

Characteristics of non-melanoma skin cancer depending upon occupational solar UV exposure dosage

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ABSTRACT

Objectives. Non-melanoma skin cancer (NMSC) is the most common human malignancy and is strongly related to solar ultraviolet (UV) radiation exposure. Occupational UV exposure is associated with a two-fold increased risk of developing NMSC, but still only few European countries recognize NMSC as an occupational disease. The study aims to analyze the clinical and histopathological features of NMSC with regard to personal cumulative occupational UV exposure doses.

Material and methods. A retrospective, analytical, comparative study was conducted during 2017-2019 with focus on outdoor workers presenting with NMSC. Occupational solar UV exposure dose was calculated based on the Wittlich algorithm and cumulative lifetime exposure of the general population of the same age was estimated according to German Standards of 130 SED/year. Subjects were divided in two groups (OW1 and OW2) according to differences between occupational exposure and estimated cumulative lifetime exposure of the general population. High-risk clinical and histopathological characteristics were compared between groups.

Outcomes. The study included 25 consecutive outdoor workers diagnosed with BCC (N=21) and SCC (N=4). Occupational solar UV exposure doses were calculated for Romanian workers and identified mean values of 17695 SED two times higher than estimative leisure cumulative lifetime solar UV exposure for a person of the same age from the general population according to German standards of 130 SED/year. Subjects were classified in two groups: group 1 (OW1) included subjects who were exposed to an additional occupational UV dose less than 50% of the cumulative lifetime exposure dose of a person of the same age from the general population according to German standards and group 2 (OW2) included subjects exposed to additional professional UV doses higher than 50%. 12 subjects were included in OW 1 and 13 subjects in OW2.

Data analysis between groups identified significant statistical differences with regard to *high-risk body locations* and *tumour size*, present in 100% of OW2 and 58.3% of OW1 (χ^2 (1, N=51) = 6.771, p=0.015) and to *high-risk histopathological subtypes*, present in 56% OW2 and 33.3% OW1 (χ^2 (1, N=51) = 4.812, p=0.036). *Ulceration* was present on the histopathological report of all subjects in OW2. OW2 was associated with higher percentages of moderate to severe *grades of actinic elastosis* and of *desmoplastic reaction* and a more *rapid evolution of lesions*.

Conclusions: Outdoor workers in Romania are exposed to an occupational solar UV dose two times higher than the cumulative lifetime exposure dose of the general population of the same age which may receive up to 130 SED/year according to German standards and they bear an increased risk of NMSC. Occupational NMSC induced by UV exposure should be recognized as an occupational disease if the subject received more than 50% additional UV exposure at the workplace.

Keywords: skin cancer, UV occupational exposure, UV dosimetry

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INTRODUCTION

Non-melanoma skin cancer (NMSC), also – more precisely – referred to as keratinocyte cancer, is the most common human malignancy in both sexes and comprises basal cell carcinomas (BCC) and squamous cell carcinomas (SCC) [1].

Exposure to solar ultraviolet (UV) radiation is considered the most important risk factor in NMSC's etiopathogenesis [2] and is included since 2012 in the category of group 1 carcinogens (carcinogens to humans) by the World Health Organization [3]. Still, few European countries recognize occupationally UV-induced NMSC as an occupational disease, such as, for example, Germany, Denmark, and Italy. In 2016, only seven European countries recognized SCC as an occupational disease and only six recognized BCC, Romania not being part of any of these categories [4].

Furthermore, recent studies demonstrated a two-fold increased risk of developing NMSC, including BCC and SCC for occupationally UV-exposed individuals when compared to the general population which only received leisure UV exposure [5,6].

The last decade provided new insights in occupationally-induced NMSC along with the introduction of UV-measuring personal dosimeters. This equipment permitted real quantitatively UV measurements for outdoor professions and therefore an objective comparison between UV exposure in terms of occupation and geographical factors. For example, in Germany, the general population is exposed to 130 SED/year (1 standard erythemal dose = 100J/cm²) while outdoor workers, for legal purposes, are considered to be exposed on average to an additional 300 SED/year [7]. Taking these aspects into consideration, in Germany, NMSC is considered an occupational disease if an outdoor worker receives more than 40% additional UV exposure by his work to his lifetime UV exposure, since this is assumed to double the risk for NMSC development [8]. More precisely, lifetime UV exposure is calculated as years of first tumor detection by 130 SED/year (for example, for first tumor detection at the age of 60, the worker is expected to have received 7800 SED lifetime UV exposure). Furthermore, for every work year, occupational UV exposure dose is calculated as working years by 300 SED/year (for example, for 15 outdoor working years, occupational exposure will be of 4500 SED). Therefore, in this example, the outdoor worker received 57% additional occupational UV exposure to his lifetime UV exposure and would be entitled to recognition of NMSC as an occupational

disease (if the tumour occurred in occupationally UV exposed body locations).

In Romania, personal dosimetry studies were recently conducted and identified alarming UV doses for outdoor workers of up to 633 SED/year [9], a value twice as high as the German values, but still this pathology is not recognized as an occupational disease. From the authors' knowledge, in Romania, no studies have correlated occupational UV doses with the presence and characteristics of NMSC, yet.

Therefore, this study aims to analyze the clinical and histopathological features of NMSC with regard to extrapolated personal cumulative occupational solar UV exposure doses.

MATERIALS AND METHODS

A retrospective, analytical, comparative study was conducted in a University Department of Dermato-venereology in Bucharest, with consecutive outdoor workers presenting with NMSC during 2017-2019.

A detailed personal history was obtained for all patients at the time of hospital admission and/or followed by additional telephone questions on a case to case basis. All patients were treated by surgical excision of tumors and all lesions underwent histopathological examinations.

Personal history was divided in two parts: (1) general information such as socio-demographic data, significant associated afflictions or risk factors and details about the evolution of lesions and (2) a thorough anamnesis based on work-related behavior which offered the possibility of determining occupational exposure dosage: hours per day and days per week spent at the work place, time intervals of outdoor activities, breaks, working years, geographical coordinates of the work place, applied sun protective measures and equipment. Occupational exposure dosage was calculated based on the Wittlich algorithm [8] – a German standardized instrument which calculates cumulative lifetime UV exposure and on recent Romanian studies [9], through which real-time measured data of UV exposure doses were obtained by personal dosimetry using the GENESIS UV system.

The Wittlich algorithm was applied for each subject included in the study. For Romania, recent studies determined 633 SED/year [9] as mean exposure level which was used for calculating occupational solar UV exposure dosage as 633 SED times (*) number of working years. Furthermore, cumulative lifetime exposure of the general popu-

lation of the same age according to German Standards was estimated as 130 SED/year [7] times (*) number of years. All values are presented in SED. These data permitted a classification of subjects in two groups according to differences between occupational UV exposure dosage and cumulative lifetime exposure dose of the general population of the same age: group 1 (OW1) included subjects exposed to an additional occupational solar UV dose less than 50% of the cumulative lifetime exposure dose of a person of the same age from the general population according to German standards and group 2 (OW2) included subjects exposed to additional professional UV doses higher than 50%.

Clinical data obtained from personal history and histopathological criteria from each patient's personal report were analyzed and correlated between groups OW1 and OW2. High-risk clinical and histopathological criteria were chosen based on National Comprehensive Cancer Centre (NCCN) recommendations [10,11]. High-risk clinical features included location and size (area L (trunk and extremities) > 20 mm, area M (cheeks, forehead, scalp, neck, and pretibial region) >10 mm, area H (central face, eyelids, eyebrows, periorbital skin, nose, lips, chin, mandible, preauricular and postauricular skin/sulci, temple, ear, genitalia, hands, and feet) and high-risk histopathological criteria included high-risk subtypes (mixed infiltrative, basosquamous BCCs, adenoid SCC).

Other analysed clinical criteria included number of lesions, tumor diameter and evolution of lesions measured in months and other histopathological criteria included tumor thickness, ulceration, desmoplastic reaction and grades of associated actinic elastosis.

Data was analyzed using the software SPSS for Windows version 20 (SPSS, Chicago, IL, USA). Mean values and standard deviations (SD) were calculated for numerical data. Statistical significance was tested for categorical data by Chi-square analysis (χ^2), corrected by Fisher's exact method in selected cases. Mean values of numerical data were compared using Independent-samples T test (Levene's test for Equality of Variances). $P < 0.05$ was considered to indicate statistical significance.

OUTCOMES

The study included 25 outdoor workers of various occupations such as construction and agriculture workers, outdoor sports teachers, workers of the oil industry and outdoor military personnel. Males were predominant (18 males, 69.2%) with

only 7 females (26.7%). 15 (57.7%) subjects came from urban environments and 10 (38.5%) from rural environments. Mean age of outdoor workers was 68.92 (SD 12.09, min 35, max 93). Studied lesions included 21 (80.8%) BCC and 4 (15.4%) SCC.

Occupational UV exposure doses identified mean values of 17,695 SED (SD 6,449, min 3,165, max 25,320), two times higher than mean values of 8,959 SED (SD 1572, min 4550, max 12090) for estimated leisure cumulative lifetime UV exposure for a person of the same age from the general population according to German standards. A detailed description of identified and estimated doses is presented in Figure 1. Obtained solar UV data permitted identification of 12 subjects (48%) in group OW1 and 13 subjects (52%) in group OW 2.

Analysis of high-risk clinical and histopathological criteria (Table 1) between groups identified significant statistical differences with regard to high-risk locations and size, present in 100% of OW2 and 58.3% of OW1 (χ^2 (1, N=51) = 6.771, $p = 0.015$) and to high-risk histopathological subtypes, present in 56% OW2 and 33.3% OW1, respectively (χ^2 (1, N=51) = 4.812, $p = 0.036$).

In OW1, 33.3% subjects associated low-risk clinical criteria such as location and size. Most frequent high-risk location and size was area M > 10 mm in both groups: 33.3% of subjects for OW 1 and 69.2% for OW2 (Table 2). Low-risk histopathological subtypes were more frequently identified in OW1 as nodular BCC in 50% of cases; in OW2, most common high-risk histopathological subtype was mixed infiltrative BCC (61.5%) (Table 3).

Table 4 presents significant statistical differences between groups in terms of presence of ulceration and presence of moderate to severe actinic elastosis and desmoplastic reaction. Ulceration was present on the histopathological report of all subjects in OW2 (χ^2 (1, N=51) = 12.745, $p < 0.001$). Moderate to severe grades of actinic elastosis were identified in 92.3% subjects from OW2 and in 75% of subjects from OW1 (χ^2 (1, N=51) = 7.164, $p = 0.017$). Moderate to severe grades of desmoplastic reaction were present in 84.6% lesions from OW2 and in 58.3% lesions from OW1 (χ^2 (1, N=51) = 4.043, $p = 0.045$).

Table 5 identified significant statistical differences regarding diameter, tumor thickness and evolution. OW2 associated higher mean diameters of lesions (7.26 compared to 4.47; t_{obt} (23) = -2.49, $p = 0.20$), increased mean values of tumor thickness on the histopathological report (1.92 compared to

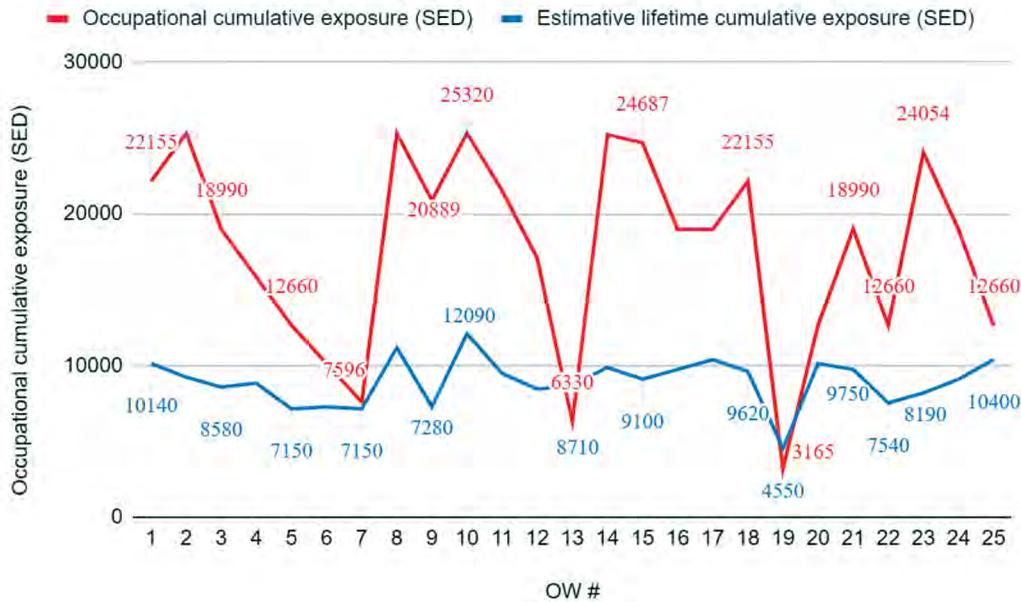


FIGURE 1. Differences between occupational cumulative UV exposure doses of subjects and lifetime cumulative UV exposure doses for the general population of the same age

TABLE 1. Overview of high-risk clinical and histopathological characteristics

High-risk Characteristics	N	%	χ^2 (1, N=25)	
High-risk location and size*	OW1	7	58.3%	6.771 (p = 0.015)
	OW2	13	100%	
High-risk histological subtype*	OW1	4	33.3%	4.812 (p = 0.036)
	OW2	10	56%	

*According to NCCN

TABLE 2. Difference between high-risk NMSC clinical criteria between groups of outdoor workers

	Clinical criteria: High-risk location and size*				Total
	Low-risk	Area L>20 mm	Area M>10 mm	Area H	
OW1	4 (33.3%)	2 (16.7%)	4 (33.3%)	2 (16.7%)	12
OW2	0	0	9 (69.2%)	4 (30.8%)	13

*According to NCCN

TABLE 3. Difference between high-risk NMSC histopathological subtypes between groups

	Histopathological criteria: Subtypes*					
	Nodular BCC	Superficial BCC	Infiltrative mixed BCC	Metatypical BCC	Well-dif. SCC	Poorly dif. SCC
OW1	6 (50%)	1 (8.3%)	2 (16.7%)	1 (8.3%)	1	1
OW2	2 (15.4%)	0	8 (61.5%)	1 (7.7%)	1	1

*According to NCCN

TABLE 4. Differences between additional high-risk NMSC histopathological criteria

Histopathological high-risk criteria	OW1 N (%)	OW2 N (%)	χ^2 (1, N=25)
Presence of ulceration	4 (33.3%)	13 (100%)	12.745 (p<0.001)
Actinic elastosis (moderate-severe)	12 (75%)	21 (92.3%)	7.164 (p=0.017)
Desmoplastic reaction (moderate-severe)	7 (58.3%)	11 (84.6%)	4.043 (p=0.045)

TABLE 5. Differences between additional characteristics between groups of outdoor workers (OW)

Characteristic	Groups	N	Mean	SD	$t_{obt}(23)$
Diameter (mm)	OW1	12	10.75	4.47	-2.49 (p=0.020)
	OW2	13	16.85	7.26	
Tumor thickness (mm)	OW1	12	1.57	0.98	-2.08 (p=0.048)
	OW2	13	2.86	1.92	
Evolution (months)	OW1	12	18.75	8.30	4.74 (p<0.001)
	OW2	13	7.15	2.881	
Number of lesions	OW1	12	1.33	0.65	-1.01 (p=0.319)
	OW2	13	1.85	1.62	

0.98; $t_{obt}(23) = -2.08$, $p=0.48$) and a more rapid evolution (mean value of 18.75 months in OW1 and 7.15 months in OW2; $t_{obt}(23) = 4.74$, $p < 0.001$). Number of lesions was not statistically different between groups ($t_{obt}(23) = -1.01$, $p = 0.319$).

DISCUSSION

The impact of occupational solar UV radiation exposure is a topic of great interest worldwide with recent literature studies emphasizing the long-term health consequences of cumulative UV exposure on both skin, with the induction of NMSC and melanomas and on other organs such as the eyes, increasing the risk of cataract and age-related macular degeneration [12].

Furthermore, the constant depletion of the atmospheric ozone layer in the last few decades caused values of UV measurements at sea level up to 15 times higher when compared to satellite estimations, significantly increasing the risk of skin cancer pathology and associated long-term associated morbidity and mortality [13].

The risk of developing NMSC may also be directly linked to types of profession. Epidemiological studies presented a stratification of NMSC's risk according to occupation. The highest risk of developing NMSC was associated with mountain guides, followed by agriculture workers and gardeners [14].

Studies with focus on personal dosimetry permitted the identification of real-time quantitatively data on European outdoor workers with alarming results. For example, outdoor workers in Denmark are exposed to 5 SED/day [15], in Switzerland up to 28.6 SED/day [16], in Spain 6.11 SED/day [17], in France 1.19 SED/day [18] and in Romania from 6.4 SED/day [19] up to 19 SED/day [20]. These data show high variability between European countries and suggest the necessity of stratifying NMSC according to exposure dosage in order to obtain

prediction models of NMSC's characteristics with regards to occupation and occupational protective behavior. Furthermore, these aspects will offer the possibility of developing specific sun protective measures for each occupation.

Recognizing NMSC as an occupational disease across Europe is a first essential step in preventing this affliction. Currently, up to 90% of the allocated healthcare budget for NMSC is invested in treatment and only 10% in prevention [21]. Therefore, development of NMSC is associated with workers absenteeism, reduced productivity at the workplace and even job loss; however, preventive measures are available and can be efficiently applied [22]. The lack of sun smart protective behavior at the work place is observed throughout Europe, with most outdoor workers using photoprotection during holidays, but not during working hours [23], noticing a big gap in the culture of prevention.

Characterizing occupationally-induced NMSC has been previously attempted, identifying the "mask area" of the face as the most common tumor localization and mixed with an aggressive component as the most frequent histopathological subtype [24].

This study related NMSCs clinical and histopathological characteristics in outdoor workers to differences between their occupational solar UV exposure compared to the cumulative lifetime exposure of the general population of the same age according to German standards of 130 SED/year. This is the first such attempt in Romania to the best of the authors' knowledge. The subjects were categorized in two groups similarly with the German NMSC recognition system, in which NMSC is considered occupationally-induced if the subject received more than 40% additional UV exposure by his work compared to his lifetime UV exposure. Since leisure solar UV dosage in Romania is not available, lifetime exposure was calculated based on the German standards of 130 SED/year. Addi-

tionally, taken into consideration that leisure UV exposure in Romania may be higher than Germany since the occupational UV exposure is higher, the threshold for categorizing subjects was set at 50% additional UV exposure at the workplace to the cumulative lifetime UV exposure.

In Romania, outdoor workers exposed to 50% additional occupational solar UV doses to the cumulative lifetime UV exposure showed statistically significant higher percentages of high-risk clinical and histopathological criteria. These included localization on high-risk areas and higher dimensions of tumors, higher percentages of high-risk histopathological subtypes, more frequent association with ulceration, high grades of desmoplastic reaction and actinic elastosis as well as a more rapid evolution of lesions.

The authors propose this classification system in Romania for recognizing NMSC, with 633 SED/year as reference value for occupational UV exposure dose and with recognition of NMSC as an occupational disease as long as the subject receives more than 50% additional UV exposure at the workplace to his lifetime cumulative exposure dose according to German standards of 130 SED/year.

Last but not least, the authors draw attention to the necessity of introducing NMSC in National Cancer Registries, as well as in the national list of occupational diseases, two topics of great interest

not only locally but also at an international level [25].

CONCLUSIONS

1. Outdoor workers in Romania are exposed to an occupational solar UV dose two times higher than the cumulative lifetime exposure dose of the general population of the same age which may receive up to 130 SED/year according to German standards.

2. Outdoor workers in Romania exposed to higher occupational solar UV doses bear an increased risk of NMSC with high-risk location and sizes, high-risk histopathological subtypes, presence of ulceration and high grades of actinic elastosis and desmoplastic reaction.

3. Outdoor workers exposed to higher occupational UV doses are associated with higher lesion diameters, increased tumor thickness and a more rapid evolution of lesions.

4. Occupational NMSC induced by UV exposure should be recognized as an occupational disease if the subject received more than 50% additional UV exposure at the workplace compared to his lifetime cumulative UV exposure dose of 130 SED/year, calculated on the base of 633 SED/year as a mean exposure dose for occupational solar UV exposure in Romanian workers.

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