Journal of Environmental and Occupational Science
www.jenvos.com
DOI: 10.5455/jeos.20170416072408

Original Research

Body site distribution and relative tumor density of different human cutaneous malignancies with emphasis on sunlight exposure: A single institution experience

Vladimír Bartoš[1], Milada Kullová[2]

ABSTRACT

Background: Different skin cancer types display disparate body site distribution, particularly related to sunlight exposure pattern. We evaluated the topographic distribution and relative tumor density (RTD) in a set of human cutaneous malignant melanoma (MM), basal cell carcinoma (BCC), and squamous cell carcinoma (SCC) cases. **Materials and Methods:** A series of 182 patients with a total of 186 MMs, 899 patients with a total of 1184 BCCs, and 114 patients with a total of 146 SCCs were analyzed. **Results:** MMs occurred most commonly on the trunk (46.8%) and the upper limbs (25.3%). While the back and the trunk in particular was sites with the most frequent MM development in males (64.3% and 45.9%), the upper limbs were the most common location in females (34.1%). BCCs and SCCs occurred predominantly on the head and neck, comprising a total of 69.0% and 81.5% of the cases. The face was a region with by far the highest RTDs in BCC and SCC patients. Men had more frequently affected extrafacial sites of the head and neck compared to women in both BCC (46% vs. 31.9%) and SCC (62.5% vs. 48.3%) cases. In BCC, the second most frequent anatomic site included the back in both genders (25.1% in males, 18.2% in females), but in SCC, it represented the trunk as a whole in males (13.6%), and the lower limbs in females (14.3%). The greatest differences in RTDs between BCC and SCC were on the back (BCC: SCC ratio, 7.5:1), especially in men (BCC: SCC ratio, 9:1). **Conclusion:** We have confirmed striking heterogeneity for skin cancer risk by anatomic site. While MMs arise predominantly on the body parts intermittently exposed to the sunlight, BCCs and especially SCCs develop most frequently on the sites that are habitually exposed to the sun.

KEY WORDS: Anatomic distribution, skin carcinomas, sunlight exposure patterns

[1]Department of Pathology, Faculty Hospital, Žilina, Slovakia, [2]Department of Dermatovenerology, Faculty Hospital, Žilina, Slovakia

Address for correspondence: Vladimír Bartoš, Department of Pathology, Faculty Hospital, Žilina, Slovakia. E-mail: vladim.bartos@gmail.com

Received: January 31, 2017
Accepted: March 09, 2017
Published: April 18, 2017

INTRODUCTION

Human skin cancers encompass a wide spectrum of malignant conditions with different epidemiologic and clinical characteristics. The three most common malignancies include basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), also referred to, collectively, as nonmelanoma skin cancer (NMSC), and malignant melanoma (MM). Although their etiopatogenesis is complex, there is persuasive evidence that an ultraviolet radiation (UVR) has a vital role in the development of each of these main tumor types [1]. However, the relative relationship between the sunlight exposure and the genesis of BCC, SCC, and MM seems to be tumor-specific [1]. These UVR-related differences result in distinct anatomic distribution of the skin cancer types. In general, while MMs arise most commonly on the trunk and limbs [2-7], the vast majority of research papers have clearly demonstrated [3,7-13] that NMSC occurs predominantly on the head and neck region. In spite of that, however, some studies [4,5,14-16] have found discrepant percentages of BCCs and SCCs at individual body parts compared with the above-mentioned papers and as a consequence, the relative tumor density (RTD) has showed wide variations. The RTD measure was first introduced by Pearl and Scott [17] in 1986, to create a standard way of comparing skin cancers distribution by anatomical sites. It considers the ratio between the proportion of tumor in a certain location and the proportion of the surface area on the same location. This index highlights the differences between the expected and observed occurrence of tumors by site. In this study, we have evaluated the topographic distribution and RTD of three types of cutaneous neoplasms mentioned above and confronted our results with eligible literature data.

MATERIALS AND METHODS

We retrospectively reviewed all patients with primary cutaneous MMs, and all patients with primary cutaneous BCCs, that were histologically diagnosed at the Department of Pathology in Faculty Hospital in Žilina (Slovakia) during 10-year period (from January 2007 to December 2016). Further, we reviewed all patients with primary cutaneous SCCs diagnosed at the same workplace during 7-year period (from January 2010 to December 2016). The participants were registered in the Pathology Archive Computer Program (PACP), from which required histopathological data were extracted. Recurrent lesions and subsequent re-excisions after incomplete tumor removal, as well as mucosal and mucocutaneous lesions were excluded. The specimens were derived from a variety of clinical sources at our hospital, especially from Surgery, Dermatology, Otorhinolaryngology, and Ophthalmology Departments. Biopsy material was fixed in buffered formalin, embedded in paraffin blocks and stained with hematoxylin and eosin. Clinical data of the patients needed for the study were obtained from their medical records. The following six anatomic locations were classified for analysis: The face, the extrafacial part of the head and neck (scalp, ears, and neck), the trunk as a whole, the back alone, and the upper and lower extremities. According to Pearl and Scott [17], present body sites comprised 2.4%, 6.6%, 32%, 10%, 19%, and 40% of entire skin surface, respectively. The RTD was calculated by dividing the proportion of tumors occurring at a specified site by the proportion of skin area of that site. Age profile of the cohort members was divided into the following three categories: ≤50, 51-70, and ≥71 years. Since, we were not able to objectively find out a personal sunlight exposure status (i.e., history of sunburns, tanning habits, total extent, and intensity of UVR throughout life), we could only suppose solar exposure patterns based on the anatomic locations involved. For the sake of simplicity, head, and neck, as well as dorsum of the hand and fingers were considered the body sites corresponding to chronic (cumulative) sunlight exposure.

RESULTS

Basic Clinicopathological Data

A series of 182 subjects (95 males, 87 females) with a total of 186 MMs (30 *in situ*, 156 invasive lesions), 899 subjects (432 males, 467 females) with a total of 1184 BCCs, and 114 subjects (79 males, 35 females) with a total of 146 SCCs (39 *in situ*, 107 invasive lesions) were evaluated in the study. Since, these participants were consecutively chosen from our PACP within a period of 10 (BCC and SCC cases) and 7 years (SCC cases), they represented all (100%) individuals with bioptically verified given cutaneous malignancies registered at our Pathology Department during that time. This explains unequal gender proportions among individual tumor types, as they differently affect men and women. Patients with MMs ranged between 22 and 93 years of age (mean 58.9 years), patients with BCCs between 25 and 97 years of age (mean 70.0 years), and patients with SCCs between 34 and 95 years of age (mean 78.3 years). There were heterogeneous percentage proportions of the age subgroups in the individual tumor types, illustrated in Figure 1. As expected, in MM, the most frequent (41.9%) age category was between 51 and 70 years. In NMSC, there were clearly rising percentages from the youngest (≤50 years) to the oldest (≥71 years) age category. However, while in BCC, it appeared to have a linear relationship; in SCC, it showed rather an exponential dependence.

Body Site Distribution and RTD

Topographic distributions and RTDs for all three cancer types in relationship to gender and are listed in Tables 1-3. Briefly, MMs occurred most commonly on the trunk (46.8%) and upper extremities (25.3%), and the least frequently on the head and neck (13.9%). No case was found on the dorsum of the hand or fingers. When we calculated the RTD, which takes into account the surface proportion occupied by body sites experiencing different amounts of UVR, the back (with RTD of 3.4) and the face (with RTD of 2.4) were the most dominant areas. Apparent gender disparities were found. While the back and the trunk in particular was sites with the most frequent MM development in males (64.3% and 45.9%, respectively), the upper extremities were the most common location in females, followed by the trunk (34.1% and 27.3%, respectively).

As for NMSC, both BCCs and SCCs occurred predominantly on the head and neck, comprising a total of 69.0% and 81.5% of the cases, respectively. The face was a region with by far the highest RTDs, representing a value of 17.6 in BCC patients and a value of 14 in SCC patients. However, regarding the head and neck region alone, the face involvement prevailed in BCC (61.3%), whereas the extrafacial parts (scalp, ears, and neck) predominated (58.8%) in SCC. Further, men had more frequently affected extrafacial sites of the head and neck compared to women in both BCC (46% vs. 31.9%) and SCC (62.5% vs. 48.3%) cases. In BCC group, the second most frequent anatomic site included the back in both genders (25.1% in males and 18.2% in females), but in SCC group,

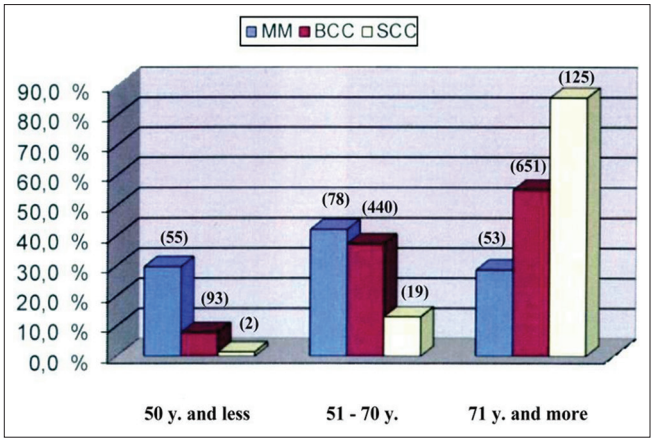

Figure 1: Percentage distributions of malignant melanoma, basal cell carcinoma and squamous cell carcinoma cases within the three given age categories (number in the brackets indicates number of lesions)

Table 1: Body site distribution and RTD of MM in a set of 186 lesions

Body site	Total		Males		Females	
	N (%)	RTD	*N* (%)	RTD	*N* (%)	RTD
Face	11 (5.9)	2.4	5 (5.1)	2.1	6 (6.8)	2.8
Scalp/ears/neck	15 (8.1)	1.2	5 (5.1)	0.7	10 (11.3)	1.7
Trunk	87 (46.8)	1.4	63 (64.3)	2.0	24 (27.3)	0.8
Back only	64 (34.4)	3.4	45 (45.9)	4.5	19 (21.6)	2.1
Upper limbs	46 (24.7)	1.3	16 (16.3)	0.8	30 (34.1)	1.8
Lower limbs	27 (14.5)	0.3	9 (9.2)	0.2	18 (20.5)	0.5

RTD: Relative tumor density, MM: Malignant melanoma

Table 2: Body site distribution and RTD of BCC in a set of 1184 lesions

Body site	Total		Males		Females	
	N (%)	RTD	*N* (%)	RTD	*N* (%)	RTD
Face	501 (42.3)	17.6	211 (34.4)	14.3	290 (50.9)	21.2
Scalp/ears/neck	316 (26.7)	4.0	180 (29.3)	4.4	136 (23.9)	6.2
Trunk	258 (21.8)	0.7	154 (25.1)	0.8	104 (18.2)	0.5
Back only	188 (15.8)	1.5	113 (18.4)	1.8	75 (13.1)	1.3
Upper limbs	76 (6.4)	0.3	54 (8.8)	0.4	22 (3.9)	0.2
Lower limbs	33 (2.8)	0.07	15 (2.4)	0.06	18 (3.1)	0.07

BCC: Basal cell carcinoma, RTD: Relative tumor density

Table 3: Body site distribution and RTD of SCC in a set of 146 lesions

Body site	Total		Males		Females	
	N (%)	RTD	*N* (%)	RTD	*N* (%)	RTD
Face	49 (33.6)	14	33 (31.7)	13.2	16 (38.1)	15.8
Scalp/ears/neck	70 (47.9)	7.2	55 (52.8)	8.0	15 (35.7)	5.4
Trunk	18 (12.3)	0.4	14 (13.6)	0.4	4 (9.5)	0.3
Back only	3 (2.0)	0.2	2 (1.9)	0.2	1 (2.4)	0.2
Upper limbs	3 (2.1)	0.1	2 (1.9)	0.2	1 (2.4)	0.1
Lower limbs	6 (4.1)	0.1	0 (0)	0	6 (14.3)	0.3

SCC: Squamous cell carcinoma, RTD: Relative tumor density

it represented the trunk as a whole in males (13.6%), and the lower extremities in females (14.3%). There was only a single case of SCC (0.6%) and only four cases of BCC (0.3%) arising on the dorsum of the hand or fingers. The greatest differences in RTDs between BCC and SCC were on the back (BCC: SCC ratio, 7.5:1), especially in men (BCC: SCC ratio, 9:1). Of note, no lower limbs' involvement was found in men with SCC. In general, in all three cancer types observed, males had systematically a higher density of tumors on the trunk than females, especially in MM cases. On the other hand, the lower limb involvement predominated in women, which was striking in SCC group. However, apart from the upper limbs in women in MM, the RTDs were below unity for anatomical areas of both upper and lower extremities in all tumor types investigated.

DISCUSSION

The incidence of human malignant skin tumors has continuously increasing trend worldwide, and they represent a serious medical and public health problem. Despite undisputed association between UVR exposure and cutaneous neoplasms, an exact relationship between the amount, pattern, and timing of exposure to UVR and the subsequent development of specific skin malignancies is not yet fully understood. Popular belief is that a crucial factor for the formation of SCC is cumulative lifetime sun exposure, while it is less important for the development of BCC, in which an intermittent solar exposure rather than chronic one may be more prejudicial etiologic determinant [1,18-20]. Even association between morphologic markers of cutaneous photodamage and an increased risk of BCC has been proven only moderate [21]. As for cutaneous MM, an intermittent intense sun exposure was shown to play considerable role as risk factor, whereas a high occupational sun exposure seemed to be inversely associated to MM development [1,18,20,22-24]. As a consequence, individual cancer types have different predominant anatomic locations. An uneven topographic distribution of cutaneous neoplasms generally parallels the indicators of UVR exposure and is one of the best surrogates for assessing the patterns of sun exposure. On the other hand, this should be interpreted with a certain degree of generalizability, because non-UVR linked factors also participate in the genesis of skin cancers, which sometimes emerge in body sites that never see the sun.

It is well-known that MMs develop most frequently on the trunk and extremities with gender disparities. Many previous cohort studies have shown [2-4,6], such as we did, the occurrence of MM was more common among males for the trunk and among females for both the upper and lower limbs. However, in NMSC, the results derived from some papers have not been so consistent. Although it is generally accepted that both BCCs and SCCs develop most frequently in the head and neck region, the percentages of tumors in this body part significantly differ among analyses conducted from various countries. Most of the published documents comprising Italian [3], Slovakian [8], Brasilian [9-11], Portuguese [12], and Romanian [7], or Iranian [13] studies have found, the head and neck represented 73.6-96.8% of all BCCs [3,7,8,10-13] and 70.2-77.6% of all SCCs [3,7-9,12] analyzed. In this study, this body part comprised 69% of BCCs and 81.5% of SCCs diagnosed, corroborating above-mentioned papers. Our results support the view, although both keratinocyte carcinomas are predominantly associated with chronic cumulative solar exposure, it seems to be more crucial etiologic factor for SCC development, compared to BCC. This is also supported by the fact, SCC individuals had a higher age. However, it is interesting that numerous Australian studies have described much lower proportional involvement of the head and neck region in NMSC lesions. For example, in BCC, the head and neck comprised only 40-67% of the cases [4,5,14-16] and in SCC, this location was even more rare, representing just 22-42.6% of all cases [4,5,14-16]. Similar data on SCC have also been documented in Saudi Arabian [25] and Ethiopian [26] studies. This finding could be at least partially explained by the fact, these geographic regions lie close to the equator with more intensive prolonged solar radiation throughout the year. As a result, native people may have a tendency to get undress those body parts, which are usually intermittently exposed to sunlight, such as the trunk and extremities. Even the disparate body site distributions of

skin cancers between women and men may reflect differences in sun exposure habits, such as clothing and work or leisure activities. In accord with many previous papers, we have showed marked sex differences in topographic sites of lesions. In MM, there was a high male to female ratio (2.6) for tumors of the trunk and low male to female ratio (0.5) for tumors of the leg. In SCC, the head and neck accounted for a larger proportion of lesions for men than women, and the lower limbs were affected more commonly (in our series exclusively) in women, justifying literature data [3,9,15,16,27]. In BCC, the trunk, especially the back, was more frequently involved in men than women, and in comparison, the head and neck region and lower limbs were more frequently affected in women, also corroborating the results from another author [10,11,15,16]. When we regarded the head and neck region alone, males had more commonly involved extrafacial part of the head and neck compared to women in both BCC and SCC lesions, similar to the findings of another study [3,4,9,10]. This is probably due to thicker and longer hair cover in females, which provide better protection against UVR-light. However, one should keep in mind that some histological subtypes of cutaneous neoplasms, for example, lentigo maligna melanoma, superficial BCC or verrucous SCC, exhibit specific etiological and clinical feature and have a predilection for certain body sites. Therefore, a precise assessment of topographic distribution of skin malignancies should also take into account their individual histological subtypes and varieties, some of which should be better evaluate separately.

In conclusion, we have observed striking heterogeneity for skin cancer risk by anatomic site. While MMs arise predominantly on the body parts intermittently exposed to the sunlight, such as the trunk and extremities, BCCs and especially SCCs develop most frequently on the sites that are habitually exposed to the sun, such as the head and neck. Although we considered anatomic location as a surrogate for assessing the patterns of solar exposure, which was the main limitation of this study, our results support an idea that development of different types of skin malignancies is influenced by distinct UVR patterns. Understanding how UVR response differs in the genesis of various skin cancers would be important for educating the public on safe sunlight behaviors and may help to improve preventive strategies.

ACKNOWLEDGMENTS

The authors wish to thank Dr. Zacharová Oĺga and Dr. Pokorný Dušan, for their educational support and technical assistance.

REFERENCES

1. Armstrong BK, Kricker A. The epidemiology of UV induced skin cancer. J Photochem Photobiol B 2001;63:8-18.
2. Bulliard JL, De Weck D, Fisch T, Bordoni A, Levi F. Detailed site distribution of melanoma and sunlight exposure: Aetiological patterns from a Swiss series. Ann Oncol 2007;18:789-94.
3. Franceschi S, Levi F, Randimbison L, La Vecchia C. Site distribution of different types of skin cancer: New aetiological clues. Int J Cancer 1996;67:24-8.
4. Youl PH, Janda M, Aitken JF, Del Mar CB, Whiteman DC, Baade PD. Body-site distribution of skin cancer, pre-malignant and common benign pigmented lesions excised in general practice. Br J Dermatol 2011;165:35-43.
5. Heal C, Buettner P, Raasch B, Browning S. Minor skin excisions in general practice in North Queensland. Aust Fam Physician 2006;35:825-8.
6. Cecconi L, Busolin A, Barbone F, Serraino D, Chiarugi A, Biggeri A, *et al.* Spatial analysis of incidence of cutaneous melanoma in the Friuli Venezia Giulia region in the period 1995-2005. Geospat Health 2016;11:422.
7. Andrese E, Solovastru LG, Taranu T, Iancu LS. Epidemiological and pathological aspects of skin cancer in North East of Romania. Rev Med Chir Soc Med Nat Iasi 2014;118:457-62.
8. Plesko I, Severi G, Obsitníková A, Boyle P. Trends in the incidence of non-melanoma skin cancer in Slovakia, 1978-1995. Neoplasma 2000;47:137-42.
9. Nasser N, Nasser Filho N, Lehmkuhl RL. Squamous cell cancer--31-year epidemiological study in a city of south Brazil. An Bras Dermatol 2015;90:21-6.
10. Souza CF, Thomé EP, Menegotto PF, Schmitt JV, Shibue JR, Tarlé RG. Topography of basal cell carcinoma and their correlations with gender, age and histologic pattern: A retrospective study of 1042 lesions. An Bras Dermatol 2011;86:272-7.
11. Ferreira FR, Pevide Bda C, Rodrigues RF, Nascimento LF, Lira ML. Differences in age and topographic distribution of the different histological subtypes of basal cell carcinoma, Taubaté (SP), Brazil. An Bras Dermatol 2013;88:726-30.
12. Andrade P, Brites MM, Vieira R, Mariano A, Reis JP, Tellechea O, *et al.* Epidemiology of basal cell carcinomas and squamous cell carcinomas in a department of dermatology: A 5 year review. An Bras Dermatol 2012;87:212-9.
13. Ghanadan A, Abdollahi P, Rabet M, Naraghi Z, Abbasi MA, Moslehi H, *et al.* Different anatomical distribution of basal cell carcinoma subtypes in iranian population: Association between site and subtype. Ann Dermatol 2014;26:559-63.
14. Subramaniam P, Olsen CM, Thompson BS, Whiteman DC, Neale RE; QSkin Sun and Health Study Investigators. Anatomical distributions of basal cell carcinoma and squamous cell carcinoma in a population-based study in Queensland, Australia. JAMA Dermatol 2016.
15. Staples MP, Elwood M, Burton RC, Williams JL, Marks R, Giles GG. Non-melanoma skin cancer in Australia: The 2002 national survey and trends since 1985. Med J Aust 2006;184:6-10.
16. Marks R, Staples M, Giles GG. Trends in non-melanocytic skin cancer treated in Australia: The second national survey. Int J Cancer 1993;53:585-90.
17. Pearl DK, Scott EL. The anatomical distribution of skin cancers. Int J Epidemiol 1986;15:502-6.
18. Kennedy C, Bajdik CD, Willemze R, De Gruijl FR, Bouwes Bavinck JN; Leiden Skin Cancer Study. The influence of painful sunburns and lifetime sun exposure on the risk of actinic keratoses, seborrheic warts, melanocytic nevi, atypical nevi, and skin cancer. J Invest Dermatol 2003;120:1087-93.
19. Calzavara-Pinton P, Ortel B, Venturini M. Non-melanoma skin cancer, sun exposure and sun protection. G Ital Dermatol Venereol 2015;150:369-78.
20. Zanetti R, Rosso S, Martinez C, Nieto A, Miranda A, Mercier M, *et al.* Comparison of risk patterns in carcinoma and melanoma of the skin in men: A multi-centre case-case-control study. Br J Cancer 2006;94:743-51.
21. Khalesi M, Whiteman DC, Doi SA, Clark J, Kimlin MG, Neale RE. Cutaneous markers of photo-damage and risk of basal cell carcinoma of the skin: A meta-analysis. Cancer Epidemiol Biomarkers Prev 2013;22:1483-9.
22. Gass R, Bopp M. Mortality from malignant melanoma: Epidemiological trends in Switzerland. Praxis (Bern 1994) 2005;94:1295-300.
23. Gandini S, Sera F, Cattaruzza MS, Pasquini P, Picconi O, Boyle P, *et al.* Meta-analysis of risk factors for cutaneous melanoma: II. Sun exposure. Eur J Cancer 2005;41:45-60.
24. Vuong K, McGeechan K, Armstrong BK; AMFS Investigators; GEM Investigators, Cust AE. Occupational sun exposure and risk of melanoma according to anatomical site. Int J Cancer

2014;134:2735-41.
25. Al Aboud KM, Al Hawsawi KA, Bhat MA, Ramesh V, Ali SM. Skin cancers in Western Saudi Arabia. Saudi Med J 2003;24:1381-7.
26. Bezabih M. Patterns in skin cancers in Tikur Anbessa hospital. Ethiop J Health Sci 2001;11:53-7.
27. Nguyen KD, Han J, Li T, Qureshi AA. Invasive cutaneous squamous cell carcinoma incidence in US health care workers. Arch Dermatol Res 2014;306:555-60.

Source of Support: Nil, Conflict of Interest: None declared.