

ORIGINAL PAPER

CLINICAL AND HISTOLOGICAL CHARACTERISTICS OF
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ABSTRACT

Introduction: Melanoma is a malignant tumor of melanocytes and it is the most malignant tumor of skin and mucous membranes. We do not have any data about incidence and characteristics of skin melanoma in Bosnia and Herzegovina.

Aim: We aimed to analyze hospital records on skin melanoma cases from the region of Tuzla during the 5-year period in order to obtain preliminary data about melanoma incidence and clinical characteristics.

Patients and methods: This retrospective study included all patients surgically treated at the University Clinical Center Tuzla, from January 2001 to December 2005, who were initially diagnosed with skin melanoma.

Results: Most of pathologically verified skin melanoma, disregarding primary tumor (T), were presented in both genders at stage T4 (41.67 %) and T2 (28.33 %). Histological analysis showed that the majority of observed skin melanoma were diagnosed in Clark level III (36.36 %) and Clark level IV (33.33 %) stage. The average tumor thickness of the examined sample, according to Breslow's classification, was found to be over than 4.0 mm.

Conclusion: Our findings are similar to those reported in other countries in the region. Further studies are necessary in order to assess the burden of the disease in the national level. A national melanoma register is of great importance for further surveillance.

Keywords: skin melanoma, epidemiology, Clark, Breslow

INTRODUCTION

Melanoma is a malignant tumor of melanocytes and the most malignant tumor of skin and mucous membranes, which originates from pathologically altered melanocytes. Every pigmented skin lesion should be viewed as a potential melanoma because the number of diagnosed skin melanoma with high thickness is increasing in our study, this reflects on survival rate. According to this it is important to work on better and successful health promotion. Surgical excision is the most frequent treatment of choice and it is obligatory. The highest incidence of melanoma in Europe is found in Norway with 14.1/100.000 of men and

15.3/100.000 of women.¹ Melanoma incidence rate in Croatia is in constant inclination (11.1/100.000 of men and 10.3/100.000 of women in 2001), while the highest prevalence is marked in the cities of Zagreb, Zadar and Dubrovnik.²

The American Joint Committee on Cancer (AJCC) is an organization best known for defining and popularizing cancer staging standards, and in 1998 AJCC founded the Melanoma Staging Committee proposed a new classification of melanoma, which was accepted in 1999 and published in 2002.³

There is no exact data about incidence and prevalence of skin melanoma in Bosnia and Herzegovina. We performed retrospective study in the region of Tu-

zla, which is the biggest region in the state, in order to obtain preliminary data about this malicious tumor.

Table 1. Skin melanoma gender distribution for a five-year period (2001 – 2005) in Tuzla region

Year of operation	Male	Female	Total
2001	2	7	9
2002	6	9	15
2003	3	8	11
2004	7	5	12
2005	10	13	23
Total	28	42	70

MATERIAL AND METHODS

This retrospective study included 70 patients surgically treated at the University Clinical Center Tuzla, from January 2001 to December 2005, who were initially diagnosed with skin melanoma in accordance to the final results obtained by histological examination of excised lesions. All the necessary macro and micro analysis of surgically obtained samples were done at the Pathology polyclinic for laboratory diagnostics of University Clinical Center in Tuzla. All the tissue specimens were formaldehyde fixed and paraffin wax embedded. Histological cuts were stained with hematoxylin-eosin. Immunohistochemical staining was performed on 5 µm tissue sections, that were placed on organosilane pretreated glass slides.

Data used in the study included gender and age of patients, tumor size, number of mitosis per observed field and histological diagnosis. Clinical staging of the disease was determined by the careful analysis of the obtained documentation. Basic methods of descriptive

statistics were used in data analysis. Given hypotheses were statistically tested at the level of $\alpha=0.05$, with the significance level of $p < 0.05$.

RESULTS

During a five-year period (from January 2001 to December 2005), 70 patients who initially diagnosed with primary skin melanoma were surgically treated at University Clinical Center of Tuzla, after consequent macro and micro histological analysis. Gender distribution showed that there were 42 (60%) female and 28 (40%) male patients diagnosed with primary skin melanoma, yielding in odds ratio 1.5:1 in favor of female patients. Patients were between the ages 20 and 90, an average age were 55 years for both genders.

Analyzing the data obtained from this study, it can be concluded that incidence for skin melanoma in the region of Tuzla is 5.6/100.000 for men and 8.4/100.000 for women. The most common sites for skin melanoma were found to be at trunk (43% of both genders or 23% of male and 20% of female), limbs (36% or 10% of male and 26% of female) and head and neck (21% of both genders or 7% of male and 14% of female). This data shows the increasing number of female patients with skin melanoma on head, neck and limbs.

Data analysis showed marked increase in the number of patients diagnosed with skin melanoma for each subsequent year in the observed five-year period. A total of 9 patients in 2001, which is 12.8% of all patients in this study, were recorded consisting of 2 males (22.2%) and 7 females (77.8%). From 2002 to 2003 there was increased number of female patients, in 2002 there were 15 patients (21.4%), 6 of them were males (40%) and 9 of them were females (60%) and 2003 there were 3 males (27.3%) and 8 females (72.7%) of 11 (15.7%) operated patients. In 2004 there was increased number of male patients, 7 (58.3%) comparing to female patients 5 (41.7%) of

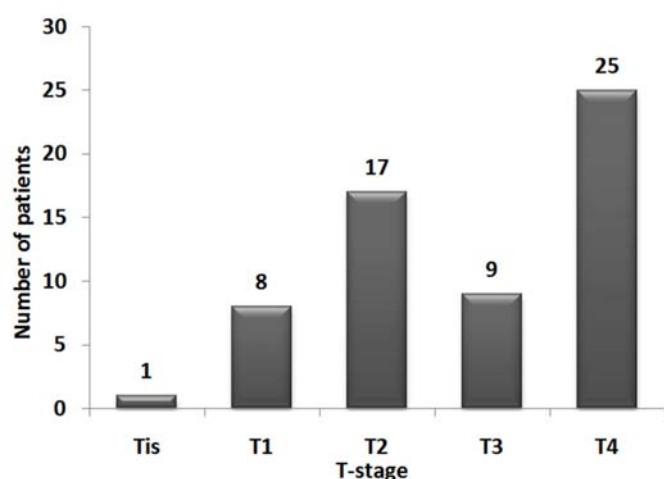


Figure 1. Distribution of patients with melanoma according to T stage

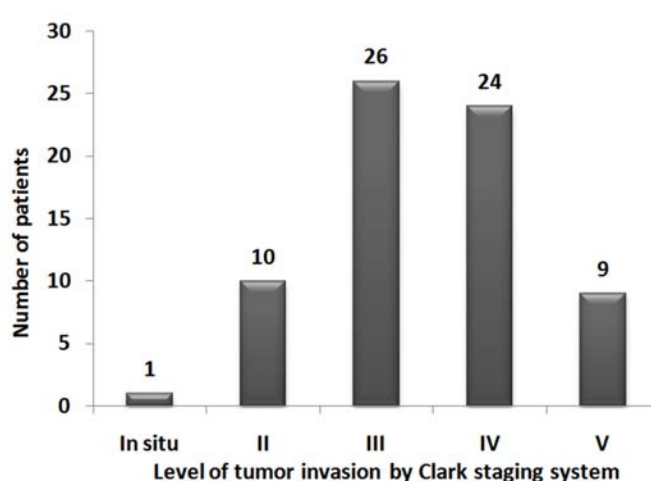


Figure 2. Distribution of skin melanoma by depth of skin invasion

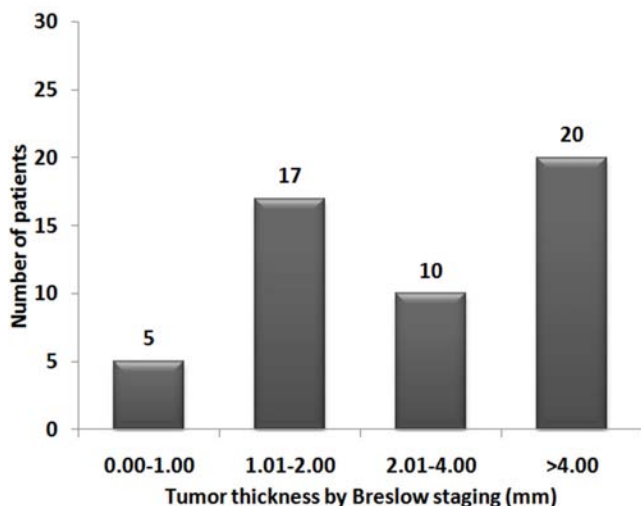


Figure 3: Distribution of skin melanoma according to tumor thickness

12 (17.1%) operated patients. In 2005 there was increased number of both genders comparing with the earlier period, total number of operated patients were 23 (32.9%), 10 (43.5%) of them were males and 13 (56.5%) were females (Table 1). Distribution of skin melanoma in relation to T stage is shown in Figure 1.

The majority of patients with skin melanoma were diagnosed in stages T4 (41.67 %), and stage T2 (28.33 %). By further histological analysis of skin melanoma, using Clark staging systems, most of the tumors were found to be at the level III (36.36 %) and level IV (33.33 %) (Figure 2). Distribution of skin melanoma according to Breslow's staging system is shows that most of the tumors had thickness over than 4.0 mm (Figure 3). Most of the examined samples of skin melanoma had ≤ 10 mitosis per 10 high power fields. Only one case was presented with 100 mitosis per 10 high power fields (Figure 4).

DISCUSSION

Melanoma is the most malignant tumor of the skin and mucous membranes. During a five-year period, 70 were surgically treated at University Clinical Center of Tuzla, with primary skin melanoma. The simple ABCDE rule (asymmetry, border irregularity, color variation, increasing diameter, elevation) should also serve as easy guidance for patients who will then be readily alerted to seek professional advice, and this helps in prevention and early diagnosis of the disease. Number of diagnosed skin melanoma with high thickness is increasing in our study, this reflects on survival rate. According to this it is important to work on better and successful health promotion. Analyzing age and gender distribution of patients diagnosed with primary skin melanoma in our study, it was noted that these tumors are usually beginning to appear in second life decade, with marked inclination up to fifth decade,

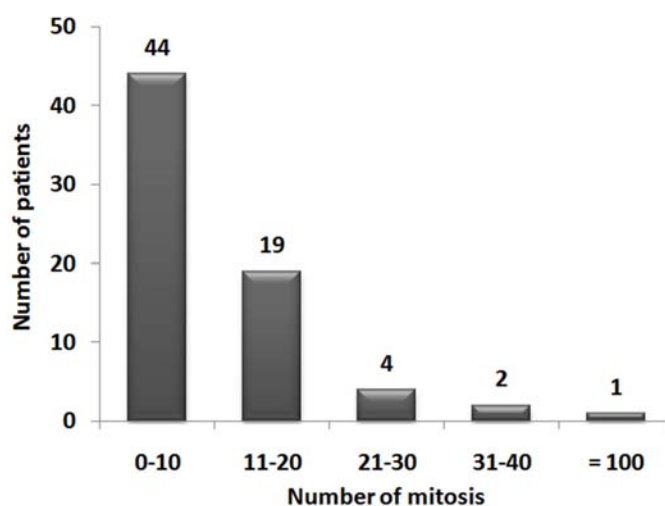


Figure 4: Distribution of melanoma in relation to the number of mitosis per 10 high power fields

with almost vertical upward slope in sixth and seventh decade with highest number of patients affected, after which the slope is gradually decreasing downward. Melanoma incidence and mortality rates are rising in many countries. Comparing to the incidence in Croatia in the cities of Zagreb, Zadar and Dubrovnik² incidence in Tuzla region is somewhat lower. This has led to development of a variety of education programmes designed for either early detection of melanoma when it can be easily cured, or prevention by taking a long term approach. Major factors associated with the incidence of melanoma include race and ethnicity, sunlight exposure, and genetic and familial predisposition.⁴

In the research conducted by Ries and al.⁵ the average age of patients diagnosed with skin melanoma were 58. In the same study 0.9% of patients diagnosed with skin melanoma were 20 years old and younger, 13.8% were between the age of 20 and 34, 19.1% were between 35 and 44; 18.5% were between 45 and 54; 18.2% were between 55 and 64; 15.8% were between 65 and 74; while 5.3% were between 75 and 84 years old.

It was also found that skin melanoma incidence for both genders were 18.2/100.000/year. If prolonged life span is taken into consideration, this gradual decrease after the seventh decade is relative, and increase in the prevalence of skin melanoma can be also expected in a much older age (after the seventh decade). The frequency of skin melanoma with thickness <0.76 mm, diagnosed in USA in the period of the early 50's, increasing from 26% to 53% to the late 70's, while the percentage of population with high-risk factors of developing skin melanoma dropped from 34% to 10%. According to National Cancer Data Base, 14.9% of patients were diagnosed with skin melanoma in stage 0, 47.7% in stage I, 23.1% in stage II, 8.9% in stage III, and only 5.3% in stage IV in accordance to TNM staging system.⁶

According to histological analysis of the examined

samples in our study, the highest number of tumors was found to be in Clark's stage III (36.36 %) while the rest were staged IV and II, thus predicting bad survival rate for those patients. AJCC's analysis of 13.581 patients with primary melanoma showed that the depth of skin invasion in melanoma presents an important factor of survival.⁷ The study showed that greatest number of skin melanoma diagnosed within the patients originated from Tuzla county during a five-year period (2001–2005), were staged T4 (41.67 %), that most frequent tumors thickness in patients diagnosed with skin melanoma was over than 4.0 mm using Breslow's staging system. In the research conducted by Krušlin and al,⁸ majority of primary tumors were diagnosed at an advanced stage (Clark III-V, Breslow III-V). The distribution of primary melanomas according to Clark and Breslow staging in our study showed same rate.

Survival rate of the patients diagnosed with skin melanoma is inversely proportional to tumor thickness which has also positive correlation with a risk for skin melanoma dissemination in regional lymph nodes.^{9,10} Most of the examined samples of skin melanoma had ≤ 10 mitosis per 10 high power fields which corresponds to data published in recent skin melanoma studies.¹¹

CONCLUSION

Our study is the first study about skin melanoma in region of Tuzla, Bosnia and Herzegovina and it shows similar results comparing with countries in a region. It shows that further studies are necessary in order to complete the picture for the whole country and to

make a national melanoma register and a malicious tumor guide.

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