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Descriptive Epidemiology of Cutaneous Squamous Cell Carcinoma in Croatia

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A B S T R A C T

The aim of the study was to investigate the squamous cell carcinoma (SCC) incidence in Croatia in the 2003–2005 period. The cases of SCC were retrospectively studied. Data were collected from University Department of Dermatology and Venereology, Zagreb University Hospital Center and National Cancer Registry. In the study period, there were 1,860 cases of SCC (934 men and 926 women). The crude incidence rate for the Croatian population of 100,000 was 14.6 for men and 13.4 for women. The age-standardized incidence rate (adjusted for the world standard population) was 8.9 for men and 5.2 for women. The head was almost exclusive localization of SCC in both sexes. The highest SCC incidence was recorded in Zadar County. These results will serve for the SCC trend monitoring in Croatia and Europe in the forthcoming years.

Key words: *squamous cell carcinoma, skin cancer, nonmelanoma skin cancers*

Introduction

Cutaneous SCC accounts for 10–20% of all skin malignancies and is the second most common skin cancer after basal cell carcinoma[1,2]. The cell of origin is the epidermal keratinocytes, which undergoes malignant transformation with repeated ultraviolet (UV) induced mutation[1,2]. It is more frequent in countries with high insolation (number of sunny days)[1,2]. SCC evolves in most cases from precursor lesions of actinic keratosis (AK) and Bowen's disease[2]. Cutaneous SCC represents a broad spectrum of disease ranging from easily managed, superficially invasive cancer to highly infiltrative, metastasing tumors that can result in death[2]. Until 2003, the incidence of SCC in Croatia was not reported. Upon initiative of the Committee of Dermatology and Venereology, Ministry of Health and Social Welfare, Republic of Croatia, since January 2003, the incidence of SCC has been monitored and studied at University Department of Dermatology and Venereology, Zagreb University Hospital Center and National Cancer Registry. Croatia is situated on the south-east of Europe on the crossing of the Mediterranean, the Middle Europe and the South-eastern Europe[3]. It is located between 42*23' and 46*33' of the northern geographical width, and 13*30' and 19*27' of the eastern geographical length[3]. The importance of the geographical location of Croatia is increased by the Adriatic Sea which, as a part of the Mediterranean Sea, spreads the deepest and the most northern towards the middle part of the European continent[3]. With approximately 2,600 hours of sunshine *per* year the Adriatic coast is one of the sunniest on the Mediterranean[3]. In the inland part of Croatia there is predominant moderate warm humid climate[3]. Territorially and politically, Croatia is divided into 20 counties of which the Istria, Split-Dalmatia, Zadar, Šibenik-Knin, Dubrovnik-Neretva Counties, and parts of the Primorje-Gorski kotar and Lika-Senj Counties are situated on the Adriatic Sea[3]. The aim of this study was to assess the incidence of SCC in Croatia during the 2003–2005 period.

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Material and Methods

This study includes all histopathologically confirmed cases of SCC in Croatia during the period from January 1, 2003 until December 31, 2005. Data were collected by use of a questionnaire designed by the Committee of Dermatology and Venereology of the Ministry of Health and Social Welfare of Croatia. The questionnaire contained information on SCC cases diagnosed at dermatology departments through Croatia and reported to the University Department of Dermatology and Venereology Zagreb, University Hospital Center. The source of the data was also hospital discharge notification called »Onco Type Cards« and outpatient »Malignant Neoplasm Notification«, submitted to the National Cancer Registry. Data were encoded according to the International Classification of Diseases Tenth Revision (ICD-10), i.e. Code C44[4]. Data on the date of diagnosis, patient's age and sex, permanent address, SCC localization and histopathologic report were recorded. Age-specific and age-standardized incidence rates were calculated per 100,000 inhabitants by direct standardization to the Croatian population and World Standard Population[5,6]. Statistical analysis was done by use of SPSS 13.0 program.

TABLE 1
ANATOMICAL DISTRIBUTION OF CUTANEOUS SQUAMOUS CELL CARCINOMA

	Males (%*)	Females (%*)
Eyelid, unspecified	15 (2)	35 (4)
Nose	79 (10)	117 (14)
Lips, unspecified	17 (2)	28 (3)
Lower lip	57 (7)	22 (3)
Tongue	3 (0.3)	0
Chin	6 (1)	4 (0.5)
Cheeks	183 (22)	298 (36)
Forehead	100 (12)	108 (13)
Scalp	51 (6)	16 (2)
Ears	124 (15)	30 (4)
Neck	43 (5)	22 (3)
Trunk, unspecified	60 (7)	44 (5)
Arm, unspecified	33 (4)	28 (3)
Hand	29 (4)	25 (3)
Leg, unspecified	16 (2)	20 (2)
Calve	9 (1)	29 (4)

* Percentage of the total number of SCC on the known localization in males and females

Results

During the study period from 2003–2005, a total of 1,860 SCC cases were registered in 1,759 patients. The majority of patients, 1,672 (95%) had one tumor. Multiple tumors were registered in 86 (5%) patients, out of two tumors in 72 (4%) patients, three tumors in 13 (0.7%) patients and five tumors in 1 patient (0.05%). The occurrence of SCC was similar in both sexes (934 in men and 926 in women). The most frequent localization of SCC was on the head and neck in both sexes, 82% in men and 83% in women, in comparison with the trunk and extremities (18% in men and 17% in women) (Table 1). The cheeks were an almost exclusive localization of SCC in both sexes (22% in men and 36% in women), followed by the ears in men (15%), forhead (12% in men and 13% in women) and nose (10% in men and 14% in women) (Table 1). The ratio of photoexposed (head, neck, hand) to non-photoexposed skin areas was 6:1. The crude incidence rate of SCC was 14.6 *per* 100,000 for men and 13.4 *per* 100,000 for women (Table 2). The age-specific incidence rate of SCC and the adjusted rates for the world standard population are listed in Table 2. The highest increase in age-specific incidence rate of SCC was after the

TABLE 2
INCIDENCE RATE OF CUTANEOUS SQUAMOUS CELL CARCINOMA

Age group (years)	Total number of SCC (males/females)	Age specific incidence rate adjusted for Croatian population*(males/females)	Incidence rate adjusted for World population† (males/females)
0–9	0/0	0/0	0/0
10–19	1/0	0.1/0	0.02/0
20–29	0/2	0/0.2	0/0.04
30–39	3/8	0.3/0.9	0.04/0.10
40–49	33/15	3.3/1.5	0.39/0.18
50–59	85/34	11.0/4.2	0.99/0.37
60–69	220/163	31.7/19.1	2.22/1.34
70–79	351/361	92.8/56.0	2.78/1.68
80+	216/325	251.6/152.8	2.51/1.53
Total	909/908	14.6/13.4	8.9/5.2

* Mean annual incidence rate for 100,000 inhabitants (Croatian population Census of 2001),

† Incidence rate for 100,000 inhabitants (World standard population at 1980).

age of 60, with the peak at the age of >80 in both sexes (Table 2). The incidence of SCC according to Croatian Counties is shown in Figures 1 and 2. The highest incidence was recorded in Zadar County, followed by the Counties in the inland, Brod-Posavina, Varaždin, Međimurje and Zagreb Counties (Figures 1 and 2). In the total number of SCC cases, the tumor localization was unknown in 109 male and 100 female patients. Patient age was unknown in 25 cases of SCC in males and 18 in females.

Discussion

Determining the true incidence of SCC is difficult because health registries exclude nonmelanoma skin cancers (NMSCs) from their databases because of the high number of cases and limited resources to collect data[7]. Some published studies confirm an increase in the incidence of SCC over the past several decades[8]. One reason for the rising incidence of SCC may be an increase in sun exposure in the general population[7]. The UV radiation

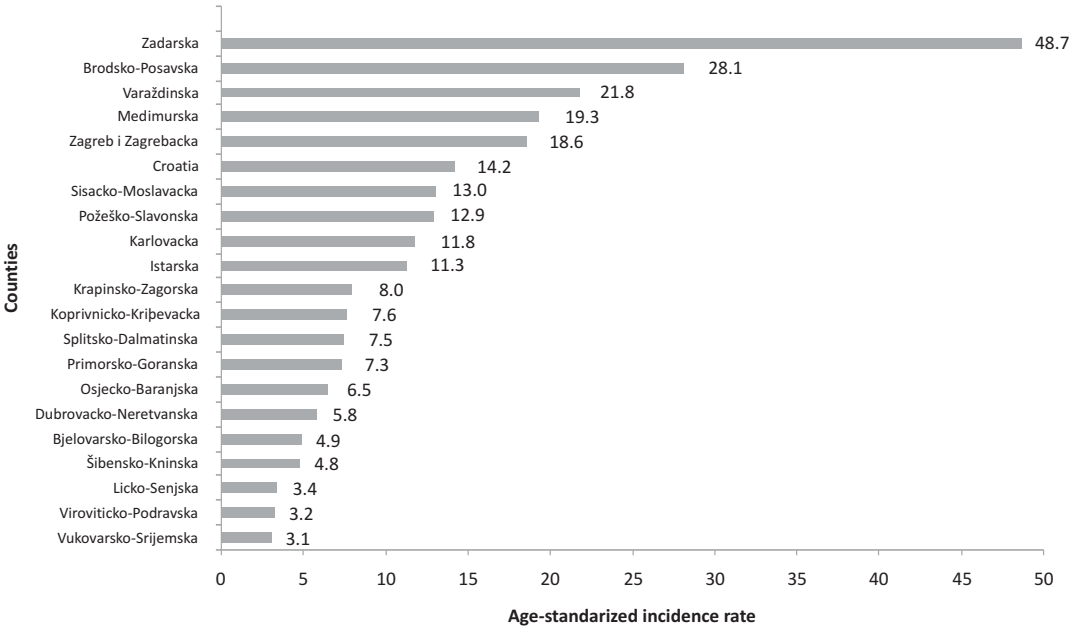

Fig. 1. The age-standardized incidence rate per 100,000 of SCC in males in Croatian counties.

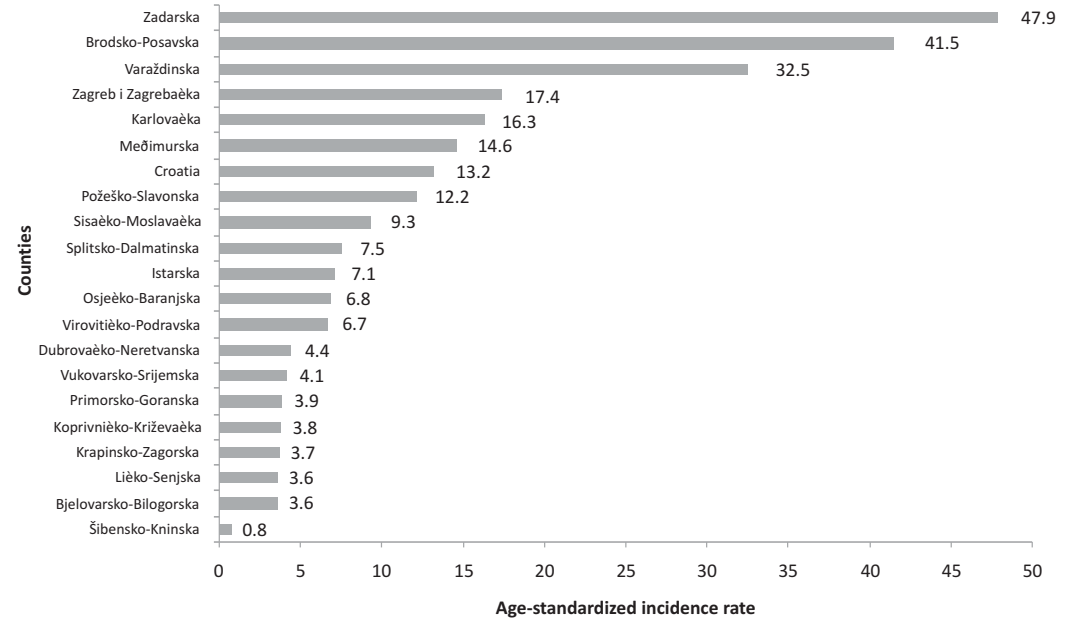

Fig. 2. Age-standardized incidence rate per 100,000 of SCC in females in Croatian Counties.

cause the mutation of the cellular DNA, when unrepaired, lead to the uncontrollable cellular growth and the occurrence of tumor[9,10]. Although, because of the immunosuppressant caused by the UV light, there is no rejecting of tumor[9]. Other factors that may contribute to the increased incidence of SCC include the advancing age of the population, earlier and more frequent diagnosis of SCC due to enhanced public awareness of skin cancer, and more frequent skin examinations by physicians[7]. Additionally, the number of patients on immunosuppressive therapy, used in solid organ transplantation and various rheumatologic and dermatologic conditions, is increasing[7]. The incidence of SCC has been reported to double with each 8- to 10-degree decline in geographic latitude and is highest at the equator[11]. The highest incidence occurs in Australia, where the age-adjusted incidence has been calculated to be 1,332 cases *per* 100,000 population for men and 755 cases *per* 100,000 population for women[12]. Again, this is likely due to large numbers of light-skinned people in this region who have had extensive sun exposure[12]. Until now, there was only one published article of the NMSCs incidence in Croatia, but it does not contain data on the regional differences of the SCC incidence among Croatian Counties[13]. In our opinion, the exact SCC incidence in Croatia is not entirely known, because the different specialists treat SCC without reporting it, which additionally makes it more difficult to collect data. During the period from 2003 until 2005 data were collected from the major clinics in Croatian Counties which had treated patients with SCC, as well as from the doctors of family medicine, but, in our opinion, that reports were not complete. The SCC incidence is influenced by the race and the skin type[2]. It is known that the individuals with fair complexion, blue eyes and red hair are more likely to developed SCC[2]. The exact data on the skin type distribution in Croatia is unknown, but, it is common knowledge that inhabitants along the coast and the seaside have darker hair and eyes and the skin type which easily gets dark and is not inclined to get sunburns. SCC is more frequent in males, which is probably the consequence of longer sun exposure during the males life than females[2]. In our study the occurrence of SCC is similar in males and females (Table 1). The longer life time of the population additionally increases the occurrence of SCC, which is more frequent after the age of 40[2]. In our study, the rapid rise of SCC incidence in males and females is after the age of 60 with the peak at the age >80 (Table 2). The probable reason has been the increased number of AK in elderly age and transition of noninvasive AK to invasive SCC. The cumulative exposure to the UV radiation is the highest risk for originating of the AK, which are the predictor in originating of the SCC[12]. By analyzing the incidence in the Counties, we have encountered an interesting data that the Zadar County has the highest SCC incidence (Figures 1 and 2). We have expected to find similar result in the other Counties in the Mediterranean Croatia, but the Šibenik-Knin County, which is territorially the closest to the Zadar County, has low SCC incidence (Figures 1 and 2). There remains a question whether such a result is credible, or it may be that the report of the SCC patients in the County of Šibenik-Knin had not been complete. Brod-Posavina, Varaždin, Međimurje, and Zagreb Counties are in the inland of Croatia, and have higher SCC incidence than the other Counties in the Mediterranean Croatia (Figures 1 and 2). We have tried to find out the possible explanation of these results in inadequate reports of SCC and by the share of agricultural population in the mentioned Counties. According to the latest agricultural register from 2003, Brod-Posavina County had 20,704 agricultural households, Varaždin 33,415, Međimurje 20,349, Zagreb 52,404 unlike Zadar County which had 14,392 agricultural households[14]. Therefore, the possible reason for the higher incidence in the inland Counties is interminent, but also the intensive sun exposure during the agricultural work, as well as the exposure to herbicides. The increased migration of the population during the war in Croatia from 1991–1995 is also a possible factor which could influence SCC occurrence in the Counties with higher incidence. Considering that SCC can give distant metastasis, the accent is on the prevention and the early detection. In the recent years in Croatia there has been an increased media campaign about the prevention and early detection of skin cancers. The prevention particularly refers to the sun protection in childhood, because childhood and adolescence are the critical periods of life for later development of skin cancers, as 80% of UV rays is being absorbed at that age[15]. Application of sun protective means during the lifetime (protective clothes, head covering, sun glasses, sun protective creams), as well as avoiding visits to tanning beds are of greatest importance. The early detection refers to the frequent examination and treatment of the individuals with the AK, as well as those who have already been treated or are under higher risk of developing SCC. It must be considered that individuals who were treated of the SCC, have 44–50% cumulative risk of developing another NMSC (18 to 30% risk of SCC) in the subsequent 3–5 years[16]. The same individuals have the higher risk of developing the other extra cutaneous cancers[17].

Conclusion

The accent on the regularity of reporting individuals with SCC is going to enable us an overall insight in the SCC incidence in Croatia, which is going to be the important data for the SCC trend monitoring in Croatia as well as in Europe in the forthcoming years.

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REFERENCES

1. NGUYEN TH, YOON J. Squamous cell carcinoma (SCC). In: RIGEL DS, FRIEDMAN RJ, DZUBOV LM, REINTGEN DS, BYSTRYN J-C, MARKS R (Eds), Dermatology (Springer-Verlag, Berlin, 2000). — 2. GROSSMAN D, LEFFELL DJ. Squamous cell carcinoma. In: FREEDBERG IM, EISEN AZ, WOLFF K, AUSTEN KF, GOLDSMITH LA, KATZ SI (Eds.). Fitzpatrick's Dermatology in General Medicine (The McGraw-Hill, New York, Chicago, San Francisco, Lisbon, London, Madrid, Mexico City, Milan, New Delhi, San Juan, Seoul, Singapore, Sydney, Toronto, 2003). — 3. Croatian homepage. Available from: URL: http://www.hr/croatia. — 4. International Statistical Classification of diseases (World Health Organisation, Geneva, 1994). — 5. Croatian Bureau of Statistics. Census of population, households and dwellings 2001. Available from: URL: http://www.dzs.hr. — 6. JENSEN OM, PARKIN DM, Cancer registration:Principles and Methods (IARC, Lyon,1991). — 7. JENNINGS J. Squamous cell carcinoma. Accessed: Aug 4,2010. Available from: URL: http://emedicine.medscape.com/article1101535-overview. — 8. GRAY DT, SUMAN VJ, SU WP, CLAY RP, HARMSEN WS, ROENIGK RK, Arch Dermatol, 133 (1997) 735. — 9. GROSSMAN D, LEFFELL DJ, Arch Dermatol, 133 (1997) 1263. — 10. HUSSEIN MR, J Cutan Pathol, 32 (2005) 191. — 11. JOHNSON TM, ROWE DE, NELSON BR, SWANSON NA, J Am Acad Dermatol, 26 (1992) 467. — 12. BUETTNER PG, RAASCH BA, 78 (1998) 5876. — 13. LIPOZENČIĆ J, CELIĆ D, STRNAD M, JURAKIĆ TONČIĆ R, PAŠIĆ A, RADOŠ J, ZNAOR A, Coll Antropol, 34 (2010) 865. — 14. Croatian Bureau of Statistics. Agricultural Census 2003. Available from: URL:http://www.dzs.hr. — 15. ŠIMIĆ D, PROHIĆ A, ŠITUM M, PENAVIĆ Ž, Coll Antropol, 34 (2010) 147. — 16. MARCIL I, STERN RS, Arch Dermatol, 136 (2000) 1524. — 17. HEMMINKI K, DONG C, Arch Dermatol, 136 (2000) 647.

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DESKRIPTIVNA EPIDEMIOLOGIJA PLANOCELULARNOG KARCINOMA KOŽE U HRVATSKOJ

SAŽETAK

Cilj ovog rada bio je istražiti incidenciju planocelularnog karcinoma kože u Hrvatskoj u periodu od 2003.–2005. godine. Slučajevi planocelularnog karcinoma su analizirani retrospektivno. Podaci su prikupljeni iz Klinike za kožne i spolne bolesti Kliničkog bolničkog centra Zagreb te Registra za rak Hrvatske. U istraživanom razdoblju, registrirano je 1860 slučajeva planocelularnog karcinoma (934 u muškaraca i 926 u žena). Gruba stopa incidencije na 100 000 stanovnika u Hrvatskoj bila je 14,6 za muškarce i 13,4 za žene. Dobno standardizirana stopa na svjetsko stanovništvo iznosila je 8,9 za muškarce te 5,2 za žene. Glava je najčešća lokalizacija planocelularnog karcinoma u oba spola. Najveća incidencija planocelularnog karcinoma registrirana je u Zadarskoj županiji. Ovi rezultati poslužit će u budućnosti za praćenje trenda planocelularnog karcinoma kože u Hrvatskoj i Europi.