

Epidemiological Data on Melanoma from the Referral Centre in Croatia (2002–2007)

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ABSTRACT

Melanoma is considered to be one of the most aggressive skin tumors. Various studies have shown that the incidence rate for this malignancy is rising rapidly all over the world. Incidence rates vary substantially worldwide with New Zealand and Australia having the highest rates. In the past 40 years in Croatia the incidence of melanoma is also in rise for more than 300%. Women and men are almost equally affected. According to anatomical site in most populations the rise is the greatest for the male trunk, and extremities in both sexes. There has been little change in rates for the head and neck. In the last decades, melanoma often occurs in relatively younger people, between the age of 25 and 40, rarely in the childhood. However, survival in patients with melanoma in Western European countries has increased markedly in recent years, due to timely recognition of the disease. Unfortunately, in Croatia the mortality remains higher even though the incidence is lower than those in some Western European countries. The authors are presenting epidemiological data on melanoma during the last 6 years (for the period 2002–2007) from the Croatian Referral Centre for Melanoma which is placed in the University Hospital »Sestre milosrdnice« in Zagreb.

Key words: melanoma, epidemiology, melanoma incidence, skin malignancy

Introduction

Melanoma is one of the most aggressive malignant tumors of the skin and its frequency is in constant rise in the last decades; with the increase higher than other malignant skin tumors. Melanoma incidence is increasing from 3 to 8% per year in different regions of the world; in Australia melanoma is the 3rd most frequent malignant tumor in women and 4th in men. In the USA there has been noticed 120.5% increase in melanoma incidence in the last two decades^{1–4}. In the period 1968–1995 in Croatia the incidence of melanoma was also in rise approximately 309% and melanoma mortality over 310%. According to Croatian National Cancer Registry there were 396 newly diagnosed melanoma patients in 2002 (209 females and 187 males), 414 in 2003 (222 females and 192 males) and 427 newly diagnosed melanoma patients in 2004 (237 females and 190 males). Also, in 2005 melanoma age-standardized (ASR-EU) incidence rate in Croatia was 11.5/100000 (10.3/100000 for women and 13.4/100000 for men). Melanoma is the 11th most com-

mon malignancy in Croatia, and represents approximately 3% of all malignancies⁵.

Patients and Methods

In Croatia, National Referral Centre (NRC) for melanoma of the Ministry of Health and Welfare is situated in the University hospital »Sestre milosrdnice« in Zagreb, including the Department of Dermatology and Venereology and the Department of Nuclear medicine and Oncology. However, in everyday practice many other departments within the hospital closely cooperate providing a multidisciplinary approach to melanoma patients. Data on all melanoma patients registered at the Department of Dermatology and Venereology in the period 2002–2007 were retrospectively analyzed according to the Department records. However, it should be noted that not all of the patients were diagnosed with mela-

noma the same year they were registered at the NRC; respectively some of them were diagnosed at some time prior to registration in the NRC. Statistical analysis was conducted using SPSS, version 12.

Results

During the 6-year period (2002–2007) there were 710 newly registered melanoma patients in the NRC, with continuous rise in number each year, starting with 60 patients in 2002 up to 191 in the year 2007 (Table 1). There were 396 (55.7%) female and 314 (44.3%) male patients (Table 2).

Most of the patients were from Zagreb and the County of Zagreb which is not surprising since the NRC is situated in Zagreb, and it also is the most populated region of Croatia with almost one million inhabitants. There were also many patients from the Northern part of the Adriatic coast namely County of Istria as well as from the County of Sisak-Moslavina, County of Karlovac, County of Split-Dalmatia and County of Slavonki Brod-Posavina and all other parts of the country.

Age distribution at the time of diagnosis is shown in the Figure 1. There were 3 patients (0.4%) in the age group 0–9 years, 6 patients (0.9%) in the age group 10–19, 41 patients (5.8%) in the age group 20–29, 84 patients (11.9%) in the age group 30–39, 144 patients (20.5%) in the age group 40–49, 172 patients (24.5%) in the age group 50–59, 153 patients (21.8%) in the age group 60–69, 82 patients (11.7%) in the age group 70–79, and 18 patients (2.6%) in the age group 80 years and older. Among 710 patients 6 were aged less than 18 and in 5 of them melanoma developed *de novo*, while in one of them melanoma developed within the pre-existing dysplastic congenital nevus. Also, out of 710 melanoma patients 23 (3.2%) were diagnosed with multiple primary melanomas; one patient had 4 melanomas, two patients had 3 melanomas, and 20 patients had 2 melanomas.

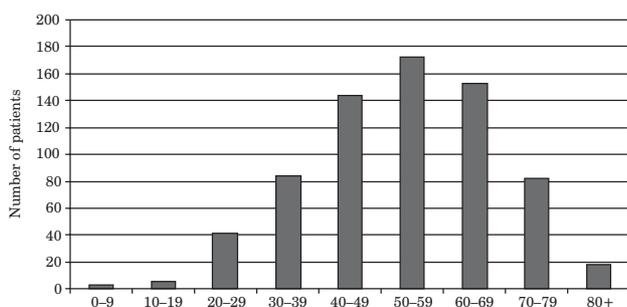


Fig. 1. Age distribution of melanoma patients.

TABLE 2
GENDER DISTRIBUTION OF MELANOMA PATIENTS REGISTERED IN THE CROATIAN REFERRAL CENTRE (2002–2007)

	N	%
Female	396	55.7
Male	314	44.3

Distribution according to tumor localization on the body showed that melanoma occurred most commonly on trunk, than on the lower extremities and other sites (Figure 2). However, a significant difference in melanoma localization between men and women was noticed (Figure 3). In men the most common site of melanoma was trunk namely on the back (40.8%) and in women the most common site of melanoma was on lower extremities (33.2%).

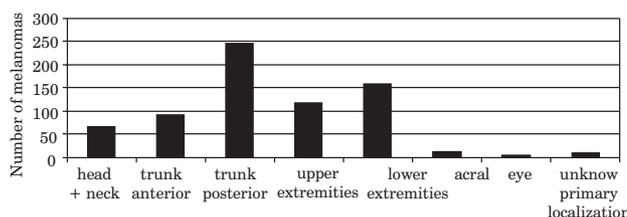


Fig. 2. Distribution of melanoma by localization.

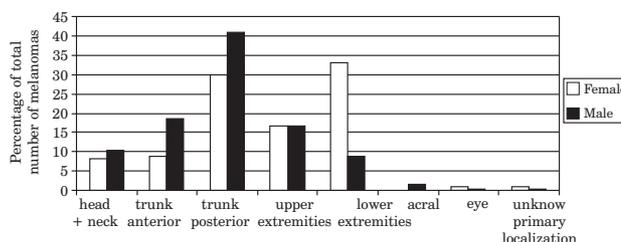


Fig. 3. Localization of melanoma in female and male patients.

According to the histopathology there were 255 (59.6%) superficial spreading melanomas (SSM), 120 (28%) nodular melanomas (NM), 31 (7.2%) lentigo maligna melanomas (LMM), and 13 (3.0%) acrolentiginous melanomas (ALM). There were also 5 (1.2%) amelanotic melanomas and approximately 1% of patients with diagnosed metastatic melanoma of unknown primary tumor (Figure 4). In both, men and women, the most common type of melanoma was SSM, however there was a significant difference in the portion of NM in the total number of melanoma among men and women, indicating that NM is

TABLE 1
NUMBER OF REGISTERED MELANOMA PATIENTS IN THE CROATIAN REFERRAL CENTRE (2002–2007)

Year of registration	2002	2003	2004	2005	2006	2007
N	60	100	121	116	122	191

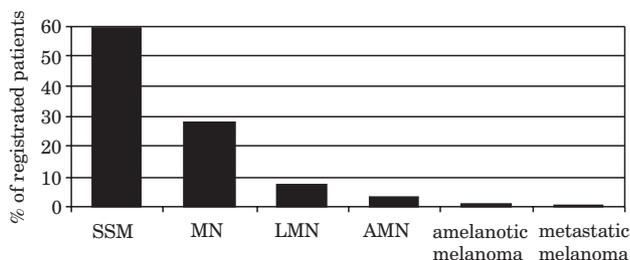


Fig. 4. Type of melanoma.

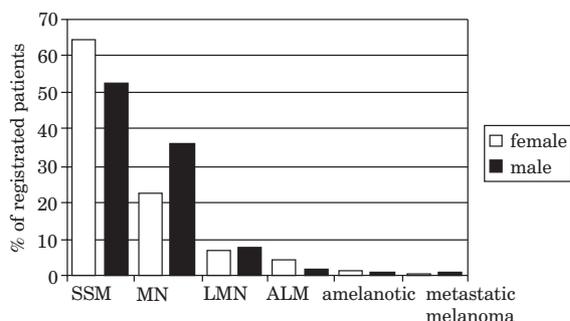


Fig. 5. Distribution of the various types of melanoma in female and male patients.

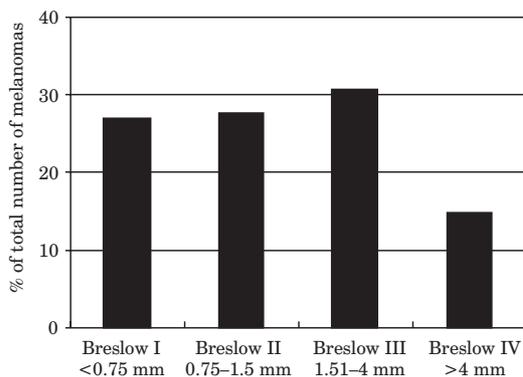


Fig. 6. Tumor thickness by Breslow classification.

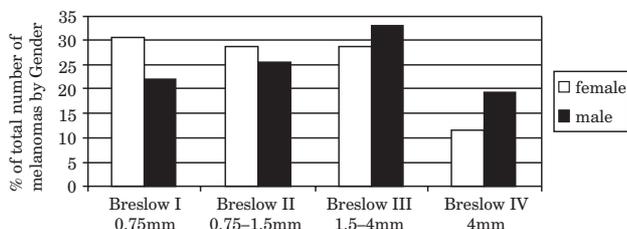


Fig. 7. Tumor thickness by Breslow for female and male melanoma patients.

TABLE 4
THE ORIGIN OF MELANOMA

Origin of melanoma	N	%
<i>De novo</i>	73	17
Acquired nevus	246	57.5
Congenital nevus	85	19.9
Lentigo maligna	24	5.6

more common in men (Figures 4 and 5). In women 64.8% were SSM, 22.4% NM, 6.8% LMM, 4.0% ALM, 1.2% amelanotic melanoma and 0.4% metastatic melanoma of unknown primary tumor. In men results were: 52.2% SSM, 36.0% NM, 7.9% LMM and 1.7% ALM, 1.1% amelanotic melanoma and 1.1% metastatic melanoma of unknown primary tumor.

The tumor thickness according to the Breslow classification (Br I = 0–0.75 mm, Br II = 0.76–1.50 mm, Br III = 1.51–4.0 mm, Br IV ≤ 4 mm) in analyzed melanoma patients is shown in Figures 6 and 7. There were 150 (27.1%) melanomas Breslow I, 152 (27.5%) Breslow II, 169 (30.6%) Breslow III, and 82 (14.8%) Breslow IV. However, a significant difference in the portion of lower Breslow melanoma stages was noticed between female and male patients. In women there were 98 (30.7%) Breslow I stage, 92 (28.8%) Breslow II, 92 (28.8%) Breslow III, and 37 (11.6%) Breslow IV. In men the results were as follows: 52 (22.2%) were Breslow I stage, 60 (25.6%) Breslow II, 77 (32.9%) Breslow III, and 45 (19.2%) Breslow IV.

The mean tumor thickness for the total number (710) of analyzed melanoma patients was 2.24 mm, with a little variation per year in the 6-year-period (2002–2007) (Table 3). Regarding the origin of melanoma, the anamnestic data was available for 428 patients. There were 73 (17.1%) newly appearing (*de novo*) melanomas, 85 (19.9%) from congenital nevus, 246 (57.5%) from pre-existing acquired dysplastic nevus, and 24 (5.6%) from lentigo maligna (Table 4).

Discussion

Epidemiological data indicates that melanoma incidence is in constant rise throughout the world.

Numerous studies have identified risk factors for the development of melanoma. The major factors include excessive sun exposure, number of melanocytic nevi, cutaneous phenotype, and family and personal history of melanoma. UV radiation from sunlight appears to be the principle environmental factor responsible for melanoma

TABLE 3
TUMOR THICKNESS BY YEAR OF REGISTRATION

Year of registration	2002	2003	2004	2005	2006	2007	2002–2007
Tumor thickness (mm)	2.21	2.21	2.24	2.32	2.49	1.77	2.24

development. This has been supported by studies which have demonstrated an inverse relationship between latitude and melanoma incidence^{6–8}.

Melanoma is uncommon in darkly-skinned people; in the United States, the incidence among blacks is only 1/10 that among whites⁹. Melanoma in blacks and Asians most often occurs at parts of the body which are not sun exposed, such as acral sites (nail beds and soles)¹⁰. During the past century, changes in clothing styles, recreational activities, chronic occupational solar exposure, longevity, and other aspects of lifestyle have resulted in increased exposure to sunlight¹¹. The incidence of melanoma increases with age, and it mostly occurs between 30–70 years of age. However, melanoma is one of the most common cancers in young adults¹². In our study most of the patients (more than 65%) were aged between 40 and 70 years with the age peak 50–59 years at the time of diagnose. Unlike the much more common skin cancers such as basal cell carcinoma and spinalioma, which are associated with cumulative UV radiation, melanomas are associated with intense intermittent exposure to UV radiation^{13–16}. Thus, melanoma occurs commonly on intermittently sun exposed body sites, such as the back in men and lower extremities in women¹². The same anatomical distribution was noticed in our group of patients, too. On the other hand, it is well known that LMM, a subtype associated with cumulative sun exposure, frequently occurs on the head and neck in older people¹⁷. Even though it is one of the most aggressive malignant tumors in humans, melanoma is curable if detected early and appropriately surgically excised. The prognosis of melanoma is related to tumor thickness. Various studies have shown that in recent years the rise in the incidence of melanoma in the Western world is mainly attributable to thin melanomas, while the number of intermediate and thick melanomas was stable¹⁸. Unfortunately, the results of our study showed that in one third of patients melanoma is diagnosed at Breslow stage III (tumor thickness 1.5–4.00 mm), with thick melanomas significantly more frequent in male patients. Tumor thickness approaching 4 mm presents a high risk of metastasis, and a diagnosis of metastatic melanoma carries with it an abysmal median survival of 6–9 months¹⁹. The major subtypes of melanoma include SSM, NM, LMM, and ALM. SSM is the most common type of mel-

noma and it represents 60–70% of all melanomas. NM are the second most common form of melanoma and usually have bad prognosis because frequently diagnosed at a thicker stage, while LMM usually has better prognosis because of very long radial growth phase. In our study in both, men and women, the most common type of melanoma was SSM, however there was a significant difference in the portion of NM in the total number of melanoma among men and women, indicating that NM is more common in men.

There are various data regarding the origin of melanoma. According to some authors in 50–60% of patients melanoma develops on previously unchanged skin (*de novo*), while only a smaller part of melanomas develop within the previously existing melanocytic nevus, of which most are congenital nevi. Approximately 25–30% of melanomas show histological signs of pre-existing melanocytic nevus and, of these nevi, 40% are congenital and 60% acquired dysplastic nevi^{20,21}. On the contrary, in our study most of the tumors developed within the pre-existing acquired dysplastic nevi. However, these results should be interpreted carefully since they are the obtained from the patients' anamnestic data which may not always be accurate.

Conclusion

The incidence of melanoma, one of the most aggressive skin tumors, is rising rapidly all over the world²². Various studies have shown that in recent years the rise in the incidence of melanoma in the Western world is mainly attributable to thin melanomas. However, in Croatia there is still a trend of diagnose at relatively thick melanoma, especially in male population. Although there have been considerable advances and breakthroughs in the treatment of melanoma, the therapy for metastatic disease is limited. Until the time comes when melanoma is curable at all stages, our efforts should be focused on risk reduction by limiting UV radiation exposure and timely recognition²³. Protection from the UV radiation is most effective when begun in early childhood. Primary prevention of melanoma and early detection are essential to reduce incidence and melanoma mortality in the future years.

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EPIDEMIOLOŠKI PODACI O MELANOMU IZ HRVATSKOG REFERENTNOG CENTRA ZA MELANOM U RAZDOBLJU 2002–2007.

S A Ž E T A K

Melanom pripada među najagresivnije maligne tumore kože i sluznica. Posljednjih desetljeća kontinuiran porast incidencije melanoma bilježi se gotovo u čitavom svijetu. Diljem svijeta incidencija melanoma varira, a najviša je u Novom Zelandu i Australiji. Unazad 40ak godina u Hrvatskoj je zabilježen porast incidencije tog tumora više od 300%. Učestalost pojavljivanja melanoma gotovo je jednaka u žena i muškaraca. Prema lokalizaciji, melanom se sve češće pojavljuje na koži trupa, a zatim na donjim ekstremitetima, dok je učestalost pojave melanoma na koži glave i vrata ostala ista. Posljednjih desetljeća melanom se sve češće dijagnosticira u mladih osoba u dobi od 25–40 godina, a rijetko u djetinjstvu. S druge strane, produljeno preživljenje bolesnika s melanomom u zapadno-europskim zemljama posljednjih godina pripisuje se ranom prepoznavanju melanoma. Na žalost, u Hrvatskoj je, u odnosu na te zemlje, mortalitet viši iako je incidencija jednaka ili niža nego u pojedinim zapadno-europskim zemljama. U radu autori izlažu epidemiološke podatke o malignom melanomu u Hrvatskom Referentnom centru za melanom KB »Sestre milosrdnice« u Zagrebu, za 6-godišnje razdoblje (2002.–2007. g.).