

Evaluation of residual tumors and recurrence rates of malignant melanoma and non-melanoma skin cancer of head and neck region

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ABSTRACT

Objective: In this study, we aimed to evaluate residual tumors and recurrence rates of malignant melanoma (MM) and a non-melanoma skin cancer of (NMSC) head and neck region.

Patients and Methods: Medical data of a total of 398 lesions of 323 patients who underwent surgical excision for a basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and malignant melanoma (MM) were retrospectively analyzed. All patients were classified according to age, sex, location of the tumor, histopathological diagnosis, lesion diameter, excision diameter, surgical margin status, and residual lesions and recurrence rates.

Results: There were 244 lesions (61.3%) in 189 males and 154 lesions (38.7%) in 134 females. The most common type of skin cancer was BCC in 268 lesions (67%), followed by SCC in 122 (31%), and MM in eight (2%), respectively. Recurrence was seen in 3% of the NMSC cases and in 25% of the MM cases. There was a statistically significant correlation between the histopathological diagnosis and recurrence rates. Compared to NMSC, MM cases had a higher risk for recurrence ($p=0.029$).

Conclusion: Our study results suggest that recurrence is associated with the localization and type of the tumor, but not with the age or sex of the patient.

Keywords: Basal cell carcinoma, Squamous cell carcinoma, Malignant melanoma, Recurrence, Residual tumor

1. INTRODUCTION

Skin cancer is the leading cancer in the world [1]. In recent years, the incidence of the skin cancer has been increasing, although, the mortality rates still remain unchanged [2]. Skin cancer can be mainly divided into two groups as malignant melanoma (MM) and non-melanoma skin cancer (NMSC). There are two main subtypes of NMSC as basal cell carcinoma (BCC) in which cancer is derived from epidermal cells of the basal layer and squamous cell carcinoma (SCC) which originates from the malignant proliferation of the epidermal keratinocytes [3-5]. However, MM originates from the melanocytes which are the pigment-generating cells of the skin [6].

Basal cell carcinoma is the dominant form of skin cancer which accounts for 80% of all cases [7]. Due to its slow-growing and non-aggressive nature, metastasis is unlikely [8]. Although, BCC is not usually fatal, it may be associated with significant morbidities and complications due to its locally invasive nature [9]. As the other form of NMSC, SCC is the second most common type of skin cancer, accounting for 20% of all NMSC cases [7,10]. In contrast to BCC, SCC acts in a more aggressive manner with a higher metastasis risk [11,12]. The major factor

for the development of NMSC is the cumulative exposure to ultraviolet radiation (UV) [13]. Consequently, the typical locations of NMSC are the areas of the skin which are regularly exposed to sun, such as head and neck region [14].

On the other hand, MM is the rarest form of skin malignancies, accounting for 1% of all skin cancer cases [15]. Although, MM is the least likely skin malignancy, it is associated with a high incidence of skin cancer-related mortality [16]. According to the American Cancer Society, MM is recognized as being the sixth most common cancer in the United States [17].

In the present study, we aimed to investigate the distribution of skin cancers of the head and neck and to evaluate the residual and recurrent cases.

2. PATIENTS AND METHODS

This retrospective study was conducted at Marmara University, Training and Research Hospital, Department of Plastic, Reconstructive and Aesthetic Surgery between January 2010

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and December 2015. This study included BCC, SCC, and MM cases of the head and neck region. The head and neck region were divided into eight subunits to obtain a systematic analysis of the retrieved data including the scalp, forehead, periauricular, periorbital, nose, cheek, perioral, and chin. In addition to benign tumors, tumors located in other areas, precursor lesions of the skin and rarer types of skin cancer (i.e., Merkel cell carcinoma, cutaneous lymphomas, Kaposi sarcoma, and skin adnexal tumors) were excluded.

Finally, a total of 1801 lesions underwent a surgical excision. After the pathology reports were classified for eligibility; 398 skin lesions of 323 patients were included in the study. Eligible cases were classified according to the age, sex, location of the tumor, histopathological diagnosis, lesion diameter, excision diameter, surgical margin status, and residual lesions and recurrence rates.

A residual lesion was defined as the presence of cancer cells in the surgical margins after the initial excision. A recurrent lesion was defined as histopathological evidence of tumor in the same excision area after the initial excision.

A written informed consent was obtained from each patient. Ethical approval was obtained for the present study from Marmara University Ethical Committee (approval number:). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Statistical analysis was performed using the STATA 10.0 software (STATA Corp., College Station, TX, USA). Descriptive statistics were expressed in mean ± standard deviation (SD), median (min-max), or number and frequency. The chi-square test was used to analyze statistically significant differences between the MM and NMSC groups. A p value of <0.05 was considered statistically significant.

3. RESULTS

A total of 398 skin lesions of 323 patients in the head and neck region were surgically excised. There were 244 lesions (61.3%) in 189 males and 154 lesions (38.7%) in 134 females. The male-to-female ratio was 1.41:1. The mean age of all patients was 66.3±15.55 (range, 6 to 59) years. The most common type of skin cancer was BCC in 268 lesions (67%), followed by SCC in 122 (31%), and MM in eight (2%), respectively. Following the initial excision, 333 cases (84%) were successfully removed, while there were 59 procedures (15%) resulting in tumor presence in the surgical margin. No data were available in six (2%) of the excisions. Recurrence was seen in 14 cases (3.5%) (Table I).

Sex

Among all excised BCC lesions, 152 (56.8%) were removed from males and 116 (43.2%) from females. A male dominance was observed in SCC in 86 procedures (70.5%) among male patients, while 36 procedures (29.5%) were performed in female patients. Of the total MM cases, six (75%) were males and two (25%) were females (Table I).

Age

The mean age was similar among BCC and SCC cases (66.4±13.03 years and 66.5±13.03 years, respectively). The mean age of MM cases was 59.8±20.72 years (Table I).

Table I. Demographic and clinical characteristics of patients

	Total	BCC	SCC	MM
Sex Male	244 (61.3%)	152 (57.8%)	86 (70.5%)	6 (75%)
Female	154 (38.7%)	116 (43.2%)	36 (29.5%)	2 (25%)
Tumor, n (%)	398 (100%)	268 (67%)	122 (31%)	8 (2%)
Age, years, mean±SD (range)	66.3±15.55 (6 to 95)	66.4±13.03 (17 to 90)	66.5±19.76 (6 to 95)	59.8±20.72 (27 to 84)
Surgical margin status (+)	59 (15%)	48 (18%)	11 (9%)	0
(-)	333 (84%)	216 (80.5%)	109 (89%)	8 (100%)
Missing data	6 (2%)	4 (1.5%)	2 (2%)	0
Recurrence, n (%)	14 (3.5%)	8 (3%)	4 (3%)	2 (25%)

BCC: basal cell carcinoma, SCC: squamous cell carcinoma, MM: malignant melanoma, SD: standard deviation

Location and sex

Most of the lesions were found in the nasal area in 111 cases (27.8%), followed by the perioral area in 68 cases (17.1%) and periorbital area in 65 cases (16.3%). The rate of skin malignancies was the lowest in around the chin and forehead in only six (1.5%) and 24 (6%) cases, respectively. Skin cancer appeared in the nasal region most commonly in both sexes. A total of 20.9% of the excisions were carried out in males and 38.9% in females. Around the periauricular region, the figures were much higher in males in 15.6% of the male population (n=38). On the other hand, only 0.8% of the female patients (n=2) had cancer in this area (Table II).

Table II. Sex of patients and location of tumors according to groups

	Total	M	F	BCC	SCC	MM
Cheek	33 (8.3%)	18 (7.4%)	15 (9.7%)	21 (7.8%)	8 (6.5%)	4 (50%)
Chin	6 (1.5%)	2 (0.8%)	4 (2.6%)	3 (1.1%)	3 (2.5%)	0
Forehead	24 (6%)	16 (6.5%)	8 (5.2%)	17 (6.3%)	7 (5.7%)	0
Nose	111 (27.8%)	51 (20.9%)	60 (38.9%)	91 (34%)	19 (15.6%)	1 (12.5%)
Periauricular	40 (10%)	38 (15.6%)	2 (1.3%)	28 (10.4%)	11 (9%)	1 (12.5%)
Perioral	68 (17.1%)	47 (19.3%)	21 (13.6%)	21 (7.8%)	47 (38.5%)	0
Periorbital	65 (16.3%)	38 (15.6%)	27 (17.5%)	50 (18.6%)	14 (11.5%)	1 (12.5%)
Scalp	51 (12.8%)	34 (13.9%)	17 (11%)	37 (13.8%)	13 (10.7%)	1 (12.5%)
Total	398	244	154	268	122	8

Data are given in number and percentage. M: male; F: female, BCC: basal cell carcinoma, SCC: squamous cell carcinoma, MM: malignant melanoma

Surgical margins

A total of 216 (80.5%) of 268 BCC cases were excised successfully, while in 48 cases (18%), there was a tumor presence in the surgical margins. Among 122 SCC cases, 109 (89%) were excised adequately and 11 (9%) were inadequately removed. All residual lesions were re-excised and clear margins were established. No inadequate margin was detected after the initial excision of all MM cases. There were missing data in six of the cases (Table III).

Table III. Margin status according to subunits

	Margin Status			Recurrence
	Negative	Positive	Missing data	
Cheek	28 (8.4%)	4 (6.7%)	1	0
Chin	4 (1.2%)	1 (1.7%)	1	0
Forehead	22 (6.6%)	1 (1.7%)	1	2 (14.3%)
Nose	91 (27.3%)	20 (33.9%)	0	6 (42.9%)
Periauricular	32 (9.6%)	7 (11.9%)	1	1 (7.1%)
Perioral	59 (17.7)	8 (13.5%)	1	2 (14.3%)
Periorbital	52 (15.6%)	12 (20.3%)	1	0
Scalp	45 (13.5%)	6 (10.2%)	0	3 (21.4%)
Total	333 (83.6%)	59 (14.8%)	6 (1.5%)	14

Data are given in number and percentage.

Recurrence rates

Recurrence was seen in a total of 3% of the NMSC cases (3% of BCC lesions, n=8 and 3% of SCC lesions, n=4), while this rate was 25% in the MM cases. There was a statistically significant correlation between the histopathological diagnosis and recurrence rates. Compared to NMSC, MM cases had a higher risk for recurrence (p=0.029), even a clear margin was achieved in all MM cases. All recurrent cases were excised and clear margins were achieved (Table IV).

Table IV. Margin status after recurrence

	Margin Status		n
	Negative	Positive	
BCC	8	0	8
SCC	4	0	4
MM	2	0	2
Total	14	0	14

BCC: basal cell carcinoma, SCC: squamous cell carcinoma, MM: malignant melanoma

4. DISCUSSION

Basal cell carcinoma is the most common type of skin cancer in Caucasians, which predominantly occurs in the exposed parts of the body, with 80% of the lesions found in the head and neck regions [18]. Our study results also showed that most of the lesions were found in the nose (27.8%), perioral (17.1%), and periorbital (16.3%) regions, which are the most prominent parts exposed to chronic sun radiation, and also in the H area.

In the literature, most of the BCC lesions are reported in the 40-79 age group with a mean age of 62 years. However, in tropical regions and in patients with a family history, BCC may occur in a younger age [19,20]. In our study, the mean age of BCC cases was 66.4 (range, 17 to 90) years with a statistically significant increase in the 60-70 and 70-80 age groups (28.9% and 27.6%, respectively). Also, in the other Mediterranean countries, it mostly affects the 70-80 age group [21-24]. Our study results regarding the age of the patients and location of the lesions were consistent with the literature.

Previous studies have demonstrated a higher rate of BCC in male patients [25-27]. In our study, there was no statistically significant difference between men (57%) and women (43%), that was consistent with previous studies [22,25,28]. According to the subunits, nose (20.9%), perioral (19.3%), periorbital (15.6%), periauricular (15.6%), and scalp (13.9%) involvement were more common in male patients. Nose (38.9%), periorbital (11%), and perioral (8.6%) involvement were more common in female patients. These can be attributed to the fact that urban life affects both sexes equally. Periauricular BCC was seen in only two female patients (0.8%), compared to male patients, which can be explained by the possible protective effect of scarf wearing in women.

The main goals of the tumor treatment are to eradicate the tumor with the safest and most cost-effective method available and to provide an aesthetically and functionally satisfactory outcome. Although, different treatment modalities for BCC have been described in the literature, surgical excision is the most effective and commonly adapted method for tumor removal [27].

In the literature, a 3-mm peripheral surgical margin is adequate for the clearance of 85% of small and well-defined BCCs, and the 4 to 5-mm margin would raise this figure to 95% [29]. This margin is 1 cm for SCCs and 1 to 2 cm for MMs, depending on the tumor depth [8]. In our study, BCCs were excised with a 3 to 5-mm clear margin, depending on the location of the tumor, while SCCs were excised with a 1-cm clear margin and MMs were excised with a 2-cm clear margin. Previous studies have shown a great variability in the re-excision rates ranging from 9% to 75% for BCCs [30]. In our study, the rate of residual tumors resulting in re-excision was 18% for BCCs, 9% for SCCs, and 0% for MMs. This relatively high rate may result from the fact that BCCs were seen around the aesthetic subunits such as nose, eyelid, and lip and there may be an effort to keep the excision margin narrow not to compromise the cosmetic results. The majority of the studies showed that BCC and SCC required a similar number of stages to obtain free margins, although some authors suggested that BCC required more stages than SCC, which was consistent with our findings [31-34]. The fewer stages required to obtain clear margins in SCC than in BCC may be due to the more aggressive behavior of the primary tumor, leading to extreme caution, and the consequent removal of more peripheral tissues per stage. Another possible explanation is that SCCs are better defined on clinical examination [35].

Review of the literature reveals that the recurrence rate for primary BCCs after surgical excision varies between 5% and 14% [29,36]. Lesions in the head and neck region are at a higher

risk for recurrence, compared to lesions in the trunk and limbs [29,36-38]. Incomplete excision has been also reported as one of the risk factors for recurrence [25,39-41]. In our series, the overall recurrence rate was 3% for NMSC (n=8 BCC and n=4 SCC) and 25% for MM (n=2). Recurrent lesions were located in the nose (n= 6), scalp (n= 3), forehead (n= 2), perioral (n=2), and periauricular (n=1) regions. The recurrence rate (2/8, 25%) seems relatively high, although this can be explained by the small number of the overall MM cases in our study. However, there was no residual tumor after MM excision in two recurrent cases. This is probably due to the aggressive behavior of MM. More interestingly, most recurrences were located in the H area which can be attributed to high recurrence rates on the embryonic fusion planes and also close margin excision tendency not to harm the aesthetic subunits [27,42-44].

Previous studies have shown a reduced residual rate of BCCs through Mohs microscopic surgery or a margin-controlled, staged surgical excision in institutions where Mohs surgery is not available [45]. In particular, in the H area where the recurrence risk is high and aesthetic subunits of the face are included, a staged surgical excision is superior to simple excision.

Nonetheless, there are some limitations to this study. Retrospective design with a relatively small sample size is the main limitation. In addition, all operations were performed by residents and specialists. Although resections were done in accordance with the current guidelines, considering the fact that learning curve may vary for each surgeon, the results might have been different for surgeons, indicating variability in surgical outcomes. Therefore, further large-scale, prospective studies are warranted.

In conclusion, our study results suggest that recurrence is associated with the localization of the tumor, but not with the age, sex, and type of the tumor. Of note, it should be kept in mind that the low recurrence rates in our series may be due to the excision with an appropriate margin and no positive surgical margins after second surgery. However, further large-scale, prospective studies are needed to establish a definite conclusion.

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