



Epidemiological data and clinicopathological features of cutaneous squamous cell carcinoma and basal cell carcinoma: A 20-year single-institution experience

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ABSTRACT

Introduction: Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the most common skin malignancies in the heterogeneous group of non-melanoma skin cancers (NMSC). Due to their increasing incidence, these tumors remain a significant health problem worldwide. The aim is to analyze the relative frequency of primary cutaneous BCC and SCC and to correlate it with the available pathological and clinical features.

Methods: We conducted a retrospective analysis to evaluate the incidence of NMSCs in our institution from 2003 to 2022 and to correlate it with patient's age and sex, together with available pathological and clinical features: Anatomical location, histopathological subtypes of prognostic implications, and size (local stage) of the tumor.

Results: We noticed that the incidence of NMSC increased between 2018 and 2022 ($p < 0.01$). Among 1570 patients diagnosed with NMSC, BCC represented 77.9% of cases. BCC was a constantly more common type of NMSC, with a statistically significant difference in the period from 2003 to 2005 and in the period from 2017 to 2022 ($p < 0.01$). Nodular subtype of the BCC was the most common, affecting primarily face. Superficial BCC occurred most commonly on trunk ($p < 0.01$), affecting younger patients than the other histological subtypes (61.29 ± 13.47 years), $p < 0.01$. BCCs were predominantly smaller tumors (< 2 cm) in contrast to SCCs, with the highest incidence in the pT2-pT4 group ($p < 0.01$). SCC patients were older (mean age 72.89 ± 9.7) than BCC patients (mean age 65.15 ± 12.80), $p < 0.01$.

Conclusion: To improve prevention strategies and prevent further increases in the incidence of NMSCs, there is a need to develop current and exact registries of these malignancies, especially separately for the most common types – BCC and SCC.

Keywords: Basal cell carcinoma; squamous cell carcinoma; non-melanoma skin cancer

INTRODUCTION

Non-melanoma skin cancer (NMSC) comprises a heterogeneous group of tumors that is mainly represented by basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) as the most common skin malignancies (1,2). BCC is the predominant type, accounting for three-quarters of lesions (3), while SCC is the major cause of death among tumors in the NMSC group (2). Histologically diverse groups of tumors, such as Merkel cell carcinoma, dermatofibrosarcoma, primary skin lymphoma, vascular lesions, and other rare tumors, comprise $< 1\%$ of NMSC (2).

Although BCC and SCC are treatable and cause mainly cosmetic defects, they remain a current public health problem. Globally, there is an increase in the incidence of NMSC, primarily due to an ageing population, prolonged sun exposure, climate changes, and the use of sunbeds (3,4).

NMSC is the most common type of cancer among Caucasians, with the highest incidence in Australia, followed by the United States of America (USA) and Europe (5). Data regarding the epidemiology of NMSC are heterogeneous. The exact incidence is difficult to establish, with the possibility that the real incidence is underestimated. One of the possible causes is the small number of studies that have examined the incidence of NMSC types separately (especially BCC and SCC). In many cancer registries, those tumors are coded under the same code (6).

The goal of the research is to analyze the relative frequency of primary cutaneous BCC and SCC according to the age and sex of the patients, as well as the correlations of these

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characteristics of NMSC with the available pathological and clinical features: Anatomical location, histopathological subtypes of prognostic implications, and size (local stage) of the tumor.

METHODS

The histopathological database of the Department of Pathology, Faculty of Medicine in Sarajevo, was retrospectively searched for confirmed diagnoses of cutaneous SCC and BCC in a 20-year period (from 2003 to 2022). The patient's age, sex, anatomical location, histopathological subtypes, and size (local stage) of the tumor were obtained from histopathological records. For easier statistical analysis, patients were divided into 10-year age interval groups. Recurrent tumors, especially in cases of incomplete surgical excision, were identified and excluded from analysis.

Histological subtypes of BCC include superficial, nodular (including pigmented nodular, nodulocystic, adenoid, and Pinkus tumor), basosquamous, infiltrative, micronodular, and less represented subtypes, grouped as other types (ulcerative, infundibulocystic, and morpheaform).

All tumors (both BCC and SCC) were classified into low- and high-risk categories. Low-risk BCCs include nodular, superficial, pigmented, infundibulocystic, and fibroepithelial types. High-risk BCC types include basosquamous, morpheaform, infiltrative, and micronodular.

Low-risk SCCs included keratoacanthoma and verrucous types, while high-risk SCCs included acantholytic, adenosquamous, and carcinosarcomatous types.

Staging, grading, and stratification of low- and high-risk tumors are done in accordance with criteria set forth in the guidelines of the national comprehensive cancer network.

An Ethical review committee approval (Number: 02-3-4-1915/23) was obtained from the Faculty of Medicine University of Sarajevo.

The data were analyzed statistically using IBM SPSS version 25.0. Data were analyzed according to type, using the Chi-square test, the Mann-Whitney U-test, the Kruskal-Wallis test, and Spearman's correlation test, where appropriate. Statistical significance was observed for $p < 0.05$.

RESULTS

Data gathered over a 20-year period showed 1570 patients (715 women and 855 men, ratio 0.84:1) diagnosed with NMSC at the Department of Pathology, Faculty of Medicine in Sarajevo. BCC was the more common type of NMSC with an incidence of 1223 (77.9%) cases (576 women and 647 men, ratio 0.89:1). Primary cutaneous SCC comprised 347 (22.1%) cases (139 women and 208 men, ratio 0.67:1).

The male-to-female ratio for NMSCs, and separately for BCCs and SCCs, did not show any significant annual differences over the 20-year analyzed period ($p > 0.05$).

Since our study shows single-institution experience with fluctuating, relatively small total number of biopsies per year, we investigated the incidence of NMSC in relation to number of skin biopsies and total number of biopsies per

year. When compared to the total number of biopsies per year, we noticed an increase in the incidence of NMSC in the 2018-2022 period ($p < 0.001$). BCC was a constantly more common type of NMSC, with a statistically significant difference in the period from 2003 to 2005 and in the period from 2017 to 2022 ($p = 0.003$) (Figure 1).

Among 1570 cases of NMSC, 68 (4.33%) patients had two or more NMSC lesions, mainly two or more BCCs ($n=59$; 86.8%), while 7 patients ($n=7$; 10.3%) had two SCCs and 2 patients ($n=2$; 2.9%) had simultaneous occurrence of BCC and SCC.

Age information was available for 1542 patients. SCC patients were significantly older than BCC patients ($p < 0.01$) (Figure 2). The mean age of patients diagnosed with SCC was 72.89 ± 9.7 (range 30-96 years), whereas the mean age of patients with BCC was 65.15 ± 12.80 (range 18-93 years) ($p < 0.01$).

Male patients diagnosed with SCC were significantly older than male patients diagnosed with BCC (mean age 71.49 ± 9.89 and 65.35 ± 2.9 ; respectively) ($p < 0.01$). Female patients diagnosed with SCC were also significantly older than female patients with BCC (mean age 74.99 ± 9.24 and 64.91 ± 12.86 ; respectively) ($p < 0.01$).

Over the 20-year period, patients with BCC were constantly younger than 70 years of age. BCC patients were the youngest in 2011 with a mean age of 61.70 ± 14.25 (range 29-82 years) and the oldest in 2016 (mean age 69.16 ± 12.65 ; range 31-88 years) ($p = 0.217$). Patients with SCC were significantly younger in the period from 2003 to 2010, compared to the period from 2011 to 2022,

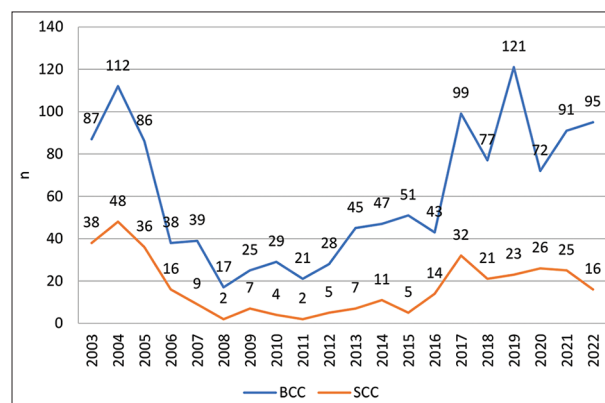


FIGURE 1. Incidence of BCC and SCC compared in a period of 20 years (between 2003 and 2022). BCC: Basal cell carcinoma, SCC: Squamous cell carcinoma.

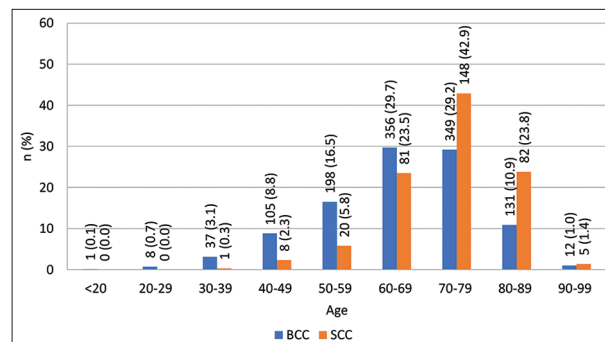


FIGURE 2. Age specific incidence rates for BCC and SCC patients. BCC: Basal cell carcinoma, SCC: Squamous cell carcinoma.

with the lowest mean age of 53.25 ± 16.80 in 2010, and highest in 2015 (81.60 ± 4.27), $p < 0.01$.

There was no significant sex predominance among age groups of patients diagnosed with NMSC ($p = 0.816$), nor in age groups of patients with BCC ($p = 0.724$). SCC was significantly more common in male patients in age groups <70 . In the female population, SCC was predominant in age groups of 70+ years ($p = 0.049$) (Figure 3).

Patients with superficial BCC were the youngest compared to patients with other histologic subtypes of BCC ($p < 0.01$) (Table 1). Among BCC cases, nodular BCC was the most frequent histologic subtype. The relative frequency of all histologic subtypes can be found in Table 2. Although we noticed a higher incidence of micronodular and basosquamous BCC, as more aggressive subtypes in female patients, the results did not reach statistical significance ($p = 0.478$). There was no significant difference in the distribution of histological subtypes of BCC among different age groups of patients ($p > 0.05$), but when analyzed according to mean age, we found that high-risk histological subtypes of BCC, such as infiltrative, basosquamous and micronodular were more frequent in older patients, compared to low-risk tumor subtypes, such as nodular and superficial BCC ($p < 0.01$).

Anatomical localization was available for 1528 NMSC, 1184 BCC, and 344 SCC cases. The most common site of both tumor types was face (71.2% for SCCs and 61.3% for BCCs) followed by trunk in BCC (22.2%) and scalp in SCC (8.6%). In both sexes, the face was the most common site for NMSC and showed no sex predominance according to predilection site ($p = 0.075$ for BCC; $p = 0.142$ for SCC). The most common site of BCCs on the face was the nose (41.7%). Other sites included lips (13.5%), forehead (11.3%), eyelids (5.5%), earlobe (4.93%), chin (0.53%), and other less common facial regions (22.5%). Most common facial sites of SCCs were lip ($n = 149$; 60.3%) and

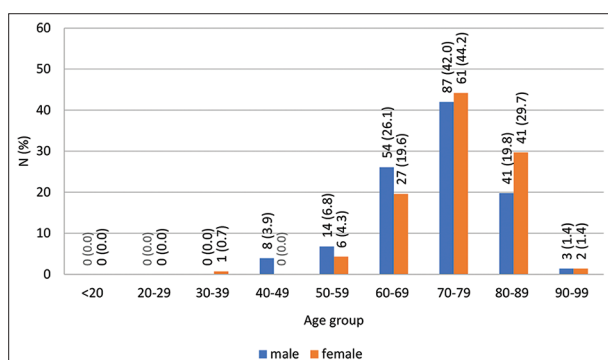


FIGURE 3. Sex-related incidence of SCC among age groups. SCC: Squamous cell carcinoma.

TABLE 1. Mean age of patients with different histological types of BCC

BCC type	n	Mean	SD	Min	Max
Superficial	224	61.29	13.47	18.00	90.00
Nodular	754	65.78	12.67	29.00	93.00
Infiltrative	170	66.71	12.43	27.00	89.00
Basosquamous	9	68.11	15.25	42.00	88.00
Micronodular	9	69.88	10.55	50.00	83.00
Other	33	66.81	11.30	38.00	91.00
Total	1199	65.15	12.88	18.00	93.00

BCC: Basal cell carcinoma

earlobe ($n = 46$; 18.6%). Face, neck and upper extremities were the most common sites for BCCs in patients of age group 70-79 years, while lower extremities, trunk, and scalp were the most common sites for BCC in age group of 60-69 years ($p = 0.004$).

All histological subtypes were most commonly located on the face. Superficial BCC occurred most commonly on the trunk ($p < 0.01$). The distribution of histological subtypes according to anatomical localization is shown in Table 2.

When stratified into low and high-risk tumor categories, both BCC and SCC showed higher incidence of low-risk tumors (81.6% and 90.8%, respectively). Patients with high-risk NMSCs were slightly older with mean age 67.58 ± 12.13 (range 27-91 years) than patients with low-risk NMSCs (mean age 66.73 ± 12.77 , range 18-96 years), but without statistical significance ($p = 0.330$). There was no statistically significant difference in the incidence of low-risk and high-risk NMSC in relation to sex and age groups of patients ($p = 0.272$; $p = 0.322$; respectively).

Table 3 shows the distribution of low-risk and high-risk BCC and SCC in relation to patient's gender and anatomical localization of the tumor. High-risk BCCs in men were more common on the head - face and scalp ($p = 0.034$), than on other sites.

Tumor size (pT) was available for 1264 (80.5%) NMSC, with predominantly pT1 tumors (83.4%), both in BCC and SCC ($n = 1082$, $n=228$; respectively). The least represented were pT4 tumors (0.6%).

We compared the incidence of different tumor sizes (from pT1-pT4) among BCC and SCC cases and found that BCCs were predominantly smaller tumors (<2 cm) in contrast to SCCs with the highest incidence in the pT2-pT4 group ($p < 0.01$) (Figure 4).

Large and advanced BCC and SCC (pT3 and pT4) were most commonly located on the face, but without statistical significance ($p > 0.05$).

DISCUSSION

All cutaneous malignancies are divided into two basic groups: Cutaneous melanoma (CM) and NMSC. Data regarding the incidence of CM are relatively consistent, unlike the heterogeneous group of NMSC which comprises not only SCC and BCC but also tumors such as Merkel cell carcinoma, adnexal malignancies, cutaneous T-cell lymphomas, Kaposi sarcoma, and other rare entities (7,8). The main problem in determining the exact incidence comes not only from relatively poor registration practice in the majority of countries but also from coding NMSCs under a single code (6,9). Other problems are related to the registration of multiple tumors. Usually, only the first case of NMSC in a patient is registered, while sub-sequent tumors or multiple tumors are not included (9,10). Among 1570 cases of non-melanotic skin cancer in our study, 4.33% of patients had two or more NMSC lesions, mainly two or more BCCs. Other multicentric studies found multiple lesions relatively common with up to 23% of patients with multiple lesions (6).

Previous data reported continuously rising trends in the incidence of NMSC worldwide (6,11-14) with many

TABLE 2. Anatomical distribution of histological types of BCC

Anatomical location			BCC type						Total
			Superficial	Nodular	Infiltrative	Basosquamous	Micronodular	Other	
Site	Face	n	63	519	128	8	6	26	750
		%	27.9	67.3	74.0	88.9	66.7	74.3	61.3
	Neck	n	6	31	2	0	1	3	43
		%	2.7	4.0	1.2	0.0	11.1	8.6	3.5
	Upper limbs	n	12	32	3	1	0	0	48
		%	5.3	4.2	1.7	11.1	0.0	0.0	3.9
	Lower limbs	n	20	16	3	0	0	0	39
		%	8.8	2.1	1.7	0.0	0.0	0.0	3.2
	Trunk	n	113	132	21	0	2	4	272
		%	50.0	17.1	12.1	0.0	22.2	11.4	22.2
	Scalp	n	2	21	8	0	0	1	32
		%	0.9	2.7	4.6	0.0	0.0	2.9	2.6
	N/D	n	10	20	8	0	0	1	39
		%	4.4	2.6	4.6	0.0	0.0	2.9	3.2
Total		n	226	771	173	9	9	35	1223
		%	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Data are presented as n (%). BCC: Basal cell carcinoma, N/D: Not defined

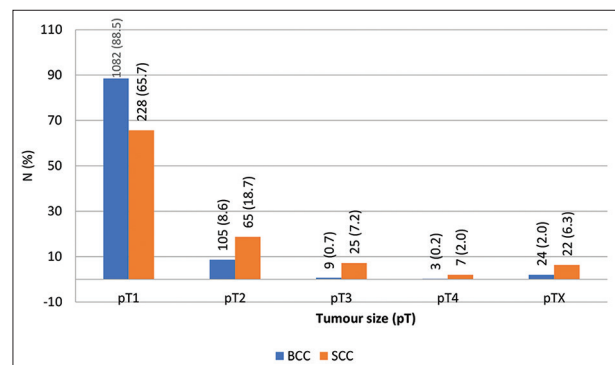
TABLE 3. Sex-dependent anatomical distribution of BCC and SCC types

Anatomical location	LRSCC	HR SCC	LR BCC	HR BCC
Men				
Face	134 (71.7)	13 (65.0)	293 (58.3)	89 (73.0)
Neck	7 (3.7)	0 (0.0)	18 (3.6)	4 (3.3)
Upper limb	8 (4.3)	1 (5.0)	32 (6.4)	4 (3.3)
Lower limb	6 (3.2)	1 (5.0)	18 (3.6)	1 (0.8)
Trunk	13 (7.0)	1 (5.0)	130 (25.8)	19 (15.6)
Scalp	19 (10.2)	4 (20.0)	12 (2.4)	5 (4.1)
N/D	1	0	16	6
Total	188	20	519	128
Women				
Face	91 (72.8)	9 (75.0)	291 (62.6)	77 (16.6)
Neck	1 (0.8)	1 (8.3)	19 (4.1)	2 (0.4)
Upper limb	13 (10.4)	0 (0.0)	12 (2.6)	0 (0.0)
Lower limb	6 (4.8)	1 (8.3)	18 (3.9)	2 (0.4)
Trunk	7 (5.6)	1 (8.3)	114 (24.5)	9 (1.9)
Scalp	7 (5.6)	0 (0.0)	11 (2.4)	4 (0.9)
N/D	2	0	14	3
Total	127	12	479	97

Data are presented as n (%). LR: Low risk, HR: High risk, BCC: Basal cell carcinoma, SCC: Squamous cell carcinoma; N/D: Not defined

factors implicated in this increase, but with the primary cause related to exposure of the skin to ultraviolet radiation (15). When compared to the total number of biopsies over 20-year period, we also noticed an increase in the incidence of NMSC, especially in the period from 2018 to 2022.

NMSC is generally a disease of the older population. Many European studies confirmed these findings (6,10,16) with higher incidence observed in the male population, especially in earlier years (13,17,18). Our results are in line with these studies, since both types of NMSC were more common in men than in women, although the male-to-female ratio for NMSCs, and separately for BCCs and SCCs, did not show any significant annual differences over the 20-year period. In our study, patients with SCC were significantly

**FIGURE 4.** Tumor size (pT) - specific incidence of NMSC. NMSC: Non-melanoma skin cancers, BCC: Basal cell carcinoma, SCC: Squamous cell carcinoma.

older than patients with BCC. These results are in line with findings of previous studies, since this type of carcinoma is more common in the older population, but the younger population is not spared from the disease either (1,6).

Due to the use of ultraviolet-emitting tanning devices, many studies conducted in Europe and USA showed evidence of women developing BCCs at younger ages and in a higher percentage than their male counterparts (14,19,20). Over the 20-year period, the mean age of BCC patients was constantly <70 years and showed no significant difference over the examined period. Our data confirm previous findings that the majority of BCC patients are between 40 and 79 years of age (6,16). We noted that patients with SCC were significantly younger in the first decade of the 2000s, compared to patients with SCC in recent years. Our results support the findings of recent studies that there is an increase in the incidence of BCC and SCC among the older population (6).

While some studies suggest that SCC is increasing in young women rather than in young men (14), others indicate a higher risk for NMSC development in the elderly, which could explain a greater proportion of cancer in women in the older age group (21). We found SCC significantly more common in male patients in age groups younger than 70.

In female patients, SCC was predominant in age groups of 70+ years.

BCC, as the most common type of NMSC, has different clinical presentations but generally is a locally invasive tumor with extremely rare metastases. It accounts for about 80% of all NMSCs (6,22), affecting primarily sun-exposed sites, such as the head and neck region, followed by the trunk (23-25).

In our study, BCC comprised a similar percentage, accounting for 77.9% of NMSC, most commonly affecting sun-exposed sites, such as the face. These findings are similar to the findings of previous studies (6,26).

Histologic subtypes of BCC differ in clinical presentation, risk of recurrence and metastasis, together with differences in treatment and prognosis (27,28).

Nodular BCC was the most frequent histological subtype in our study, comprising 63.0% of cases. These results are in concordance with the findings of other studies (29,30). The majority of nodular BCC cases were located on the face. The second most common histological form of BCC is superficial, affecting predominantly the trunk and extremities of younger patients, as well as the head/neck (31). Our results confirm these findings (Table 2).

Superficial BCC shows a high propensity for recurrence since the lesions are quite difficult to define clinically. Furthermore, this type is prone to having multiple lesions (31,32). In our study, among 59 patients with multiple BCCs, 11 (18.6%) had multiple superficial BCCs.

In our study, high-risk BCCs histologic subtypes, such as infiltrative, basosquamous, and micronodular (33-35), showed tendency to develop more frequently in older patients, with slight female predominance. High-risk BCCs in men were more common on head-face and scalp ($p = 0.034$). Other studies also found high-risk histologic subtypes most commonly on head-and-neck area (6,34).

SCC, as the second most common type of NMSC, is more invasive than BCC with a greater predisposition to develop in certain cervicofacial regions, such as in the ears and lower lip (36). Our study is in line with these findings since the head region was the most common site of SCCs, including the lower lip and earlobe.

The pathological characteristics related to the aggressiveness of SCC include the size, depth, location, and differentiation of the lesion, that is, tumors larger than 2 cm in diameter are more likely to recur and metastasize (37). Staging of SCC is done according to lesion size, depth of invasion, differentiation, and perineural invasion (38).

We compared the incidence of different tumor size (local extension of tumor) among BCC and SCC cases and found that BCCs were predominantly smaller tumors (<2 cm) in contrast to SCCs which showed tendency for advanced local extension, confirming higher aggressiveness of SCCs.

We noted high-risk SCCs most frequently in age group of 70-79 years, but without statistical significance. High-risk SCCs were most commonly located on face and scalp in men and on face in women.

CONCLUSION

Although NMSC are malignancies with low mortality rates, they represent a significant economic burden to health

services, especially due to a noted increase in incidence and significant morbidity, which is especially related to tumors located in the head-and-neck region.

In the past years of research, an increase in the frequency of NMSC was observed in relation to the total number of biopsies analyzed in our Institute. The nodular subtype was the most common subtype of BCC and by far the most frequently occurring in the facial region, which is overall the most common location of BCC. Compared to the others, high-risk BCC subtypes appeared at a significantly older age and most often in the face and scalp region. Patients with SCC were significantly older than patients with BCC. SCCs most often appeared in the region of the face and scalp, and unlike BCC, they were most often in the high-stage group (pT2-pT4) at the time of surgery.

All the above results are in full agreement with the results of significant international studies of NMSC, showing that the population in our country is exposed to the same external risk factors for the development of NMSC as the population of other countries of the world.

DECLARATION OF INTERESTS

Authors declare no conflict of interest.

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