Prognostic Factors and Epidemiological Characteristics of Cutaneous and Mucosal Head and Neck Melanoma

Anna Berzina, Kristine Azarjana, Ingrida Cema, Dace Pjanova, Alexander Rivosh

SUMMARY

The objective. To describe the prognostic factors and epidemiological characteristics of cutaneous and mucosal head and neck melanoma and to identify the variables associated with mortality from this disease.

Material and methods. Patients treated for head and neck melanoma in the Oncology Centre of Latvia, Riga during a 10-year period were identified. Records from 124 cases were analyzed in a descriptive, retrospective study. For each patient, information regarding age, sex, tumor anatomic site, as well as ulceration, histological tumor subtypes, Breslow thickness and Clark invasion level was viewed. Disease specific survival rates were calculated. The frequencies of all study variables and their 95% confidence intervals were determined. Kaplan-Meier survival curves were produced to illustrate the survival diferences for each variable.

Results. The patients' mean age was 67.36 years. The study included 81 females (65.32%) and 43 males (34.67%). The prevalent anatomical site for cutaneous head and neck melanoma was the cheek – 49% (n=55) and the intraocular site for mucosal melanoma (61.5%). A high percentage of thick cutaneous melanoma was detected. In 53 cases (47.3%) out of 112 cutaneous melanoma the tumor ulceration was found. Nodular melanoma subtype was predominating (38%). The incidence of cutaneous melanoma has increased unequally whereas mucosal melanoma of the head and neck is an uncommon cancer and the incidence rates in Latvia during a ten year period are decreasing.

Conclusion. Female sex, advanced age, facial skin, tumor thickness, nodular subtype and ulceration carried a relevant risk of poor prognosis.

Keywords: head and neck melanoma, survival, mortality.

INTRODUCTION

Melanoma is a potentially fatal cancer derived from abnormally proliferating melanocytes, although the process called "melanomagenesis" has not yet been fully understood [1]. Cutaneous melanoma only accounts for 3% of all skin tumors, however this malignant cancer presents high mortality rates, accounting for 75% of all deaths due to cutaneous malignant neoplasms [2,3,4].

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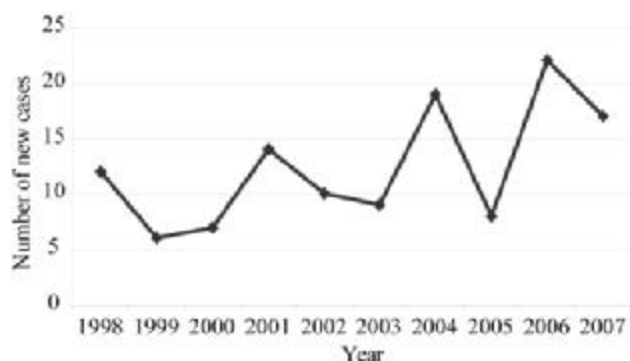*E-mail address: berzina.anna@gmail.com*

The incidence of cutaneous melanoma has increased dramatically since the early 1970s [5]. The rates of incidence and mortality rise in the Caucasians with each year all over the world [6,7,8,9]. The reason for these increases is probably related to changes in people's habits, including types of leisure and clothes, which in case of head and neck melanoma expand the influence of ultraviolet light [10,11,12,13]. Factors like the relationship between skin immunity and melanoma development as well as genetic predisposition are also known [14].

Although cutaneous and mucosal head and neck melanoma (CMHNM) is not the leading anatomical site, the tumor arising from this region has a worse prognosis and require better understanding of the factors that play a role in the disease.

The aim of the study is to describe the epidemiological features of cutaneous and mucosal head and neck melanoma and to identify factors associated

Fig. 1. Number of new cases of cutaneous and mucosal head and neck melanoma in a ten year period
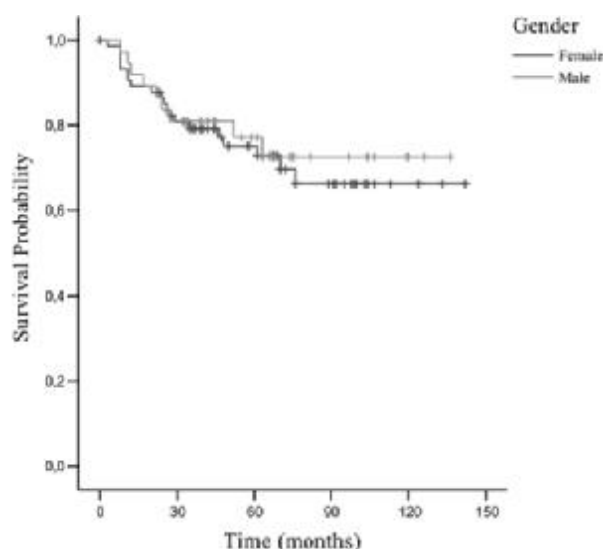

Fig. 2. Difference in mortality between sexes

with mortality from this disease. By identifying the factors that affect survival of patients, we could invent preventive and therapeutic strategies to change the mortality rates from melanoma as well as contribute towards better comprehension of the disease [2,15,16,17]. In relation to mucosal melanoma, Breslow thickness and Clark level data are typically not applicable for this tumor, we tried to generalize the epidemiological characteristics of this tumor.

MATERIALS AND METHODS

This is a retrospective, descriptive study. The records of 124 cases of CMHNM diagnosed as having or treated between January 1, 1998, and December 31, 2007 were obtained from The Onclogy Centre of Latvia, Riga. For each patient, information regarding age, gender, tumor localization as well as ulceration, histological subtypes, the predominant cell type, melanoma Breslow thickness and Clark invasion level was viewed. The depth of invasion of melanoma was categorized by objective measurement – Breslow thickness (measured in milimeters). The

measurement of tumor thickness according to this method is one of the most significant microscopic parameters to predict metastasis [18,19]. The Clark's levels of melanoma invasion represent a description of the magnitude of invasion of the tumor. It is defined through the different microscopic levels of the skin from the epidermis to the subcutaneous tissue [18]. The data included also patient's vital status (alive or dead). In addition, the patients were separated into two groups: up to 60 years and over 60 years. Descriptive statistics were calculated and 95% confidence intervals were defined for all the variables. Such measure as age was summarized using means and standard deviations, while categorical measures were summarized in counts and percentages. Death from melanoma was the survival outcome of interest. All the remaining were considered as censored. The Kaplan-Meier survival curves were used to illustrate the differences of survival for each categorical variable. Kaplan-Meier estimator is designed to estimate the probability of an event that eventually will occur for all patients, ie, death. Statistical differences with a p value <0.05 were considered significant [19].

RESULTS

The study group was composed of 43 males (34.67%) and 81 women (65.32%). The mean age of the cohort was 67.36 years, aged from 25 to 93 years (standard deviation, 14.50 years). The mean age for women exceeds the mean age of men, accordingly 69.55 to 63.23 years.

The number of new cases of CMHNM increased irregularly – from 12 cases in 1998 to 17 in 2007 (Figure 1).

Female patients were most of the cohort with 68.75% deaths compared with 31.25% in male patients. Females were more likely to die (confidence interval, CI=0.51 to 0.82; p=0.68) (Figure 2).

The mean age of women patients with cutaneous and mucosal head and neck melanoma in the first decade (year 1998 till 2002) (n=34) was 70.08 years, while in the second analyzed decade (year 2003 till 2007), the mean age was 69.17 years (n=47). In relation to men patients, the mean age of the first decade was higher comparing to the second one, respectively 64.8 years and 62.0 years (n=15 and n=27).

The most frequent anatomical site of CMHNM was the cheek (n=55, 49%), followed by the ear (n=14, 13%) and neck (n=12, 11%). Melanoma was least frequent on the lips, palate tonsil and hard palate (n=1, 0.81% each) (Figure 3).
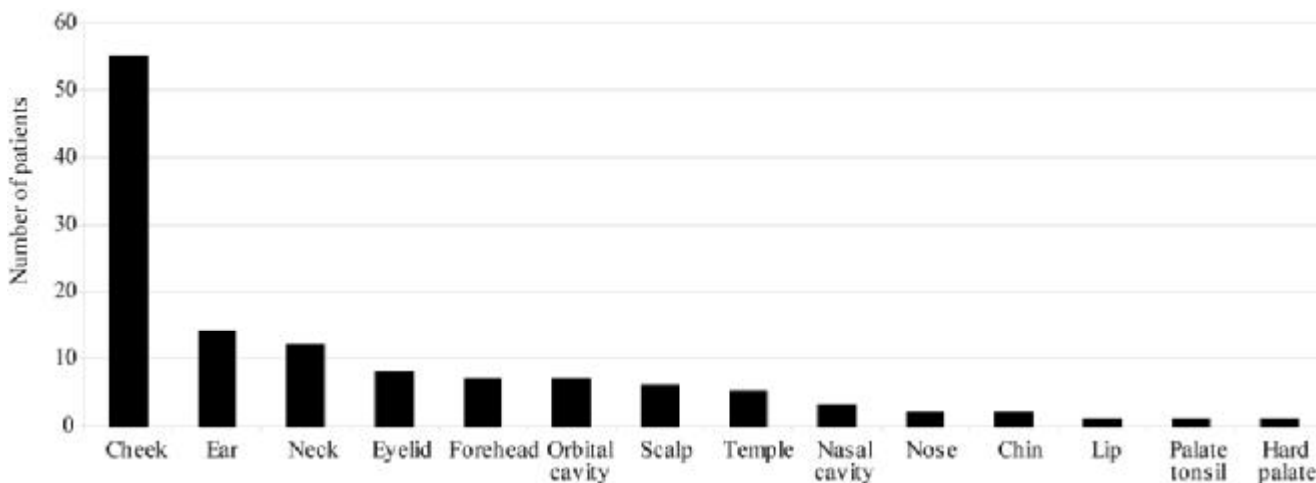
Patients with lesions of the scalp, neck and ear

Fig. 3. Number of cutaneous melanoma cases in relation to the primary lesion site

were more likely to die, comparing to the anatomic site of the face (Figure 4).

Nodular melanoma was the most common histological feature and was diagnosed in 38.39% of all cutaneous melanoma cases. Superficial spreading melanoma was found in 8 cases (7.14%), lentigo maligna melanoma in 6 cases (5.36%). Nearly half of the cohort (49.11%) was histologically unclassified (Figure 5).

Of all morphological features, nodular melanoma carried substantially worse prognosis in accordance with patients' survival (Figure 6).

The presence of ulceration was more frequently found in women after the age of 60 years (n=25; 29.76%), whereas until the age of 60 years in 7 cases (25%). In the group of patients under the age of 60, males had the ulceration of tumor in 9 cases (32.14%), but over the age of 60 – 14.29 % (12 cases). Ulceration was significantly associated with melanoma's prognosis (Figure 7).
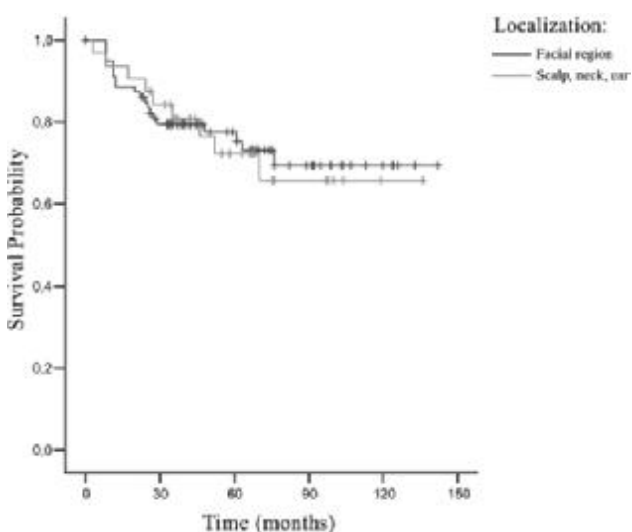
For the purpose of the analyses, tumor thickness was categorized into 3 groups: thin ($\leq$1 mm), intermediate (>1-3,9 mm) and thick ($\geq$4 mm) melanoma. The mean thickness of the primary tumors was 4.99 mm. In 19 cases it was not possible to obtain such data. Thick melanomas ($\geq$4 mm) in the group of age over 60 years for both sexes were diagnosed predominantly, correspondingly 45.67% (n=22) for women and in 8 cases (33.33%) for men. Younger patients (under the age of 60) had characteristic of thick melanomas to a lesser extent. Women were diagnosed with thick melanomas in 7 cases (46.67%), whilst men – in 8 cases (61.54%). The total amount of thick melanomas was 45, out of which 16 cases (35.56%) in men and 29 cases (64.44%) in women. Thin tumors ($\leq$1mm) were characteristic of rarely occurence in the age group of younger patients – only one case (6.67%) in women and accordingly 1 case (7.72%) in men. In
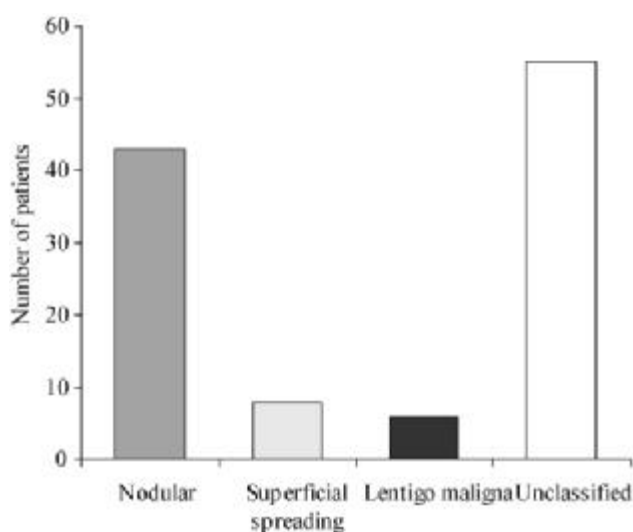

Fig. 4. The risk of mortality for cutaneous melanoma

Fig. 5. Distribution of the cutaneous melanoma cases, according to the subtype of tumor
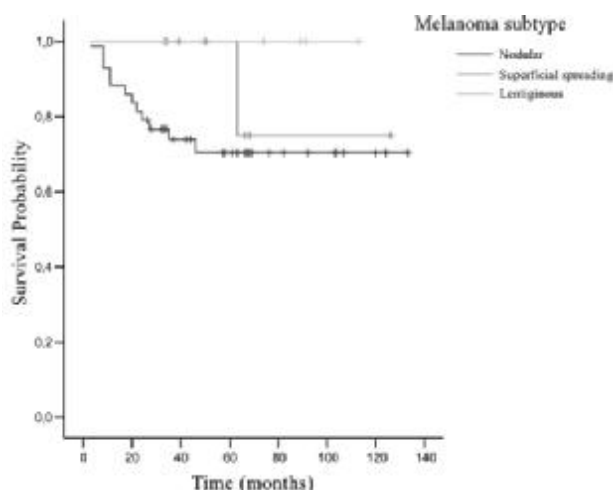
Fig. 6. Mortality from different subtypes of melanoma

Fig. 7. Kaplan-Meier survival curve for ulcerated and non-ulcerated melanomas

the age group of 60 years and older thin melanomas were diagnosed in 11 cases – 13.33% (n=8) in women and 12.5 % (n=3) in men (Figure 8).

Tumors with greater thickness had an unfavorable prognosis (Figure 9).

Clark invasion level V had the highest mortality. The lesser the invasion level was, the more decreased the mortality (Figure 10). In most cases (28%, n=32) both gender patients Clark level was III. In 29% of men patients (n=11) Clark invasion level was IV.

DISCUSSION

Melanoma is a potentially fatal malignant tumor with increasing incidence over the last few decades in many countries of the world [2,5,21,22]. Although, head and neck anatomic location for melanoma was not highlighted and described in every scientific paper mentioned above, the fact of steady increase in the incidence of melanoma is mentioned in the vast majority of corresponding scientific papers, which is
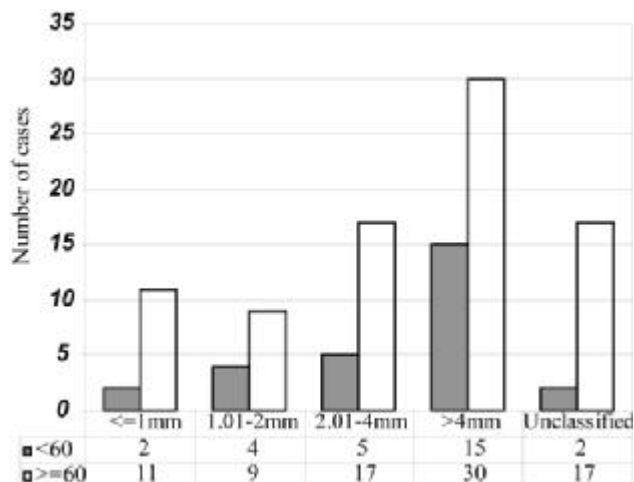
different from our data. The amount of patients with cutaneous and mucosal head and neck melanoma in Latvia is inconsistent and could not be described as a persistent increase.

According to other authors, the mean age of melanoma patients is 53.7 to 59 years [2,19,23,24], thus playing a substantial role in loosing a prominent amount of years of life. As we analyzed the head and neck region of the body, contrary to some papers mentioned above, patients with cutaneous and mucosal head and neck melanoma in Latvia are featured elderly. As prognosis worsens with increasing age, patients drawn in our study are all subdued to a worse prognosis concerning the survival and complications.

Numerous studies have demonstrated that male melanoma patients outnumber females [7,8,15,21,25]. According to the Cancer Register of Latvia, the incidence of melanoma in men patients in year 2009 was 6.2/100000, however in women 7.7/100000. Comparatively – this rate in year 1988 was 3.3/100 000 for both genders. Reduced melanoma incidence

	<=1mm	1.01-2mm	2.01-4mm	>4mm	Unclassified
<60	2	4	5	15	2
>=60	11	9	17	30	17

Fig. 8. Distribution of the cases by patient's age, according to melanoma Breslow thickness
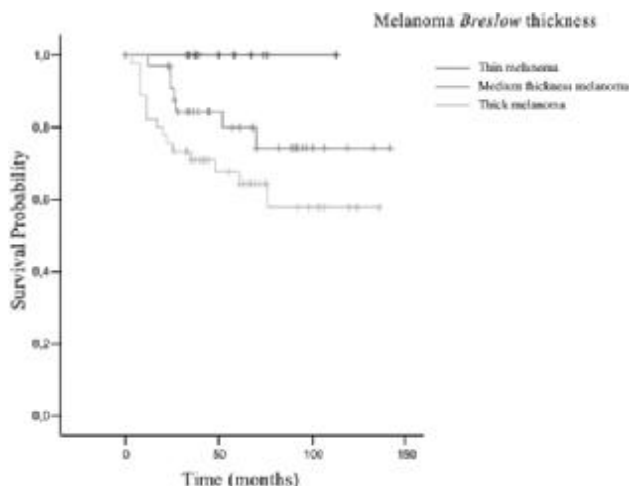

Fig. 9. Kaplan-Meier survival curve for differet Breslow thickness melanomas
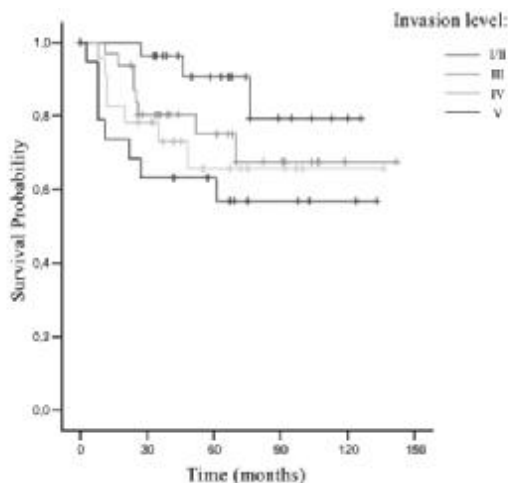
Fig. 10. Difference in mortality between Clark levels of invasion

rate in men probably is related to infrequent self examination, as well as less pronounced participation in primary and secondary melanoma prevention campaigns [26,27].

The authorities in the field of melanoma claim that head and neck melanoma carry the worst prognosis, comparing with other anatomical sites [15,28]. Scalp, neck and ear melanoma has a poor prognosis, which has been proven not only in other scientific studies [15,29], but also in ours. As head and neck melanoma is localized in an anatomical site which can be seen to any speciality of doctors, it should increase the probability of being diagnosed early.

The prognosis of melanoma is very good if the tumor is thin at the time of diagnosis. In this case 5-year survival is 95-97% [30]. The risk of metastasis radically increases when melanoma is diagnosed in a late stage (tumor Breslow thickness >4mm). Thereby, early diagnosis of melanoma is invaluably essential as it improves the prognosis of the disease. Having a good knowledge in the epidemiologic characteristics and prognostic factors of melanoma, primary and secondary prevention of this malignant tumor can be upgraded. Tumor Breslow thickness is the most powerful prognostic value [28], whilst increasing Clark invasion

level also is associated with more frequent mortality [15]. We found that Clark level of invasion V, thick melanomas (Breslow thickness ≥4 mm) and ulcerated tumors carried a significantly worse prognosis.

According to other authors superficial spreading melanoma is the most frequent histopathologic tumor subtype [2,21,25,28]. In our study nodular subtype of melanoma was the most common and the cummulative survival curve demonstrated the worse prognosis for these patients.

Although cutaneous malignant melanoma is one of the most preventable and treatable of cancers [30], the mortality rates have risen during the past 20 years [2,21,32]. In Latvia, in the year of 2008, 34 cases of death due to body melanoma were recorded in male gender, while 45 – in women. Respectively, in the year of 1988 - 11 cases of death in men and 22 in women. Number of cases of death from head and neck melanoma are instable and does not have a convincing tendency to grow. During the period of 10 years that was analyzed in our study, most of all death cases from head or neck melanoma was found in the year of 2006 (n=5).

CONCLUSIONS

The prognosis of most of the analyzed cases is poor, according to survival, local recurrence and distant metastasis due to delayed diagnosis.

In our study we found the predominance of female gender and advanced aged patients, as well as nodular, ulcerated and thick melanomas, mostly localized on the face - factors all of which carry a relevant risk of poor prognosis.

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