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Skin Cancers in Croatia, 2003–2005: Epidemiological Study

Jasna Lipozenčić[1], Dijana Celić[2], Marija Strnad[3], Ružica Jurakić Tončić[1], Aida Pašić[1], Jaka Radoš[1] and Ariana Znaor[3,4]

[1] Department of Dermatology and Venereology, School of Medicine, Zagreb University, Zagreb, Croatia
[2] Medikol Outpatient Department, Zagreb, Croatia
[3] National Institute of Public Health, Zagreb, Croatia
[4] National Cancer Registry, Zagreb, Croatia

A B S T R A C T

This study presents the incidence of major nonmelanoma skin cancers (major NMSCs), other nonmelanoma skin cancers (other NMSCs) and malignant melanoma (MM) in Croatia. The skin cancers recorded between 1 January 2003 and 31 December 2005 were retrospectively analyzed. Until 2003, the incidence of major NMSCs and other NMSCs was not estimated in Croatia. Incident cases of NMSCs were identified by the use of a questionnaire distributed to dermatology departments in Croatia and then collected at the University Department of Dermatology and Venereology, Zagreb University Hospital Center, and from the records kept at the National Cancer Registry. Incident cases of MM were extracted from the National Cancer Registry. During the 3-year period, 9,479 cases of major NMSCs are recorded, 4,622 (49%) in male and 4,857 (51%) in female patients. The crude incidence rate was 72.1/100,000 for males and 70.3/100,000 for females. Basal cell carcinoma (BCC) was the most common major NMSC in both sexes. In the total number of major NMSCs, there were 7,244 cases of BCC. Squamous cell carcinoma (SCC) was the second most common major NMSC. There were 1,860 SCC cases. The crude incidence rate was 54.9/100,000 for BCC in males, 53.9/100,000 in females, and 14.6/100,000 for SCC in male and 13.4/100,000 in female patients. Other NMSCs were registered in 119 cases (53% male and 47% female). The crude incidence rate was 0.9/100,000 for male and 0.8/100,000 for female patients. MM was registered in 1,427 cases (48% male and 52% female.) The crude incidence rate was 10.7/100,000 for males and females. These results will serve as reference for studying the patterns of descriptive epidemiology of major NMSCs, other NMSCs and MM in Croatia and Europe in the forthcoming years.

***Key words**: skin cancers, melanoma, epidemiology, incidence, Croatia*

Introduction

Nonmelanoma skin cancers (NMSCs) comprise the most common group of skin cancers in the different parts of the world[1,2]. In clinical practice major NMSCs refers to squamous cell carcinoma (SCC), basal cell carcinoma (BCC) and neoplasms with high malignant potential such as Merkel cell carcinoma[1,3,4]. Major NMSCs and malignant melanoma (MM) incidence is increasing worldwide[5–7]. Dermatologists have repeatedly criticized that the public health importance of skin cancers is not appropriately reflected by the patient-based cancer incidence rates of population-based cancer registries[2]. Until 2003, the incidence of major NMSCs and other NMSCs in Croatia was not reported. Upon the initiative of the Committee of Dermatology and Venereology, Ministry of Health and Social Welfare, Republic of Croatia, since January 2003, the incidence of major NMSCs and other NMSCs has been monitored and studied at the University Department of Dermatology and Venereology, Zagreb University Hospital Center and National Cancer Registry. Health institutions and private practice offices are obliged to submit notification of all skin cancers to the National Cancer Registry. In Croatia, malignant melanoma (MM) has been registered since 1962 by the National Cancer Registry[8]. The aim of the present study

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was to assess the incidence of major NMSCs, other NMSCs and MM in Croatia during the 2003–2005 period.

Materials and Methods

Cases of major NMSCs, other NMSCs and MM recorded from January 1, 2003 to December 31, 2005 were retrospectively analyzed. Data were derived from hospital discharge notification called »Onco type card« and outpatient »Malignant neoplasm notification«, submitted to the National Cancer Registry. The Croatian National Cancer Registry at the Croatian National Institute of Public Health was founded in 1959[8]. Since 1994, it has been a full member of the International Association of Cancer Registries (IARC), and the data on cancer incidence in Croatia have been included in the last three volumes of Cancer Incidence in Five Continents publications[5–7]. Under the Statistical Research Program promulgated by the Parlament, health institutions and private health practitioners are required to submit cancer notification to the Registry. To improve data coverage, Committee of Dermatology and Venereology of the Ministry of Health and Social Welfare of Croatia designed the questionnaire which contained information on major NMSCs and other NMSCs diagnosed at major Dermatology departments in Zagreb, Split, Rijeka and Osijek, and General Hospitals in Zadar, Karlovac, Slavonska Požega, Slavonski Brod, Vukovar and Dubrovnik. The questionnaire, »Onco type card« and »Malignant neoplasm notification« contained information on each patient (personal identification data, sex, date of birth, place of residence, histopathologic type of skin cancer and therapy) and information on the hospital where patients were treated (name of the hospital/clinic and department, address, date of admittance and date of discharge). The 38% of major and other NMSCs were reported by the questionnaire and 62% by the Registry. All incident cases of MM were extracted from the National Cancer Registry[8]. Patients living abroad, reports received in duplicate and cancer recurrences were excluded. All skin cancers were verified by histopathology. Keratoacanthoma and Bowen's disease were studied separately from invasive squamous cell carcinoma (SCC). Data were encoded according to the International Classification of Diseases Tenth Revision (ICD-10), i.e. code C44 for basal cell carcinoma (BCC), squamous cell carcinoma (SCC), basal-squamous cell carcinoma, Bowen disease, Merkel cell carcinoma, malignant neoplasms of sebaceous and sweat glands and extramammary Paget disease, C46 for Kaposi sarcoma, C49 for sarcoma of connecting and soft tissues and unspecified sarcoma, C84 for lymphoma cutis and C43 for MM[9]. Group of major NMSCs included BCC, SCC, basal-squamous cell carcinoma, Bowen disease, Keratoacanthoma and Merkel cell carcinoma. Paget disease, lymphoma cutis, sarcoma cutis, porocarcinoma, pilomatrix carcinoma, trichilemmal carcinoma, sebaceous gland carcinoma and malignant fibrous histiocytoma were classified as other NMSCs. Crude rate and age-specific incidence rate were calculated on the basis of 2001 Croatian census[10]. Age-standardized incidence rate of major NMSCs and MM was calculated by the direct standardization method, using the World Standard Population[11]. It was not calculated for other NMSCs since it appeared in a statistically irrelevant number.

Statistical analysis was done by use SPSS 13.0 software.

Results

During the period from January 1, 2003 until December 31, 2005, a total of 9,479 major NMSCs were reported, i.e. 4,622 (49%) in male and 4,857 (51%) in female patients, male to female ratio 0.9 (Table 1). In the total number of major NMSCs, the highest incidence was recorded for BCC (Table 1). There were 7,244 BCC cases, i.e. 3,519 (76%) in male and 3,725 (77%) in female patients. SCC was the second most common major NMSC, with the total of 1,860 SCC cases, 934 (20%) in males and 926 (19%) in females. The total of 119 other NMSCs were

TABLE 1
MAJOR NONMELANOMA SKIN CANCERS AND MELANOMA IN CROATIA FROM 2003–2005

	Total number		Percentage		Crude rate/100,000		Incidence (World)/100,000	
	Males	Females	Males	Females	Males	Females	Males	Females
Basal cell carcinoma	3,519	3,725	76*	77*	54.9	53.9	33.6	24.5
Squamous cell carcinoma	934	926	20*	19*	14.6	13.4	8.9	5.2
Basal-squamous cell carcinoma	25	38	0.5*	0.8*	0.4	0.5	0.2	0.2
Merkel cell carcinoma	6	2	0.1*	0.04*	0.09	0.02	0.05	0.005
Bowen disease	110	142	2*	3*	1.7	2.0	1.0	0.9
Keratoacanthoma	28	24	0.6*	0.5*	0.4	0.3	0.03	0.2
Total of major NMSCs	4,622	4,857	49*	51*	72.1	70.3	56.1	36.4
Melanoma	685	742	48†	52†	10.7	10.7	7.3	6.4

* Percentage of the total number of major NMSCs, † Percentage of the total number of MM

TABLE 2
OTHER NONMELANOMA SKIN CANCERS IN CROATIA FROM 2003–2005

	Total number		Percentage*		Crude rate/100,000	
	Males	Females	Males	Females	Males	Females
Paget disease (extramammary)	1	7	2	13	0.01	0.1
Mycosis fungoides	16	9	25	16	0.2	0.1
Lymphoma, unspecified	5	3	8	5	0.07	0.04
Kaposi sarcoma	15	13	24	23	0.2	0.2
Leiomyosarcoma	7	3	11	5	0.1	0.04
Dermatofibrosarcoma protuberans	4	3	6	5	0.06	0.04
Sarcoma, unspecified	8	7	13	13	0.1	0.1
†Other skin cancers	7	11	11	20	0.1	0.2
Total	63	56	53	47	0.9	0.8

* Percentage of the total number of other NMSCs, †Porocarcinoma, Pilomatrix carcinoma, Trichilemmal carcinoma, Sebaceous gland carcinoma and Malignant fibrous histiocytoma

registered, i.e. 63 (53%) in male and 56 (47%) in female patients, male to female ratio 1.1 (Table 2). Other NMSCs that appeared in a statistically irrelevant number were classified in the group of other skin cancers that included porocarcinoma (3 cases in male and 0 female), pilomatrix carcinoma (1 male and 1 female), trichilemmal carcinoma (0 male and 2 female), malignant fibrous histiocytoma (1 male and 2 female) and sebaceous gland carcinoma (2 male and 6 female) (Table 2). MM was recorded in the total of 1,427 cases, i.e. 685 (48%) in male and 742 (52%) in female patients, male to female ratio 0.9 (Table 1). The age-specific incidence rate of BCC increases rapidly after the age of 60 in males and females, reaching the peak at the age group 80–85 in both sexes (Figure 1). In male and female patients, the age-specific incidence rate of SCC has showed an increase after the age of 60, with an abrupt rise and peak at the age of >80 (Figure 2). The age-specific incidence rate of MM continuously increased in all age groups in females, with a peak after the age of 80, and in males with a peak at the age group 55–59 and at the age of >85 (Figure 3). Table 3 shows the age-standardized incidence rate adjusted to the World Standard Population for skin cancers (C44) and MM (C43) in Croatia and in different world areas.

Discussion

BCC and SCC are the most common cancers in humans which are usually not life threatening[12]. Despite the low mortality, the economic costs from major NMSCs are enormous[13]. Preston and Stern estimated that the treatment of major NMSCs in the USA costs 500 million dollars yearly[14]. A high number of these cancers were recorded during the 2003–2005 period in Croatia. However, we believe that it is still underestimated due to variable recording and reporting by the many different specialists involved in the management of major NMSCs. The timing and periodicity of the ultraviolet light (UVL) exposure appears to be important in its effect on subsequent skin cancer risk[2]. The risk of BCC is increased by recreational exposure to the sun during childhood and adolescence[15]. Intense intermittent sun exposure is associated with a higher risk of BCC than as a similar degree of continuous exposure[15]. SCC appears to be strongly related to cumulative sun exposure[15]. Exposure to ionizing radiation, arsenic and metoxsalen and UV-A radiation has also been linked to the development of BCC and SCC[15,16]. Acute intermittent UVL exposure elevates the risk of MM in the future[17]. The regular use of sunscreen has been shown to inhibit the development of potential precursors to invasive skin cancers such as actinic keratoses**,** Bowen disease and dysplastic nevi[18–20]. Croatia is partly a Mediterranean country whose coast and islands have more than 2,600 hours of sunshine *per* year[21]. In the inland there are a lot of agricultural households[22] which contributes to intensive periodical sun exposure of the population. The data on occupational and recreational exposure to the UVL and other risk factors for skin cancers in Croatian population are not available. Until now there was only one published article on the regional differences of the BCC incidence among certain

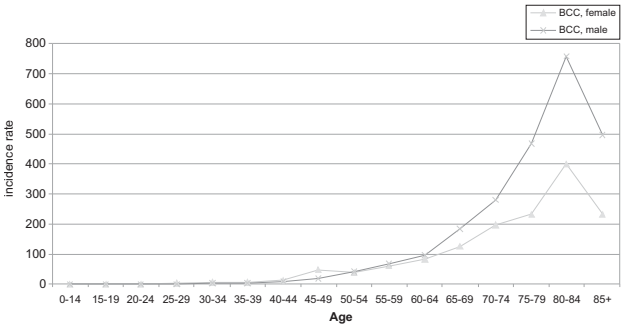

Fig. 1. The age-specific incidence rate of basal cell carcinoma according to sex (mean per *year).*

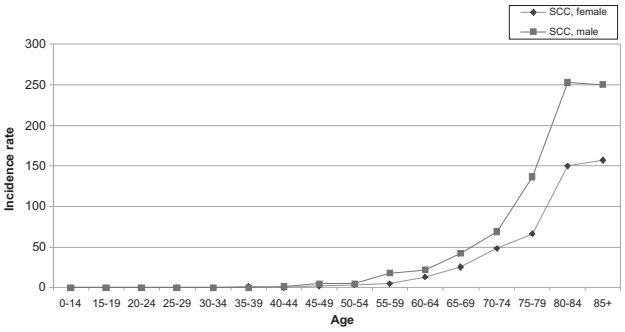

Fig. 2. The age-specific incidence rate of squamous cells carcinoma according to sex (mean per *year).*

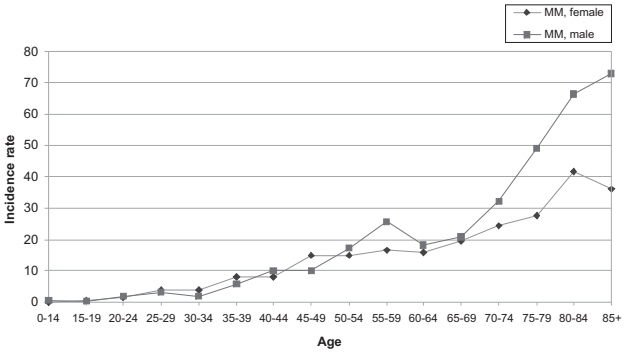

Fig. 3. The age-specific incidence rate of malignant melanoma according to sex (mean per *year).*

parts of Croatia[23]. The major NMSCs and MM incidence is rising all over the world[5–7]. In Europe, a doubling of MM rates every 10–20 years has been observed since 1970s[24]. The trend has stabilized in Northern European countries, but rapidly increasing rates are still observed in Southern and Eastern Europe[24]. MM incidence rates increase with proximity to the Equator, however, in Europe, the highest incidence rates are observed in the Northern Europe[5–7]. MM incidence in Croatia is lower than in the neighboring Slovenia, but higher than in areas of more Southern latitude in some other Mediterranean countries, such as Spain and Italy[5–7]. Due to much lower coverage of incidence data worldwide[5–7] the epidemiology of major NMSCs has not been so extensively studied. The latest edition of the Cancer Incidence in Five Continents publication presents cancer incidence data for the period from 1998 to 2002[7]. The data on skin cancers (C44) and MM (C43) incidence for selected registries are presented in Table 3. Of the member registries included in the publication, Brazil (Goiania) had the highest age-standardized incidence rate of NMSCs (C44) (198.1/100,000 for males and 177.1/100,000 for females)[7]. In Europe, the highest rates are observed in Switzerland, Geneva (133.1/ 100.000 for males and 113.0/100,000 for females)[7]. The age-standardized incidence rates for skin cancers (C44) and MM (C43) in Croatia were higher than in most of the Mediterranean countries. However, the manifold differences incidence of NMSCs observed be-

TABLE 3
THE AGE-STANDARDIZED INCIDENCE RATE ADJUSTED FOR THE WORLD STANDARD POPULATION FOR SKIN CANCERS (C44) AND MELANOMA (C43) IN DIFFERENT WORLD AREAS

	Male/C44	Female/C44	Male/C43	Female/C43
Switzerland, Geneva	133.3	113.0	18.5	19.0
Malta	72.2	39.4	5.5	5.1
Italy, Genoa Province	60.5	39.0	7.9	7.4
Italy Veneto Region	71.7	46.3	9.4	10.0
Italy, Varese Province	58.7	35.0	7.8	7.8
Croatia	55.3*	36.3*	6.9†	5.8†
Spain, Murcia	51.0	31.5	6.5	7.0
Slovenia	41.0	29.8	9.0	8.7
Italy, Naples	22.0	12.7	3.9	3.4
Austria	24.2	16.3	8.6	7.8
Serbia	24.1	17.6	4.0	3.8
Turkey, Antalya	19.8	15.4	1.3	1.0
Tunisia, Centre, Sousse	13.4	10.5	0.6	0.5
Algeria, Setif	7.7	4.5	0.2	0.4
Egypt, Gharbiah	6.8	2.5	0.3	0.3
Israel	3.4	3.0	11.2	9.5
Portugal, Porto	0.4	0.6	2.6	3.5

Source: Cancer Incidence in Five Continents, Vol IX, IARC (1998–2002), except C44 for Croatia
*The data of skin cancers (C44) in Croatia for the period from 2003–2005
†The data of melanoma for the period 1998–2002

tween the areas of the similar latitude suggest severe underreporting in some registration areas. Until this effort, the major NMSCs, as well as other NMSCs, such as mycosis fungoides have been underreported in Croatia as well, and further improvements in registration completeness are expected. To date, Croatia has not reported data on the incidence of major NMSCs to the IARC, the results presented will serve as reference data for the study of descriptive epidemiology of skin cancers in Croatia and Europe in the forthcoming years.

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D. Celić

Medikol Outpatient Department, Radnička cesta 80, 10000 Zagreb, Croatia
e-mail: dermatologija@medikol.hr

KARCINOMI KOŽE U HRVATSKOJ, 2003–2005

SAŽETAK

U radu je prikazana incidencija nemelanomskih tumora kože (»major NMSCs«), ostalih nemelanomskih tumora kože (»other NMSC«) i malignog melanoma (MM) u Hrvatskoj. Slučajevi navedenih neoplazmi kože registrirani između 1. siječnja 2003. i 31. prosinca 2005. godine su retrospektivno analizirani. Do 2003. godine, incidencija nemelanomskih i ostalih nemelanomskih tumora kože nije bila poznata. Slučajevi nemelanomskih i ostalih nemelanomskih tumora kože registrirani su putem upitnika upućenog dermatološkim ustanovama u Hrvatskoj i potom prikupljenih u Klinici za dermatologiju i venerologiju Kliničkog bolničkog centra Zagreb te putem prijava u Nacionalnom registru za rak. Slučajevi melanoma dobiveni su iz Nacionalnog registra za rak. Tijekom 3-godišnjeg perioda, registrirano je 9479 slučajeva nemelanomskih tumora kože, 4622 (49%) u muškaraca i 4857 (51%) u žena. Stopa incidencije iznosila je 72,1/100.000 za muškarce i 70,3/100.000 za žene. Bazocelularni karcinom (BCC) je bio najčešći nemelanomski tumor u oba spola. Od ukupnog broja nemelanomskih tumora, bilo je 7244 slučajeva BCC. Planocelularni karcinom (SCC) je drugi najčešći nemelanomski tumor. Registrirano je 1860 slučajeva SCC. Stopa incidencije iznosila je 54,9/100.000 za BCC u muškaraca, 53,9/100.000 za BCC u žena te za SCC 14,6/100.000 u muškaraca i 13,4/100.000 u žena. Ostali nemelanomski tumori registrirani su u 119 slučajeva (53% muškarci i 47% žene). Stopa incidencije bila je 0,9/100.000 za muškarce i 0,8/100.000 za žene. MM je registriran u 1427 slučajeva (48% muškarci i 52% žene.) Stopa incidencije bila je 10,7/100.000 za muškarce i žene. Ovi rezultati poslužit će kao referentni podaci za buduće deskriptivne epidemiološke studije o nemelanomskim, ostalim nemelanomskim tumorima kože te melanomu u Hrvatskoj i Europi.