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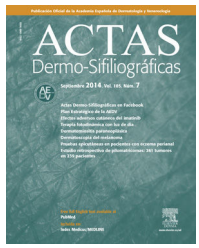

ORIGINAL ARTICLE

Clinical and Pathological Features of Melanoma in Europeans Living on the Western Costa del Sol in Southern Spain☆

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KEYWORDS
Melanoma;
Recreational sun exposure;
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Abstract

Objective: To compare clinical and pathological features of melanoma in Spanish patients with those of patients from Central or Northern Europe living in the health district of Costa del Sol Occidental in southern Spain.

Methods: We conducted a descriptive cross-sectional study of all cases of primary cutaneous melanoma histologically confirmed between 2005 and 2011 in the health care district covered by Hospital Costa del Sol in Marbella. We analyzed clinical and pathological features and performed a descriptive analysis of the 2 populations, in addition to univariate analysis with place of birth (Spain vs Central or Northern Europe) as the independent variable.

Results: Compared with Spaniards, patients from Central or Northern Europe were 10 years older at the time of melanoma diagnosis (66.2 vs 56.2 years, $P < .001$), had lighter skin (types I or II) (90.3% vs 67.1%, $P < .001$), and greater recreational sun exposure (93.7% vs 66.2%, $P < .001$). In addition, multiple melanomas (17.6% vs 4.4%, $P = .001$), nonmelanoma skin cancer (47.2% vs 15.7%, $P < .001$), and a family history of melanoma (9.5% vs 2.3%, $P = .01$) were more common in these patients. Central and Northern Europeans also had a higher overall frequency of melanoma on the trunk (46.3% vs 38.7%) and melanoma in situ (54.7% vs 41.8%, $P = .03$).

Conclusion: Differences in melanoma presentation between Spanish patients and patients from Central or Northern Europe appear to be linked to phenotypic and lifestyle factors. A better understanding of these differences will help to tailor melanoma prevention and follow-up programs for multicultural populations, such as those on Spain's Costa del Sol.

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PALABRAS CLAVE
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Características clínico patológicas del melanoma en residentes europeos de la Costa del Sol occidental

Resumen

Objetivo: Estudiar las diferencias clínico-patológicas del melanoma entre grupos de población española y centro-norte europea en el área sanitaria pública de la Costa del Sol occidental.

Métodos: Se realizó un estudio descriptivo, transversal, que incluyó todos los casos de melanoma cutáneo primario confirmados histológicamente durante el periodo 2005-2011 en el área sanitaria del Hospital Costa del Sol. Se analizaron las características clínicas y patológicas. Se realizó un análisis descriptivo y un análisis univariado tomando como variable de comparación de subgrupos el país de nacimiento (España vs norte y centro de Europa).

Resultados: En comparación con los españoles, los pacientes centro-norte europeos presentaron una edad al diagnóstico 10 años superior (66,2 vs 56,2; $p < 0,001$) una mayor frecuencia de fototipos bajos (I o II 90,3% vs 67,1%; $p < 0,001$), fotoexposición recreativa (93,7% vs 66,2%; $p < 0,001$), antecedentes familiares de melanoma (9,5 vs 2,3; $p = 0,01$), melanomas múltiples (17,6% vs 4,4%; $p = 0,001$) y una mayor asociación con carcinomas cutáneos (47,2% vs 15,7%; $p < 0,001$). Además, destacó un mayor número de melanomas del tronco (46,3% vs 38,7%) y melanomas *in situ* (54,7% vs 41,8%; $p = 0,03$).

Conclusión: Las diferencias fenotípicas y en los estilos de vida entre la población española y la centro-norte europea parecen determinar patrones diferentes de presentación del melanoma. Conocer estas diferencias permitirá orientar más adecuadamente las estrategias de prevención, así como el seguimiento de los pacientes con melanoma en poblaciones multiculturales como la de la Costa del Sol.

Introduction

The incidence of melanoma is growing at an annual rate of between 3% and 7% in the white population.[1] This rise in incidence has been attributed to a combination of factors, including an ageing population, depletion of the ozone layer, and changes in lifestyle habits related to a desire for a tan. Sun exposure is now considered one of the main modifiable risk factors for melanoma.

The western Costa del Sol, which is located in southern Spain and includes the city of Malaga, has over 300 days of sun a year and is one of the top destinations for both tourists and retirees. At least 31.8% of its population (148 320 inhabitants, of whom 25 664 are aged over 65 years) are from European countries with less sunshine than Spain (data from 2010 census). Our Mediterranean climate has a lot to offer this population, who, with a distinct phenotype and genotype to ours and very different sun exposure habits, are drawn to Spain in search of sun, sand, and golf.

The prevalence of melanoma in the province of Malaga is underestimated due to a lack of records, and there is currently no information on the frequency of melanoma among foreigners residing in tourist spots such as the Costa del Sol. The combination of light skin types, risk-related sun exposure habits, and a high incidence of melanoma make the western Costa del Sol health care district an ideal place for epidemiological studies comparing Spaniards and Central-Northern Europeans.

The aims of this study were to analyze melanoma cases registered at Hospital Costa del Sol and to study clinical and pathological differences between Spanish patients and patients from Central and Northern Europe. Hospital del Sol, the referral hospital for our health care district, serves a population of 465 217 inhabitants between the cities of Fuengirola and Manilva (2010 census).

Materials and Methods

This was a descriptive, cross-sectional study of all patients from Spain and Central or Northern Europe with primary cutaneous melanoma histologically confirmed between 2005 and 2011. The data were collected from the pathology department's skin cancer registry at Hospital Costa del Sol and from electronic medical records. Patient nationality is recorded in the administrative section of the medical record. All the data were recorded anonymously, with strict adherence to Spanish data protection laws (Organic Law 15/1999 of 13 December on Data Protection and Law 41/2002 of 14 November on Patient Autonomy).

We analyzed epidemiological variables (country of origin, age, sex, skin type, sun exposure habits) and clinical and pathological features of melanoma (tumor thickness and location, melanoma subtype, family history of melanoma, presence of multiple melanomas, and a histologic diagnosis of nonmelanoma skin cancer (NMSC) (Table 1).

We performed a descriptive analysis using measures of central tendency and dispersion for quantitative variables and distribution of frequencies for qualitative variables. The independent variable used in the univariate analysis to compare subgroups was place of origin (Spain vs Central or Northern Europe). The *t* test was used for quantitative variables, and the X^2 test corrected for continuity (or the Fisher test where appropriate) was used for qualitative variables.

Table 1 Characteristics of Patients and Melanomas.

Age, mean (SD), y	58.3 (16.6)
	No. (%) of Patients
Sex	
Male	154 (50.8)
Female	149 (49.2)
Place of origin	
Spain	229 (75.6)
Central or Northern Europe	74 (24.4)
Skin type	
I	42 (14.7)
II	166 (58.2)
III	74 (26.0)
IV	3 (1.1)
Sun exposure	
Recreational	188 (73.6)
Occupational	70 (26.4)
Tumor site	
Trunk	122 (41.5)
Head and neck	76 (25.9)
Lower extremities	51 (17.4)
Upper extremities	35 (11.9)
Tumor thickness	
In situ	165 (42.6)
< 1 mm	92 (23.8)
Melanoma subtype	
Superficial extending melanoma	177 (55.1)
Nodular melanoma	25 (9)
Lentigo maligna melanoma	67 (20.5)
Other	50 (15.4)

Significance was set at a *P* value of less than .05. All analyses were performed using SPSS version 15 (Table 2).

Results

The final sample included 340 patients with 387 melanomas. In total, 229 patients were Spanish and 74 were from Central or Northern Europe. Specifically, 48.6% were from the United Kingdom. Just over half of the patients (50.8%) were male. The mean (SD) age was 58.3 (16.6) years. The most common skin types were phototypes I-II (72.3%) and most sun exposure (73.6%) occurred in recreational settings. The trunk was the most common site for melanoma and the main subtype was superficial spreading melanoma (SSM) (55.1%).

In the univariate analysis, patients from Central-Northern Europe were on average 10 years older than their Spanish counterparts at the time of diagnosis (66.2% vs 56.2%, $P < .001$). There were no differences between the groups in terms of distribution of men and women (male to female ratio, 1:1). Skin types I-II and recreational sun exposure were more common in the Central-Northern European population (90.3% vs 67.1% $P < .001$ and 93.7% vs 66.2% $P < .001$, respectively). The most common site for melanoma in both groups was the trunk, followed by the head and neck. In the sex-stratified analysis, the head and neck, followed by the trunk, was the most common tumor site in women from Central-Northern Europe. In women from Spain, it was the trunk, followed by the lower extremities. There were no differences in tumor site between the men according to place of origin. On analyzing the age of patients according to tumor site, Central-Northern Europeans were older than Spaniards for all sites: head and neck (73.5 vs 67.9 years, $P = .063$), trunk (64.0 vs 51.7 years, $P < .01$), lower extremities (62.9 vs 51.9 years, $P = .037$), and upper extremities (65.8 vs 53.6 years, $P = .01$).

SSM, followed by lentigo maligna (LM), was the most common melanoma subtype observed in both groups. SSM was located mainly on the trunk, while LM was located mainly on the head and neck. On analyzing differences in tumor thickness, melanoma in situ was more common in the Central-Northern European population (54.7% vs 48.1%, $P = .03$). A family history of melanoma was also more common in this population (9.5% vs 2.3%, $P = .01$), as was the presence of a second melanoma, with a 4-fold difference (17.6% vs 4.4%, $P = .001$). A histologic diagnosis of NMSC was also 3 times more common in Central-Northern Europeans (47.2% vs 15.7%, $P = .001$). The most common type of NMSC was basal cell carcinoma.

Discussion

This is the first epidemiological study of melanoma in a multicultural population in Spain to reveal significant differences between Spanish patients and patients from Central-Northern Europe.

On average, 55 new cases of melanoma were recorded annually between 2005 and 2011 in the health care district of Hospital Costa del Sol. Of these, 25% corresponded to patients from Central-Northern Europe, most of whom were from the United Kingdom. Although this hospital-based incidence is high (11.8 cases/100 000 inhabitants/year), we cannot compare it to rates reported for Spain or the United Kingdom, as these correspond to population-based and not hospital-based data. The highest rate in Spain has been recorded in women in Girona (8.24 cases per 100 000 population per year),[2] while in the United Kingdom rates of up to 13.2 cases per 100 000 population a year have been reported.[3]

Compared with the Spaniards in our series, Central-Northern Europeans were older at the time of diagnosis, had a lighter skin type (I-II), and a higher rate of recreational sun exposure. These features are all melanoma risk factors[4,5] and describe the typical profile of retired foreigners in Spain who devote many hours to sport and other outdoor pursuits. We do not have information on the prevalence of melanoma in younger individuals who come to Spain in search of sun and sand, as the majority are not seen in our health care system. In some countries such as Norway, the increase in the number of inhabitants who travel to the sun for their holidays has had a detectable effect on national melanoma incidence rates.[6]

In contrast to other epidemiological studies,[2,3] we detected no sex-related differences in melanoma incidence in either population group. This trend is becoming increasingly evident in countries with a high rate of melanoma incidence, such as the United States, Australia, New Zealand,

Table 2 Comparison of Spanish and Central-Northern European Patients With Melanoma.

Variables	Spain No. (%) of Patients	Central or Northern Europe No. (%) of Patients	*P* Value
Age, mean (SD), y	56.2 (16.9)	66.2 (14.1)	< .001
Sex			
Male	115 (50.2)	39 (52.7)	< .71
Female	114 (49.8)	35 (47.3)	
Skin type			
I-II	143 (67.1)	65 (90.3)	< .001
III-IV	70 (32.9)	7 (9.7)	
Sun exposure			
Recreational	129 (66.2)	59 (93.7)	< .01
Occupational	66 (33.8)	4 (6.3)	
Tumor site			
Trunk	92 (38.7)	50 (46.3)	< .08
Head and neck	57 (23.9)	33 (30.6)	
Lower extremities	47 (19.7)	11 (10.2)	
Upper extremities	30 (12.6)	13 (12)	
Melanoma subtype			
Superficial extending melanoma	117 (53.9)	60 (58.8)	.083
Nodular melanoma	18 (8.3)	7 (6.9)	
Lentigo maligna melanoma	44 (20.3)	23 (22.5)	
Tumor thickness			
In situ	97 (41.8)	58 (54.7)	.034
Family history of melanoma			
Yes	5 (2.3)	7 (9.5)	.01
Multiple melanoma			
Yes	10 (4.4)	13 (17.6)	< .01
Other type of NMSC			
Yes	35 (15.7)	34 (47.2)	= .001
No	188 (84.3)	38 (52.8)	
Type of NMSC			
Basal cell carcinoma	30 (13.5)	29 (40.3)	< .001
Squamous cell carcinoma	5 (2.2)	3 (4.2)	

Abbreviation: NMSC, nonmelanoma skin cancer.

Norway, Finland, and Italy, among others.[3] One theory is that the proportion of melanoma cases in males and females is related to incidence. In other words, melanoma rates will be similar in males and females in countries with a high incidence and exposure to intense UV radiation.[7]

In series reported in Spain, the most common site for melanoma is the trunk, followed by the lower extremities.[8,9] In our series, the trunk, followed by the head and neck, was the most common tumor site in both Spaniards and Central-Northern Europeans. Nagore et al.[10] and Lipsker et al.[11] reported identical findings for Spanish and French patients, respectively. Lipsker et al. proposed the existence of 3 distinct types of melanoma depending on location. The first type is a slow-growing melanoma typically located in intermittently sun-exposed areas (the trunk). This type has been linked to changes in lifestyle habits and its incidence is increasing in almost epidemic proportions. The second type, also slow-growing, typically affects chronically sun-exposed areas (head and neck). Its rising incidence has been linked to the ageing of the population. The third type is a very fast-growing melanoma with an aggressive course but stable incidence. In the Spanish population in our study, the trunk was the most common site for melanoma, taking over from the lower extremities, which have traditionally occupied first place.[1,2] As in other countries, this new situation is a reflection of changes in sun exposure habits and the use of clothing that leave the trunk bare.[12]

SSM was the most common subtype of melanoma in both groups in our series, coinciding with findings for several other Spanish studies.[2,8,9] In situ melanoma was the most common type of melanoma in Central-Northern Europeans. We cannot compare this observation to those of other studies, as not all skin cancer registries record in situ forms of melanoma.[13] The higher rate of in situ melanoma detected in our series is probably due to the impact of skin cancer prevention campaigns and early diagnosis in at-risk populations, and also possibly reflects more acute sun exposure in later years of life. In other words, the melanomas would not

yet have had time to invade deeper layers. It is also possible that other factors, such as protocol-based follow-up of patients at Hospital Costa del Sol's Melanoma Unit, systematic use of dermoscopy,[14] and use of specific electronic medical records have led not only to higher rates of early diagnosis but also to the recording of more cases.

Approximately 5% of all invasive cutaneous melanomas occur in families with at least 2 cases of melanoma in close relatives, indicating that low-frequency, high-penetrance genes are involved in a small minority of patients. Furthermore, the phenotype that is typically seen in patients with melanoma—white skin, red or blonde hair, and blue eyes—indicates that high-frequency, low-penetrance genes, such as *MC1R*, may interact with environmental factors (and sun exposure in particular).[15] We believe that this was probably case in our Central-Northern European population.

The high percentage of Central-Northern Europeans with multiple melanomas and NMSC in our series is noteworthy. The rate is higher than rates reported for both Spain[8,16] and abroad,[17–19] and is undoubtedly the result of the interaction between endogenous factors (phenotype, genetic determinants), exogenous factors (UV index, sunburn), and behavioral factors (recreational sun exposure habits) in our setting. Although cumulative skin damage and a reduced immune response in elderly patients are obvious explanations for the increased frequency of multiple melanomas and NMSC, it is also true that older people tend to attach less importance to skin changes and self-examination than their younger counterparts.[20] The high proportion of multiple melanomas and NMSC detected might also be explained by the existence of systematic follow-up programs, which would contribute to the early diagnosis of tumors in less chronically sun-exposed areas that might otherwise be missed. The most common form of NMSC in our series was basal cell carcinoma. This is understandable considering that NMSC, like melanoma, is associated with intense and intermittent sun exposure[21] and a history of sunburn.

A recent comparative study of NMSC in Spanish and Central-Northern European patients in our health care district showed that the latter group had a higher frequency of multiple carcinomas (22.5% vs 13.4%) and less aggressive subtypes (48.3% for superficial basal cell carcinoma vs 34.7% for in situ squamous cell carcinoma).[22]

This study has certain limitations. For instance, the follow-up time was variable and there was no information on how long the patients from Central-Northern Europe had been living in Spain. Furthermore, sun exposure habits was classified into just 2 categories (occupational and recreational), as no additional information was available in the patients' medical records. Finally, our analysis is limited to patients seen in the public health care system, and therefore excludes anyone treated in private practice.

In conclusion, differences in melanoma presentation between Spanish patients and patients from Central-Northern Europe appear to be linked to phenotypic and lifestyle factors. A better understanding of these differences will help to tailor melanoma prevention and follow-up programs for multicultural populations, such as those on Spain's Costa del Sol.

Future studies should investigate individual and environmental risk factors associated with the development of melanoma in multicultural populations such as ours.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Ethical Disclosures

Protection of humans and animals. The authors declare that no tests were carried out in humans or animals for the purpose of this study.

Confidentiality of data. The authors declare that they have followed their hospital's protocol on the publication of data concerning patients.

Right to privacy and informed consent. The authors declare that no private patient data appear in this article.

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