Coll. Antropol. 36 (2012) 1: 133–137
Original scientific paper

Descriptive Epidemiology of Cutaneous Squamous Cell Carcinoma in Croatia

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ABSTRACT

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 carcinoma1,2. The cell of origin is the epidermal keratinocytes, which undergoes malignant transformation with repeated ultraviolet (UV) induced mutation1,2. 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 disease2. Cutaneous SCC represents a broad spectrum of disease ranging from easily managed, superficially invasive cancer to highly infiltrative, metastasizing tumors that can result in death2. 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 Europe3. It is located between 42°23’ and 46°33’ of the northern geographical width, and 13°30’ and 19°27’ of the eastern geographical length3. 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 continent3. With approximately 2,600 hours of sunshine per year the Adriatic coast is one of the sunniest on the Mediterranean3. In the inland part of Croatia there is predominant moderate warm humid climate3. 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 Sea3. The aim of this study was to assess the incidence of SCC in Croatia during the 2003–2005 period.

Received for publication October 7, 2009
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. 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. Statistical analysis was done by use of SPSS 13.0 program.

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%), forehead (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>
<thead>
<tr>
<th>Age group (years)</th>
<th>Total number of SCC (males/females)</th>
<th>Age specific incidence rate adjusted for Croatian population*(males/females)</th>
<th>Incidence rate adjusted for World population† (males/females)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–9</td>
<td>0/0</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>10–19</td>
<td>1/0</td>
<td>0.1/0</td>
<td>0.02/0</td>
</tr>
<tr>
<td>20–29</td>
<td>0/2</td>
<td>0/0.2</td>
<td>0.0/0.04</td>
</tr>
<tr>
<td>30–39</td>
<td>3/8</td>
<td>0.3/0.9</td>
<td>0.04/0.10</td>
</tr>
<tr>
<td>40–49</td>
<td>33/15</td>
<td>3.3/1.5</td>
<td>0.39/0.18</td>
</tr>
<tr>
<td>50–59</td>
<td>85/34</td>
<td>11.0/4.2</td>
<td>0.99/0.37</td>
</tr>
<tr>
<td>60–69</td>
<td>220/163</td>
<td>31.7/19.1</td>
<td>2.22/1.34</td>
</tr>
<tr>
<td>70–79</td>
<td>351/361</td>
<td>92.8/56.0</td>
<td>2.78/1.68</td>
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<tr>
<td>80+</td>
<td>216/325</td>
<td>251.6/152.8</td>
<td>2.51/1.53</td>
</tr>
<tr>
<td>Total</td>
<td>909/908</td>
<td>14.6/13.4</td>
<td>8.9/5.2</td>
</tr>
</tbody>
</table>

* 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, Medimurje 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. Some published studies confirm an increase in the incidence of SCC over the past several decades. One reason for the rising incidence of SCC may be an increase in sun exposure in the general population. The UV radiation...
cause the mutation of the cellular DNA, when unrepaired, lead to the uncontrollable cellular growth and the occurrence of tumors\textsuperscript{6-10}. Although, because of the immunosuppressant caused by the UV light, there is no rejecting of tumor\textsuperscript{6}. 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\textsuperscript{7}. Additionally, the number of patients on immunosuppressive therapy, used in solid organ transplantation and various rheumatologic and dermatologic conditions, is increasing\textsuperscript{7}. The incidence of SCC has been reported to double the rate of SCC incidence (Figures 1 and 2). We have expected to find an interesting data that the Zadar County has the highest SCC incidence (Figures 1 and 2). We have expected the SCC incidence to be influenced by the race and the skin type\textsuperscript{2}. It is known that the 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\textsuperscript{8}. In our study the occurrence of SCC is similar in males and females (Table 1). The longer life time of the population, earlier and more frequent diagnosis of SCC, which is more frequent after the age of 40\textsuperscript{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\textsuperscript{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, Medimurje, 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, Medimurje 20,349, Zagreb 52,404 unlike Zadar County which had 14,392 agricultural households\textsuperscript{14}. Therefore, the possible reason for the higher incidence in the inland Counties is intermittent, 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\textsuperscript{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\textsuperscript{16}. The same individuals have the higher risk of developing the other extra cutaneous cancers\textsuperscript{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.

**Acknowledgements**

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DESKRIPTVNA EPIDEMIOLOGIJA PLANOCELULARNOG KARCINOMA KOŽE U HRVATSKOJ

SAŽETAK