

Risk Factors for Malignant Melanoma and Preventive Methods

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Practice Points

- Our study revealed the following common risk factors associated with higher melanoma incidence: light eye color (ie, blue, green, gray), Fitzpatrick skin types I and II, frequent sunburns during childhood and adolescence, and higher level of education.
- Prevention campaigns should be implemented to improve awareness of melanoma to reduce exposure to UV radiation among high-risk patient populations.

UV radiation is an important environmental risk factor for cutaneous melanoma; however, information concerning UV exposure in many populations is lacking. The aim of our study was to investigate risk factors for malignant melanoma (MM), particularly those related to UV exposure behavior in the Czech Republic and Germany. This case-control study included 207 patients who were consecutively diagnosed with MM in 2 dermatology clinics in Prague, Czech Republic, and Munich, Germany. Controls were 235 patients with other dermatologic conditions. All 442 participants completed a questionnaire on sociodemographic data and factors related to UV exposure. The association between risk factors and MM was assessed using multivariate logistic regression. Patients with Fitzpatrick skin types I and II had a higher likelihood of developing melanoma than those with Fitzpatrick skin type III. Frequent

sunburns during childhood and adolescence were strongly related to developing melanoma. A higher level of education also was associated with a higher melanoma incidence. Variables related to UV exposure were strongly associated with melanoma in our study population. Prevention campaigns should be implemented to improve awareness of melanoma to reduce exposure to UV radiation among high-risk patient populations.
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Cutaneous melanoma is a malignant tumor of the skin that develops from melanin-producing pigment cells known as melanocytes. The development of melanoma is a multifactorial process. External factors, genetic predisposition, or both may cause damage to DNA in melanoma cells. Genetic mutations may occur de novo or can be transferred from generation to generation. The most important environmental risk factor is UV radiation, both natural and artificial. Other risk factors include skin type, ethnicity, number of melanocytic nevi, number and severity of sunburns, frequency and duration of UV exposure, geographic location, and level of awareness about malignant melanoma (MM) and its risk factors.¹

Melanoma accounts for only 1% to 2% of all tumors but is known for its rapidly increasing

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incidence.² White individuals who reside in sunny areas of North America, northern Europe, Australia, and New Zealand seem to be at the highest risk for developing melanoma.³ The global incidence of MM from 2004 to 2008 was 20.8 individuals per 100,000 people.⁴ In Central Europe, 10 to 12 individuals per 100,000 people were diagnosed with melanoma, and 50 to 60 individuals per 100,000 people were diagnosed in Australia. In 2011, the lifetime risk of being diagnosed with melanoma was 1% in Central Europe and 4% in Australia.² The incidence of melanoma is lower in populations with darker skin types (ie, Africans, Asians). In some parts of the world, the overall incidence and/or severity of melanoma has been declining over the last few decades, possibly reflecting improved public awareness.⁵

Cutaneous MM is an aggressive skin cancer that has fatal consequences if diagnosed late. Chances of survival, however, increase dramatically when melanoma is detected early. Collecting and analyzing data about a certain disease leads to a better understanding of the condition and encourages the development of prevention strategies. Epidemiologic research helps to improve patient care by measuring the occurrence of an event and by investigating the relationship between the occurrence of an event and associated factors; in doing so, epidemiologic research directly enables a better understanding of the disease and promotes effective preventive and therapeutic approaches.⁶

Although risk factors for melanoma are well established, current epidemiologic research shows that information on UV exposure and its association with this disease in many parts of the world, including Central Europe, is lacking. The aim of this study was to investigate behavioral and sociodemographic factors associated with the development of MM in the Czech Republic and Germany.

Materials and Methods

This hospital-based, case-control study was conducted in the largest dermatology departments in the Czech Republic (Clinic of Dermatology and Venereology, Third Faculty of Medicine, Charles University, Prague) and Germany (Department of Dermatology and Allergology, Ludwig Maximilian University, Munich). Data from the Czech Republic and Germany were not evaluated separately. These 2 countries were chosen as a representative sample population from Central Europe.

Study Population—The study population included 207 patients (103 men; 104 women) aged 31 to 94 years who were consecutively diagnosed with MM (cases). Patients with acral lentiginous melanoma were excluded from the study due to the

generally accepted theory that the condition is not linked to UV exposure. Melanoma diagnosis was based on histopathologic examination. The study population also included 235 randomly selected controls (110 men; 125 women) from the same 2 study centers who had been hospitalized due to other dermatologic diagnoses with no history of any skin cancer. Among patients asked to take part in the study, the participation rates were 83% among cases and 62% among controls.

Assessment—Various sociodemographic factors and factors related to UV exposure were assessed via administration of a structured questionnaire that was completed by all 442 patients.

Four statistical models concerning variables were constructed. The basic model, which was part of all subsequent models, included age, sex, education, and history of skin tumors. Variables included in the biological model were eye color (light vs dark) and Fitzpatrick skin type (I–V). Variables included in the lifestyle model were the use of sunscreen (never and rarely; often; always; always and repetitively), sun exposure during work (yes/no), and seaside vacation (never, rarely, regularly, more than once per year). The variable in the exposure model was the number of sunburns during childhood and adolescence (none, 1–5 times, 6–10 times, ≥ 11 times).

Sociodemographic characteristics (sex, age, education) and prior incidence of skin tumor were included in each model. Although there were no statistically significant differences in the incidence of melanoma associated with sex and age, those variables were kept in the models to control the impact of other variables by sex and age.

Other variables were added into the model one by one, and the likelihood ratio was tested step-by-step. Only the variables that improved the model fit were kept in the final model. Impact of variables on dependent variables also was tested; variables with no significant impact on dependent variables were left out of the model.

Statistical Analysis—The association between risk factors and MM was assessed using multivariate logistic regression. In total, 4 models were included in the results, which were presented as odds ratios (ORs) and 95% confidence intervals (CIs). A significance level of $\alpha=.05$ was chosen. The statistical program Stata 11 was used for all analyses.

Results

Descriptive data on the 442 patients surveyed are shown in Table 1. The results of the logistic regression in all studied models are shown in Table 2.

Basic Model—There was no difference in the proportion of men and women in the melanoma and

Table 1.

Study Collective Characteristics: Questions Concerning Behavioral Characteristics

Survey Question With Answer Options	Melanoma Group, n (%) (n=207)	Control Group, n (%) (n=235)
Achieved level of education		
University degree	56 (27.1)	31 (13.2)
High school	112 (54.1)	122 (51.9)
Primary school	39 (18.8)	82 (34.9)
No. of sunburns sustained during childhood and adolescence		
None	17 (8.2)	76 (32.3)
1–5	11 (5.3)	94 (40.0)
6–10	37 (17.9)	30 (12.8)
≥11	142 (68.6)	35 (14.9)
Do you use sunscreen while being exposed to the sunlight?		
Never	14 (6.8)	3 (1.3)
Rarely	42 (20.3)	12 (5.1)
Often	40 (19.3)	63 (26.8)
Always (once per period of sun exposure)	49 (23.7)	84 (35.7)
Always and repetitively	62 (30.0)	73 (31.1)
Do you use tanning beds?		
Never	153 (73.9)	174 (74.0)
Sometimes (once in 2 mo)	46 (22.2)	59 (25.1)
Often (every week)	8 (3.9)	2 (0.9)
Do you spend your free time in direct sunlight?		
Never	65 (31.4)	13 (5.5)
Sometimes (30% of free time)	105 (50.7)	177 (75.3)
Often (60% of free time)	32 (15.5)	39 (16.6)
Almost always (90% of free time)	5 (2.4)	6 (2.6)
Do you spend your working time in direct sunlight?		
Never	74 (35.7)	114 (48.5)
Sometimes (30% of free time)	105 (50.7)	96 (40.9)
Often (60% of free time)	24 (11.6)	18 (7.7)
Almost always (90% of free time)	4 (1.9)	7 (3.0)
Do you spend your vacation at the seaside?		
Never	53 (25.6)	62 (26.4)
Rarely	75 (36.2)	50 (21.3)
Regularly (every year)	41 (19.8)	96 (40.9)
More than once per year	38 (18.4)	27 (11.5)
Do you spend your vacation in the mountains?		
Never	102 (49.3)	67 (28.5)
Rarely	40 (19.3)	45 (19.1)
Regularly (every year)	50 (24.2)	53 (22.6)
More than once per year	15 (7.2)	70 (29.8)
Do you perform self-examination of your skin?		
Yes	31 (15.0)	141 (60)
No	176 (85.0)	94 (40)

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Table 1. (continued)

Survey Question With Answer Options	Melanoma Group, n (%) (n=207)	Control Group, n (%) (n=235)
Do you know about the possibility of a whole-body examination by a skin specialist?		
Yes	159 (76.8)	228 (97.0)
No	48 (23.2)	7 (3.0)
Do you visit a dermatologist?		
Never	21 (10.1)	22 (9.4)
Rarely	40 (19.3)	49 (20.9)
Regularly	146 (70.5)	164 (69.8)
What was the reason for having your lesion examined?		
Change of size/form/color of the lesion	48 (23.2)	115 (48.9)
Bleeding from the lesion	23 (11.1)	0 (0)
Itching of the lesion	39 (18.8)	3 (1.3)
Aesthetic reasons	3 (1.4)	53 (22.6)
Preventive or other reasons	94 (45.4)	64 (27.2)

control groups. We observed that more patients in the melanoma group had a university degree than patients in the control group. Patients in the melanoma group with a history of MM showed 4.2 times higher risk for developing another melanoma.

Biological Model—Eye color and Fitzpatrick skin type were the focus of the biological model. The odds of being diagnosed with melanoma were 2.5 times greater in respondents with a light eye color (ie, blue, green, gray) than in respondents with a dark eye color (ie, brown, black). Respondents with Fitzpatrick skin types I and II had a significantly higher association with melanoma (OR, 4.25 and 6.98; 95% CI, 2.13-8.51 and 3.78-12.88) than Fitzpatrick skin type III (OR, 1.0) ($P < .001$ for both). Respondents with darker skin types (IV and V) also were present in our study population. The numbers were low, and the CI was too wide; nevertheless, the results were statistically significant ($P < .001$).

Lifestyle Model—The lifestyle model included patients' use of sunscreen and level of sun exposure at work and on vacation. Respondents who did not use sunscreen were 12 times more likely to develop melanoma than those who always used it (95% CI, 5.56-27.14); however, individuals who used sunscreen always and repetitively (ie, more than once during 1 period of sun exposure) had a higher likelihood of melanoma compared to those who always used it. The incidence of melanoma was lower in respondents who regularly spent their vacations

by the sea than those who did not vacation in seaside regions. Respondents who worked in direct sunlight were approximately 2 times more likely to present with melanoma than individuals who did not work outside.

Exposure Model—The number of sunburns sustained during childhood and adolescence was assessed in the exposure model. Respondents with a history of 1 to 5 sunburns during childhood and adolescence did not show a statistically significant increase in the incidence of melanoma diagnosis; however, those with a history of 6 or more sunburns during these periods showed a significant increase in the odds of developing melanoma (OR, 4.95 and 25.52; 95% CI, 2.29-10.71 and 12.16-53.54) ($P < .001$ for both).

Comment

In this study, we concentrated on UV exposure and various sociodemographic factors that were possibly connected to a higher risk for developing melanoma. We observed that the majority of patients in the melanoma group had achieved a higher level of education than the control group. Most of the melanoma group patients had light-colored eyes and spent more time in direct sunlight at work. Although seaside vacations did not correlate with a higher occurrence of melanoma, it was noted that the melanoma patients used sunscreen much less often than the control group. Major differences among respondents in the melanoma group versus the control group were

seen in the reported number of sunburns sustained in childhood and adolescence. More sunburns during these periods seemed to play the most important role in the risk for melanoma. Some of the patient responses to the questionnaire may be biased, as respondents answered the questions by themselves.

Because risk factors for and preventive methods against melanoma are well established, one would assume that general knowledge regarding melanoma is adequate. On the contrary, it has been shown that knowledge about melanoma is insufficient, even among professionals and individuals with higher levels of education. In a study based on a questionnaire administered to plastic surgeons, only 37.5% (27/72) of respondents correctly identified the duration of action of sunscreen to be 3 to 4 hours.⁷ Approximately half of the respondents (37/72) did not know that geographical conditions such as altitude and latitude as well as shade can alter sunscreen efficacy and also were not aware of the protective action of clothing. These results are alarming and indicate that even medical professionals, who should play a main role in improving the health knowledge of the general population, have an unsatisfactory level of education in prevention of melanoma. Another important part of better education of specialists treating skin disorders is good knowledge of dermatoscopy. In fact, the Annual Skin Cancer Conference 2011 in Australia emphasized the importance of dermatoscopy in primary and secondary prevention of skin cancer.⁸ Teaching dermatoscopy should be part of melanoma campaigns for professionals.

Our basic model demonstrated that a higher level of education was connected to a higher occurrence of MM, which may seem surprising, considering that most diseases, along with their incidence, prevalence, and mortality, usually are associated with lower levels of education or lower socioeconomic status. A similar trend also was reported in prior studies, with higher socioeconomic groups showing higher incidences of cutaneous melanoma; colon cancer; brain cancer in men; and breast and ovarian cancer in women. Additionally, patients with higher socioeconomic status have been shown to have a survival advantage.⁹ Individuals with higher socioeconomic status can afford to travel more often for vacation and are more frequently exposed to direct sun. Individuals with higher levels of education also are generally more aware of the importance of disease prevention and therefore go for preventive check-ups more often. The detection of melanoma in this socioeconomic group should be higher.

Our biological model demonstrated that respondents with lighter eyes had melanoma almost 3 times more often than individuals with darker

eyes. Fitzpatrick skin types I and II also were significantly associated with the development of melanoma ($P < .001$). These findings are generally confirmed in the literature. In a study of the incidence of melanoma in Spain, statistically significant risk factors included blonde or red hair ($P = .002$), multiple melanocytic nevi ($P = .002$), Fitzpatrick skin types I and II ($P = .002$), and a history of actinic keratosis ($P = .021$) or nonmelanoma skin cancer ($P = .002$).¹⁰ A group in Italy also has investigated the main risk factors for melanoma. This study suggested dividing patients into high-risk subgroups to help minimize exposure to UV radiation and diagnose melanoma in its early stage.¹¹

The results from our study confirmed the importance of concentrating melanoma prevention campaign efforts on high-risk patients. Dividing these patients into subgroups (eg, individuals who play outdoor sports, individuals with occupations associated with UV exposure, individuals who use indoor tanning beds, individuals with a family history of melanoma) may be helpful. A case-control study on sun-seeking behavior in the Czech Republic showed that the most alarming risk factors were all-day sun exposure during adolescence, frequent holidays spent in the mountains, and inadequate use of sunscreen in adulthood.¹² We investigated the effects of sunscreen use on the incidence of melanoma in our lifestyle model and discovered that it decreased the risk for melanoma. Respondents who used it always had a much lower risk for developing melanoma than those who never or rarely applied it. Individuals who used sunscreen always and repetitively (ie, more than once per period of sun exposure) did not show a lower risk than those who used it once per period of sun exposure. This finding could mean that patients who are known to get sunburns or who feel a certain discomfort on direct exposure to the sun tend to use sunscreen always and repetitively.

It is important to note that some investigators disagree with the importance of some generally accepted means of prevention, such as the effect of sunscreen products. Due to insufficient evidence, the role of sunscreen use in reducing the risk for skin cancer, especially cutaneous MM, is controversial.¹³ Although we could prove there is a considerable difference in the incidence of melanoma in patients who claimed to use sunscreen always versus those who never use it, we agree that more evidence on this topic is needed. Furthermore, it has been reported that risk for melanoma has increased with rising intermittent sun exposure and indoor tanning bed use.^{14,15}

Respondents who regularly traveled to seaside regions showed a surprisingly lower incidence of

Table 2.
Variables Influencing the Incidence of Malignant Melanoma^a

Variables and Subgroups	Basic Model ^b			Biological Model ^c			Lifestyle Model ^d			Exposure Model ^e		
	OR	P Value	95% CI	OR	P Value	95% CI	OR	P Value	95% CI	OR	P Value	95% CI
Sex												
Male	1.0			1.0			1.0			1.0		
Female	0.97	.86	0.65-1.44	1.22	.38	0.78-1.91	0.94	.78	0.61-1.46	1.40	.19	0.85-2.32
Age, y												
≤40	1.0			1.0			1.0			1.0		
41-55	0.45	.16	0.15-1.36	0.50	.25	0.15-1.64	0.36	.11	0.10-1.25	0.64	.53	0.16-2.55
56-69	0.46	.19	0.15-1.47	0.49	.26	0.14-1.68	0.47	.26	0.13-1.73	0.78	.74	0.18-3.38
≥70	0.61	.40	0.20-1.89	0.93	.90	0.27-3.12	0.56	.38	0.15-2.06	1.57	.54	0.38-6.54
Achieved level of education												
Primary school	1.0			1.0			1.0			1.0		
High school	2.04	.01	1.26-3.31	1.81	.03	1.08-3.04	3.3	<.001	1.73-5.31	0.95	.87	0.52-1.74
University degree	3.16	<.001	1.68-5.92	3.71	<.001	1.85-7.43	3.42	.01	1.66-7.02	3.26	.01	1.52-7.01
History of a skin tumor												
Yes	4.19	<.001	2.77-6.35	4.23	<.001	2.70-6.62	3.77	<.001	2.38-5.99	3.13	<.001	1.88-5.22
No	1.0			1.0			1.0			1.0		
Eye color												
Dark (brown, black)				1.0								
Light (blue, green, gray)				2.46	.01	1.45-4.18						
Fitzpatrick skin type												
III				1.0								
I				4.25	<.001	2.13-8.51						
II				6.98	<.001	3.78-12.88						
IV, V				4.57	<.001	1.96-10.62						

Variables and Subgroups	Basic Model ^b			Biological Model ^c			Lifestyle Model ^d			Exposure Model ^e		
	OR	P Value	95% CI	OR	P Value	95% CI	OR	P Value	95% CI	OR	P Value	95% CI
Sunscreen use												
Never and rarely							12.28	<.001	5.56-27.14			
Often							1.62	.13	0.87-3.03			
Always (once per period of sun exposure)							1.0					
Always and repetitively							2.19	.01	1.23-3.91			
Seaside vacation												
Never							1.0					
Rarely							1.8	.06	0.97-3.35			
Regularly (every year)							0.46	.03	0.22-0.93			
More than once per year							2.7	.09	0.88-4.87			
Sun exposure during work												
No							1.0					
Yes							1.73	.03	1.06-2.82			
No. of sunburns sustained during childhood and adolescence												
None										1.0		
1-5										0.65	.34	0.27-1.56
6-10										4.95	<.001	2.29-10.71
≥11										25.52	<.001	12.16-53.54

Abbreviations: OR, odds ratio; CI, confidence interval.

^aThe fit of the models is compared with the basic model.

^bLikelihood ratio, -296.30; *P*<.001.

^cLikelihood ratio, -257.60; *P*<.001.

^dLikelihood, -246.60; *P*<.001.

^eLikelihood ratio, -204.80; *P*<.001.

melanoma than respondents who did not spend their vacations in seaside locations. It is possible that individuals who choose not to spend their vacations at the seaside are more prone to sunburns and therefore do not prefer to spend their free time in direct sunlight. Another possible explanation is that individuals who regularly travel to seaside regions actively try to protect themselves from sunlight and sunburns. A higher incidence of melanoma also was observed in respondents who reported sun exposure during work.

In our exposure model, we demonstrated that a history of sunburns is the strongest risk factor for melanoma. Frequent sunburns during childhood and adolescence were strongly associated with the development of MM. This association has been supported in a systematic review on sun exposure during childhood and associated risks.¹⁶

Conclusion

To improve patient knowledge about melanoma prevention, we suggest directing targeted campaigns that address high-risk population groups, such as individuals with red hair and/or light eyes, people with an occupation associated with frequent UV exposure, and individuals with higher levels of education. With regard to younger populations, parents as well as physicians and teachers should be aware that frequent sunburns during childhood and adolescence and use of tanning beds are 2 main risk factors for MM.

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