z = 2.11, p = 0.017) and compared of 14.29% of cases with moderately differentiated SCC (Z = 2.32, p = 0.01); and in the age group 70-79 years, it appeared significantly more frequently differentiated moderate SCC (57.14%) compared to 0% with metatypic SCC (Z = 1.69, p = 0.045). In the age group 70-79 years, appeared significantly more frequently in situ SCC / Bowen's disease (60%) compared to 14.29% with well-differentiated SCC (Z = 2.18, p = 0.01) and compared of 0% with metatypic SCC (Z = 1.70, p = 0.04).

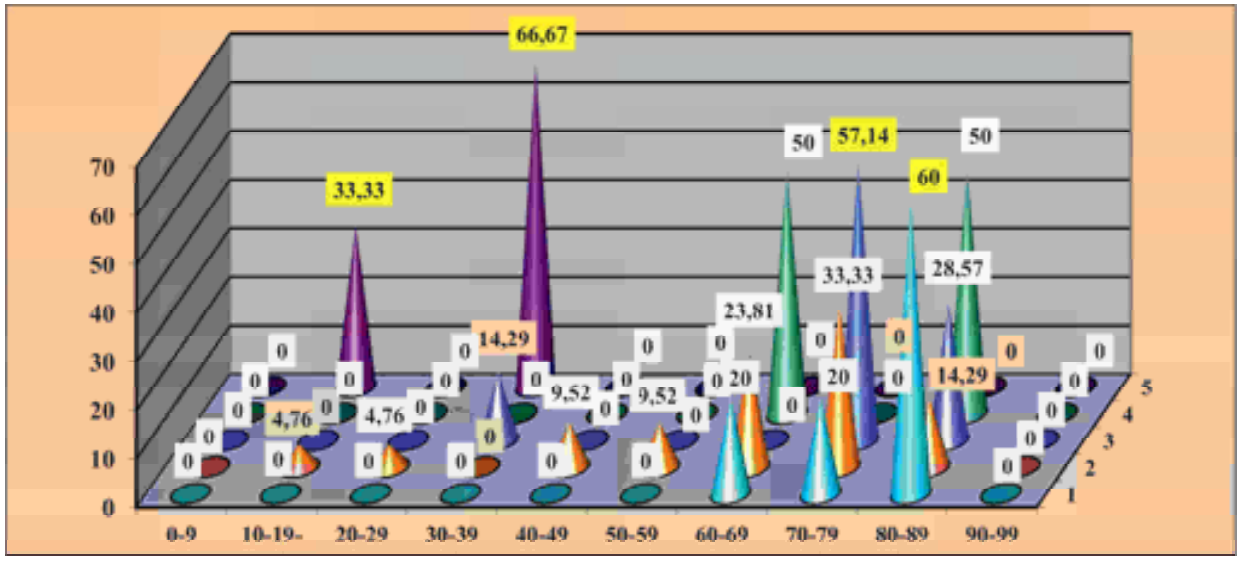
Comparison of the frequency of manifestation of SCC diagnosed histopathologically on different anatomical regions (Table III, Fig. 3) showed that SCC in situ / Bowen's disease appeared significantly more frequently on the lower limbs (without plants), 2 cases out of 2 (100%) compared to 2 cases out of 21 (9.52%) in the head and neck region, Z = 3.23, p = 0.0006.

Moderate differentiated SCC occurred significantly more frequently on the oral mucosa (one case in 1 compared to 5 cases in 21 in the head and neck region, Z = 1.67, p = 0.047; poorly differentiated SCC occurred only in the head and

Table II. Distribution of squamous cell carcinomas diagnosed histopathologically depending on age groups

Age groups	Histopathologically diagnosed squamous cell carcinomas										Significant differences	
	1		2		3		4		5			
	N	%	N	%	N	%	N	%	N	%	Z	p
0-9	0	0	0	0	0	0	0	0	0	0		
10-19	0	0	1	*4,76↓*	0	*0↓*	0	0	1	**33,33**	1,67; 1,61	**0,05; 0,047**
20-29	0	0	1	4,76	0	0	0	0	0	0		
30-39	0	0	0	*0↓*	1	*14,29↓*	0	0	2	**66,67**	2,11; 2,32	**0,017; 0,01**
40-49	0	0	2	9,52	0	0	0	0	0	0		
50-59	0	0	2	9,52	0	0	0	0	0	0		
60-69	1	20	5	23,81	0	0	1	50	0	0		
70-79	1	20	7	33,33	4	**57,14**	0	0	0	*0↓*	1,69	**0,045**
80-89	3	**60**	3	*14,29↓*	2	28,57	1	50	0	*0↓*	2,18; 1,70	**0,01; 0,04**
90-99	0	0	0	0	0	0	0	0	0	0		
Total	5	100	21	100	7	100	2	100	3	100		

1: In situ / Bowen's disease 2: Well differentiated / keratoacanthoma 3: Moderately differentiated 4: Poorly differentiated 5: Metatypical



1: In situ / Bowen's disease 2: Well differentiated / keratoacanthoma 3: Moderately differentiated 4: Poorly differentiated 5: Metatypical

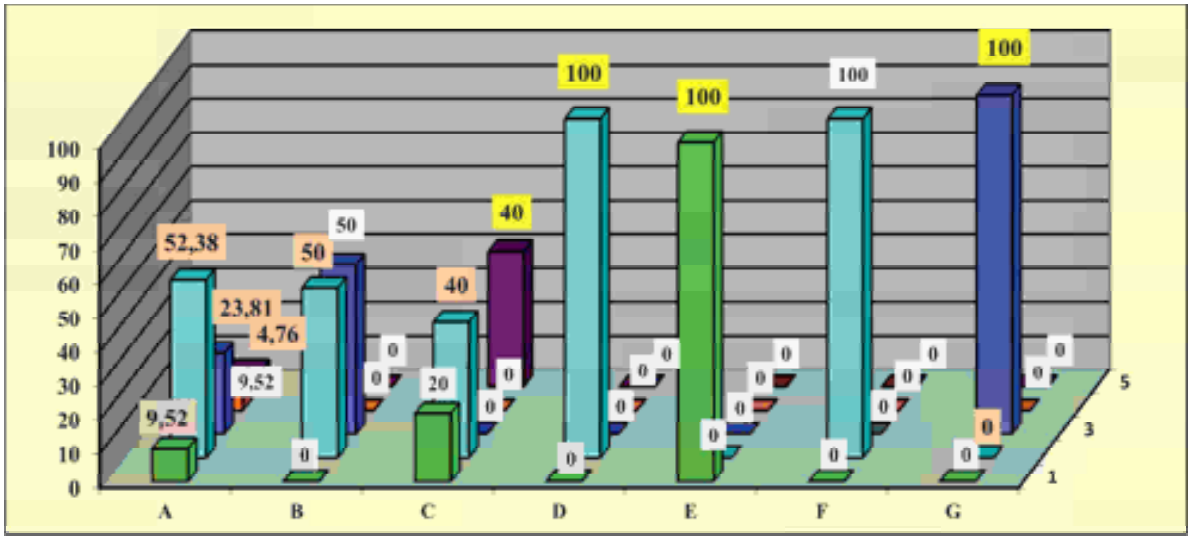
Fig. 2. Differences in the frequency of forms of CCS depending on age groups

neck area, 9.52% compared to 0% in the other anatomical regions, metatypic SCC occurred significantly more frequently in the posterior thoracic region + lumbosacral region, 2 cases out of 5 (40%) compared to a case out of 21 (4.76%) from the head and neck region, Z = 2.22, p = 0.01). Well-differentiated SCC was diagnosed significantly more frequently on the upper limbs (without palms), 5 cases out of 5 (100%) compared to 11 cases out of 21 (52.38%) in the head and neck region, Z = 1.97, p = 0.02, as well as compared to 1 case in 2 (50%) of the anterior thoracic region + abdomen, Z = 1.71, p = 0.04 (Table III, Fig. 3).

Table III. Distribution of squamous cell carcinomas diagnosed histopathologically depending on the anatomical region

SCC	Anatomical region														Significant differences	
	1		2		3		4		5		6		7			
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	Z	p
1	2	9,52↓	0	0	1	20	0	0	2	10 ↑	0	0	0	0	3,23	0,0006
2	11	52,38 ↓	1	50 ↓	2	40 ↓	5	10 ↑	0	0↓	2	10 ↑	0	0↓	1,97;1,71;2,0 ? 2,65;2,45	0,02;0,04;0,0 ? 0,004; 0,007
3	5	23,81 ↓	1	50	0	0	0	0	0	0	0	0	1	10 ↑	1,67	0,047
4	2	9,52	0	0	0	0	0	0	0	0	0	0	0	0		
5	1	4,76↓	0	0	2	40	0	0	0	0	0	0	0	0	2,22	0,01
Total	21	100	2	10 0	5	10 0	5	10 0	2	10 0	2	10 0	1	10 0		

1: In situ / Bowen's disease 2: Well differentiated / keratoacanthoma 3: Moderately differentiated 4: Poorly differentiated 5: Metatypical
Anatomical regions: 1: head and neck; 2: anterior thorax + abdomen; 3: posterior thorax + lumbosacral region; 4: palmo-plantar limbs; 8: oral mucosa



1: In situ / Bowen's disease 2: Well differentiated / keratoacanthoma 3: Moderately differentiated 4: Poorly differentiated 5: Metatypical
Anatomical regions: 1: head and neck; 2: anterior thorax + abdomen; 3: posterior thorax + lumbosacral region; 4: palmo-plantar limbs; 8: oral mucosa

Fig. 3. Differences in SCC frequency depending on the anatomical region

Discussions

Existing epidemiological data in specialized studies [12] illustrate that skin tumors are the most common forms of cancer, and SCC is the second most common skin neoplasm after basal cell carcinoma, the proportion being 1/5. It is also estimated that over 700,000 new cases of SCC are diagnosed annually in the United States. The incidence of SCC appears to be increasing from 50% to 200% over the last three decades [12].

However, there are reports that the incidence of SCC now appears to be increased and equal to that of basal cell carcinoma among the US population [13].

Causes of SCC include exposure to UV radiation, ionizing radiation, genodermatosis, human papillomavirus (HPV), substances such as arsenic, polycyclic aromatic hydrocarbons, immunosuppression, chronic ulcers, scars or pre-existing chronic dermatoses. In most cases it is due to the progressive mutagenic effects of exposure to ultraviolet radiation, noting the disposition on chronically exposed areas [11]. The incidence in males is higher, the data recorded in the literature [14] indicating a male / female ratio of 3/1, most likely due to longer lifetime exposure to ultraviolet radiation in males.

The classification of SCC based on the degree of histological invasiveness indicates SCC carcinomas in situ, in which changes in cellular atypia of the epidermis do not cross the basement membrane, while invasive forms of SCC show atypical cells that cross the basement membrane with the invasion of the underlying dermis. SCC in situ is commonly called Bowen's disease. The most common presentation of SCC in situ is that of erythematous-squamous plaque or a slightly elevated plaque that often appears on the sun-exposed skin of an elderly individual. However, it can develop in younger individuals with significant photodamage or even in places protected from the sun. SCCs frequently occur in preneoplastic lesions such as actinic keratoses or chronic ulcers. Bowen's disease can occur de novo or from pre-existing actinic keratosis [15]. In the present study, between 2015-2019 in the Dermatology Clinic, the County Emergency Clinical Hospital "St. Spiridon "from Iași, the analysis of the frequency of the histo-pathologically diagnosed forms of SCC did not differ significantly depending on the sex or environment of origin. When comparing the frequency of cases with SCC diagnosed according to the year of hospitalization, the results obtained indicated that the frequency of in situ SCC / Bowen's disease had an oscillating evolution. Thus, its frequency increased from 0% in 2015 to 14.29% in 2016, then decreased to 0% in 2017 and 2018, after which it increased significantly to 36.36% in 2019.

Also, the results of the current study revealed that in the age group 10-19 years, the metatypical form appeared significantly more frequently (33.33%) compared to 4.76% of cases with well-differentiated SCC ($Z = 1.67$, $p = 0.05$) and compared to 0% of cases with moderately differentiated tumors ($Z = 1.61$, $p = 0.047$). In the age group 70-79 years, Bowen's disease appeared significantly more frequently (60%) compared to 14.29% with a well-differentiated form and compared to 0% with a metatypical form ($Z = 1.70$, $p = 0, 04$). Other epidemiological studies have indicated that the incidence of SCC increases with age; the average age of onset is in the mid-1960s [14]. In recent years, the number of skin cancers in people aged 65 and over has increased dramatically, and the typical age at presentation for SCC is about 70 years. However, this varies widely and in certain high-risk groups (eg organ transplant patients, patients with bullous epidermolysis), carcinoma often manifests at a much younger age [13].

According to the staging of the National Comprehensive Cancer Network (NCCN) guideline, version 1.2021 [16], risk factors for classification as low, high and very high risk of recurrence include SCC including tumor parameters such as size (less than 2 cm, respectively, 2-4 cm with localization on the trunk and extremities), and with a diameter greater than 4 cm with any localization in the case of CSC tumors with a very high risk of recurrence. Bowen's disease occurred significantly more frequently on the lower limbs (without plants) than in the head and neck region ($Z = 3.23$, $p = 0.0006$); well-differentiated SCC appeared significantly more frequently on the upper limbs (without palms), respectively 5 cases out of 5 (100%) compared to 11 cases out of 21 (52.38%) in the head and neck region. Other epidemiological reports have indicated that the head and neck region, followed by the extremities and trunk, are the most common sites reported as anatomical location of the SCC [15].

Conclusions

SCC is the malignant proliferation of epidermal keratinocytes that occurs most frequently on skin exposed to chronic sunlight in

elderly patients. The typical age at presentation for SCC is about 70 years. However, this variation greatly, and in certain high-risk groups (eg, organ transplant patients, patients with bullous epidermolysis), the carcinoma often manifests at a much younger age. More population-based studies on incidence and mortality are needed to better quantify the impact of SCC on the health system around the world.

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Conflict of interest
NONE DECLARED

Correspondance address: Ioana-Adriana Popescu
Dermatology Department, 'Grigore T. Popa' University of Medicine and Pharmacy, Faculty of Medicine, University Street 16, 700115 Iași
e-mail: oana.manolache@yahoo.com