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ORIGINAL ARTICLES

Clinical-Pathological Features of Cutaneous Melanomas Diagnosed in a Mediterranean Tertiary Hospital Between 1990 and 2004: A Comparison Between Sexes and Age Groups and Analysis of Long-Term Outcomes

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Abstract. *Background.* The incidence of malignant melanoma has increased over recent decades. Early diagnosis continues to be essential for effective treatment. Our objective was to analyze cutaneous malignant melanomas diagnosed over a 15-year period in a tertiary hospital for trends towards earlier diagnosis and to identify subgroups with poorer prognosis.
Material and methods. Retrospective analysis of primary cutaneous melanomas analyzed in the pathology department of Hospital La Paz, Madrid, Spain, between 1990 and 2004.
Results. In total, 526 melanomas were diagnosed. The mean (SD) Breslow thickness was 2.63 (4.84) mm and the median thickness was 0.98 mm (range, 0-65 mm). The mean size (widest point) was 16.59 (12.11) mm. The most common histological type was surface-spreading melanoma and the most common site was the trunk. Melanomas detected in men were generally larger and thicker than in women (*P*=.05). Individuals aged over 60 years consulted for significantly thicker and larger tumors than younger individuals. The incidence of malignant melanomas has increased steadily over the years whereas the mean Breslow thickness and size have decreased.
Conclusions. Diagnosis of melanoma in Spain is made increasingly earlier, although locally advanced tumors are still sometimes seen in men and in individuals aged over 60 years.

Key words: melanoma, epidemiology, early diagnosis, Spain, Mediterranean population.

CARACTERÍSTICAS CLÍNICO-PATOLÓGICAS DE LOS MELANOMAS CUTÁNEOS DIAGNOSTICADOS EN UN HOSPITAL TERCIARIO MEDITERRÁNEO ENTRE 1990 Y 2004: COMPARACIÓN ENTRE SEXOS, POR GRUPOS DE EDAD Y EVOLUCIÓN A LO LARGO DEL TIEMPO

Resumen. *Introducción.* En las últimas décadas está aumentando la incidencia de melanoma maligno (MM) y el diagnóstico precoz sigue siendo esencial para conseguir su curación. Nuestro objetivo fue analizar los MM cutáneos diagnosticados durante 15 años en un hospital terciario para comprobar si existe una tendencia favorable hacia un diagnóstico cada vez más precoz e intentar identificar grupos de población con MM de peor pronóstico.
Material y métodos. Análisis retrospectivo de los melanomas cutáneos primarios analizados en el Departamento de Anatomía Patológica del Hospital La Paz entre 1990 y 2004.
Resultados. Se diagnosticaron en total 526 melanomas. El espesor medio de Breslow fue de 2,63 mm (desviación estándar [DE] 4,84) y la mediana de 0,98 mm (0-65 mm); el tamaño medio (diámetro mayor) fue de 16,59 mm (DE 12,11); el tipo histológico más frecuente fue el melanoma de extensión superficial y la localización más habitual el tronco. Los melanomas detectados en varones tendieron a ser más grandes y de mayor espesor (p =0,05) que los de las mujeres. Los mayores de 60 años consultaron con tumores significativamente más gruesos y de mayor diámetro que los pacientes más jóvenes. A lo largo de estos años, ha aumentado progresivamente el número de MM, pero han disminuido el Breslow medio y el tamaño.
Conclusiones. El diagnóstico del melanoma en nuestro medio es cada vez más precoz, pero los varones y los mayores de 60 años en ocasiones aún consultan con tumores localmente avanzados.

Palabras clave: melanoma, epidemiología, diagnóstico precoz, España, población mediterránea.

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Introduction

Malignant cutaneous melanoma incidence and mortality have increased worldwide in recent decades, so much so that this cancerous tumor has become one of the leading causes of cancer-related death in young patients.[1-3] Although malignant melanoma accounts for just 1.5% to 7% of all malignant skin tumors, it is responsible for 65% of all skin cancer deaths and 80% to 90% of such deaths in patients under 65 years.[4] Mortality has risen less than incidence thanks to the ever earlier detection of the disease, leading to the gradual improvement in 5-year survival figures.[2,5-7]

Tumor thickness at the time of removal is directly associated with survival.[8] Prognosis is invariably poor in patients with organ metastases and few improvements have been seen in recent years due to a lack of major advances in the treatment of disseminated melanoma. In view of the high mortality and resistance to treatment associated with advanced-stage malignant melanoma, primary prevention and early diagnosis have become the most important weapons in the fight against this cancer.[9,10]

The aim of the present study was to determine the fundamental clinical and pathologic characteristics of primary skin melanomas excised from patients treated at Hospital Universitario La Paz in Madrid, Spain, or any of the centers in its catchment area (health district V of the Autonomous Community of Madrid) between 1990 and 2004. By analyzing changes in these characteristics over time, we also aimed to determine whether or not there was a trend towards an increasingly early diagnosis of malignant melanoma in this health district and whether analysis by sex and age groups could help to identify patients with a poorer prognosis.

Materials and Methods

We studied all the primary skin melanomas excised from patients treated at any of the centers in health district V of the Autonomous Community of Madrid and sent to the pathology department at Hospital Universitario La Paz for analysis between January 1, 1990 and December 31, 2004. Tumors removed and studied histologically in other centers were not included in our study, even if the patients were subsequently monitored at Hospital Universitario La Paz. We included nail apparatus melanomas but not primary ocular malignant melanomas (except those located on the eyelid), melanomas on mucosal or semi-mucosal surfaces, or soft tissue melanomas.

The melanomas were identified using the computerized database held by the pathology department at our hospital. Clinical and pathologic data were retrieved from the patients' medical records, the forms requesting histopathologic analysis, and the final pathology reports. No histologic review of the tumors was performed for the purpose of this study. The same person (D.A.S.) performed the medical record review and collected the data in all cases.

The following clinical data were recorded for each melanoma included in the study: age and sex of the patient, date of diagnosis, and tumor location and size (largest diameter in mm). Not all of the data were available in all cases (Table 1). Tumor size was included because it is an indirect marker of the time to diagnosis, and more importantly, of the likelihood of suspicion, which can vary greatly from one case to another.

The histologic features analyzed were Breslow thickness, Clark level of invasion, and histologic type. Breslow thickness is the most important prognostic factor in malignant melanoma and is associated with how early a tumor is diagnosed. We were unable to obtain this information for 29 cases either because of inappropriate surgical technique or the practice of just a diagnostic incisional biopsy in patients with metastatic melanomas or inoperable tumors. Histologic ulceration was not analyzed as this information was missing from many pathology reports completed before 2001 and included in this study, the year in which melanoma ulceration was incorporated into the staging system for cutaneous melanoma recommended by the American Joint Committee on Cancer.[8]

Table 1. Clinical and Pathologic Data Collected for Malignant Melanomas (n=526) and Availability of Information by Number of Melanomas

Data	*No. of Melanomas*
Date of diagnosis	526
Age of patient at time of tumor excision	524
Sex	526
Breslow thickness	497
Clark level	489
Size (largest diameter), mm	502
Tumor location (head and neck; trunk; upper limbs, not counting palms and nails; lower limbs, not counting soles and nails; acral sites [palms, soles, and nails])	478
Histologic type (lentigo maligna, melanoma in situ, lentigo maligna melanoma, superficial spreading melanoma, acral lentiginous melanoma, nodular melanoma, other [nevoid, spitzoid, and desmoplastic variants, unclassifiable, etc.])	526

Within the group of malignant melanomas in situ (Clark level 1), lesions diagnosed as lentigo maligna were considered as a separate group due to their clinical and epidemiologic particularities.

The data collected were analyzed for the group as a whole and also grouped by sex and age. In addition, we examined changes over time by dividing the study period into three 5-year periods: 1990 to 1994, 1995 to 1999, and 2000 to 2004.

Statistical Analysis

Statistical analyses were performed using version 9.1 of the Statistical Analysis System program and statistical significance was set at *P* less than .05.

The χ^2 test was used to examine associations between qualitative variables. Significant associations were then further examined using simple correspondence analysis to determine which categories were interrelated. Analysis of variance (ANOVA), together with nonparametric tests (median analysis, Mann-Whitney, Wilcoxon, and Kruskal-Wallis) were used to test for differences between quantitative variables and the Duncan multiple range test to determine significant between-group differences.

Results

Melanoma Characteristics for the Overall Group and a Comparison of Subgroups Defined by Sex

A total of 526 melanomas from 506 patients were studied. Table 2 shows the full clinical and pathologic data for the series and the most relevant findings are described below.

Of the 526 malignant melanomas studied, 44.5% were found in men and 55.5% in women. The mean (SD) age of the patients was 56.6 (18.3) years, with no significant differences detected between sexes. The median age was 56.8 years (range, 14.6-96.5 years).

The mean Breslow thickness was 2.63 (4.84) mm and the median thickness was 0.98 mm (range, 0-65 mm). The mean tumor size was 16.59 (12.11) mm and the median, 14 mm (range, 2-80 mm). Tumors diagnosed in men tended to be deeper (mean Breslow thickness, 3.14 mm) and larger (mean size, 17.77 mm) than those in women (2.23 mm and 15.67 mm, respectively), although the differences were not statistically significant (*P*=.05).

The most common tumor site for the group as a whole was the trunk, followed by the lower limbs and the head and neck. There were significant differences between men and women in terms of tumor site, with a clear predominance of lesions on the trunk in the former and of lesions on the lower limbs, followed by lesions on the trunk and head, in the latter (χ^2, simple correspondence analysis). The most common histologic type detected for the study period (15 years) was superficial spreading melanoma, with no significant sex-related differences.

Characteristics of Melanomas for Subgroups Defined by Age

Table 3 shows the characteristics of the melanomas studied according to the age of the patients at the time of diagnosis. As can be seen, there were clear differences between patients over and under 60 years in all of the clinical and pathologic variables analyzed.

Tumors detected in patients older than 60 years were significantly larger and deeper than those in younger patients (ANOVA, Duncan multiple range test).

The most common lesion sites were the trunk and the lower limbs in patients under 60 years; in those over 60 years the head and neck were the most common sites, though there was less predominance for specific sites. Acral sites were also common in patients aged over 60 years (16.8% of all melanomas), contrasting with the situation in the other age groups (Figure 1) (χ^2, simple correspondence analysis).

Our analysis of histologic type revealed that patients over 60 years of age had a greater prevalence of lentigo maligna, lentigo maligna melanoma, nodular melanoma, and acral lentiginous melanoma than younger patients (χ^2, simple correspondence analysis), although the most common histologic type across all ages was superficial spreading melanoma.

Characteristics of Melanomas According to the Treatment Period and Changes Over Time

Table 4 shows the findings of our analysis of melanomas by treatment period, the most relevant of which are described below.

The total number of malignant melanomas diagnosed increased from 124 between 1990 and 1994 (first period) to 217 between 2000 and 2004, with no significant changes in the age of patients at the time of diagnosis.

The increase in incidence was accompanied by a decrease in mean tumor thickness and size at the time of diagnosis. There were statistically significant differences in mean tumor thickness between the first

Table 2. Characteristics of the Overall Series and Comparison Between Sexes

	Overall Series	*Men*	*Women*	*Statistical significance*
Malignant melanomas, No. (No. of patients)	526 (506)	234 (219)	292 (287)	
Mean (SD) age, y	56.6 (18.3)	56.30 (17.7)	56.89 (18.8)	NS
Mean (SD) Breslow thickness, mm	2.63[a] (4.84)	3.14[a] (5.96)	2.23[a] (3.70)	*P*=.05
Median thickness, mm (range)	0.98 (0-65)	1.15 (0-65)	0.84 (0-26)	
Breslow thickness				NS
≤1 mm	258 (51.91%)[a]	103 (47.25%)[a]	155 (55.56%)[a]	
1.01-2 mm	89 (17.91%)	43 (19.72%)	46 (16.49%)	
2.01-4 mm	60 (12.07%)	25 (11.47%)	35 (12.54%)	
>4 mm	90 (18.11%)	47 (21.56%)	43 (15.41%)	
Clark level				NS
I	58 (11.86%)	22 (10.33%)	36 (13.04%)	
II	126 (25.77%)	49 (23%)	77 (27.90%)[a]	
III	139 (28.43%)[a]	66 (30.99%)[a]	73 (26.45%)	
IV	126 (25.77%)	58 (27.23%)	68 (24.64%)	
V	40 (8.18%)	18 (8.45%)	22 (7.97%)	
Mean (SD) diameter, mm	16.59[a] (12.11)	17.77[a] (13.07)	15.67[a] (11.24)	*P*=.05
Median diameter, mm (range)	14 (2-80)	15 (2-80)	12 (2-80)	
Diameter				*P*<.05
≤5 mm	51 (10.16%)	24 (10.86%)	27 (9.61%)	
5.01-10 mm	149 (29.68%)	51 (23.08%)	98 (34.88%)	
10.01-20 mm	191 (38.05%)[a]	92 (41.63%)[a]	99 (35.23%)[a]	
>20 mm	111 (22.11%)	54 (24.43%)	57 (20.28%)	
Location				P<.0.0001
Head and neck	85 (17.8%)	34 (15.9%)	51 (19.3%)	
Upper limbs	51 (10.7%)	24 (11.2%)	27 (10.2%)	
Trunk	187 (39.1%)[a]	114 (53.3%)[a]	73 (27.7%)	
Lower limbs	105 (22%)	19 (8.9%)	86 (32.6%)[a]	
Acral sites	50 (10.5%)	23 (10.7%)	27 (10.2%)	
Histologic type, No. (% of total)				NS
Lentigo maligna	15 (2.85%)	5 (2.14%)	10 (3.42%)	
Melanoma in situ	42 (7.98%)	17 (7.26%)	25 (8.56%)	
Lentigo maligna melanoma	41 (7.79%)	14 (5.98%)	27 (9.25%)	
Superficial spreading melanoma	250 (47.53%)[a]	117 (50%)[a]	133 (45.55%)[a]	
Melanoma on congenital nevus	32 (6.08%)	15 (6.41%)	17 (5.82%)	
Acral lentiginous melanoma	50 (9.51%)	22 (9.40%)	28 (9.59%)	
Nodular melanoma	61 (11.60%)	29 (12.39%)	32 (10.96%)	
Other	35 (6.65%)	15 (6.41%)	20 (6.85%)	

Abbreviation: NS, not significant.
[a] Most common value in each analysis.

and the second 2 periods; a reduction in tumor thickness was also noticeable between the second and the third period, although to a lesser extent (ANOVA, Duncan multiple range test). In the case of tumor size, significant differences were found between the 3 periods (ANOVA, Duncan test) (Figure 2). The increase in incidence was related to a greater number of melanomas with a Breslow thickness of less than 1 mm. Nonetheless, although the proportion of melanomas with a thickness of over 4 mm gradually decreased over time, practically no changes were detected in their number.

While the location of tumors did not vary during the study period, their histologic features did, with an increase in melanomas in situ and a decrease in the proportion but not in the absolute number of nodular melanomas (χ^2, simple correspondence analysis) (Figure 3).

Table 3. Characteristics of Melanomas (n=524) by Age Group

	Less than 40 Years	*40-60 Years*	*Over 60 Years*	*Statistical Significance*
Malignant melanomas, No.	105	192	227	
Mean (SD) Breslow thickness, mm	1.47[a] (2.11)	1.69[a] (2.84)	3.97[a] (6.53)	*P*<.0001
Median thickness, mm (range)	0,60 (0-10)	0,69 (0-25)	1,50 (0-65)	
Breslow thickness				*P*<.0001
≤1 mm	70 (67.96%)[a]	106 (57.92%)[a]	82 (39.23%)[a]	
1.01-2 mm	14 (13.59%)	39 (21.31%)	35 (16.75%)	
2.01-4 mm	9 (8.74%)	25 (13.66%)	26 (12.44%)	
>4 mm	10 (9.71%)	13 (7.10%)	66 (31.85%)	
Clark level				*P*<.0001
I	13 (12.75%)	19 (10.80%)	26 (12.44%)	
II	37 (36.27%)[a]	55 (31.25%)[a]	34 (16.27%)	
III	34 (33.33%)	52 (29.55%)	52 (24.88%)	
IV	15 (14.71%)	45 (25.57%)	66 (31.58%)[a]	
V	3 (2.94%)	5 (2.84%)	31 (14.83%)	
Mean (SD) diameter, mm	11.16[a] (8.72)	15.0[a] (10.32)	20.51[a] (13.62)	*P*<.0001
Median diameter, mm (range)	8 (2-70)	10 (2-60)	15 (2-80)	
Diameter				*P*<.0001
=5 mm	23 (22.77%)	20 (10.75%)	8 (3.76%)	
5.01-10 mm	40 (39.60%)[a]	63 (33.87%)	46 (21.60%)	
10.01-20 mm	30 (29.70%)	69 (37.10%)[a]	91 (42.72%)[a]	
>20 mm	8 (7.92%)	34 (18.28%)	68 (31.92%)	
Location				*P*<.0001
Head and neck	4 (4.3%)	16 (9.1%)	64 (30.8%)[a]	
Upper limbs	13 (13.8%)	20 (11.4%)	18 (8.7%)	
Trunk	48 (51.1%)[a]	89 (50.9%)[a]	50 (24%)	
Lower limbs	25 (26.6%)	39 (22.3%)	41 (19.7%)	
Acral sites	4 (4.3%)	11 (6.3%)	35 (16.8%)	
Histologic type, No. (% of total)				*P*<.0001
Lentigo maligna	0 (0%)	3 (1.56%)	12 (5.29%)	
Melanoma in situ	12 (11.43%)	16 (8.33%)	14 (6.17%)	
Lentigo maligna melanoma	2 (1.90%)	5 (2.60%)	33 (14.54%)	
Superficial spreading melanoma	61 (58.10%)[a]	120 (62.50%)[a]	69 (30.40%)[a]	
Melanoma on congenital nevus	13 (12.38%)	13 (6.77%)	6 (2.64%)	
Acral lentiginous melanoma	1 (0.95%)	11 (5.73%)	38 (16.74%)	
Nodular melanoma	6 (5.71%)	13 (6.77%)	41 (18.06%)	
Other	10 (9.52%)	11 (5.73%)	14 (6.17%)	

Abbreviation: NS, not significant.
[a] Most common values in each analysis.

Discussion

The general epidemiologic aspects associated with the present series are similar to those described for other recently analyzed series in Spain in terms of the mean age of patients at the time of diagnosis, distribution by sex, most common tumor locations, and histologic subtype.[11-14] The only parameter which has varied between studies is tumor location, with several studies reporting the legs to be the most common site for melanomas.[15-17] While the mean Breslow thickness detected in our study is similar to that reported by other studies,[11-13,16] we found a somewhat greater percentage of tumors penetrating deeper than 4 mm than other studies did.[11,13,14] This could be because the health district analyzed serves a large rural population that does not live near specialist centers; this population is characterized by certain sociocultural factors that might have a negative effect on the speed with which they seek medical attention.

In our sample, we found that women tended to have smaller, thinner tumors located predominantly on the

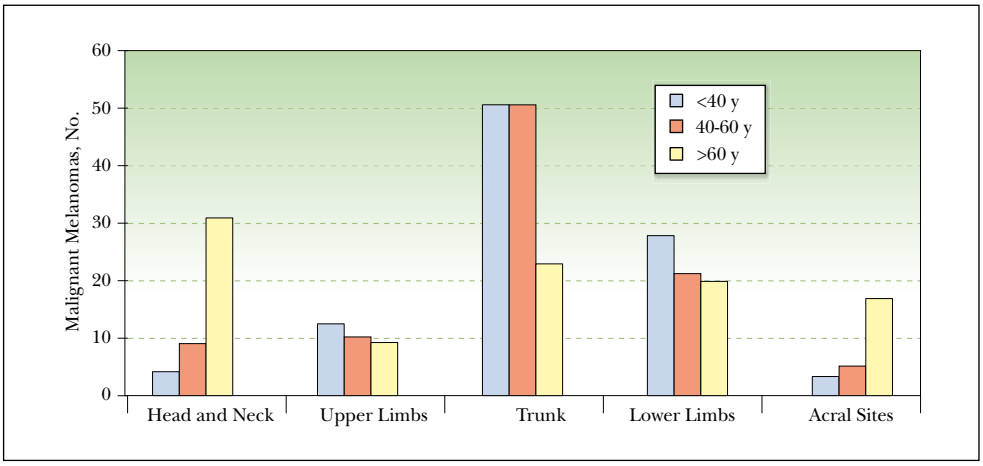

Figure 1. Location of malignant melanomas by age group (percentage of total for each group). Melanomas of the head and acral sites were the most common locations in patients over 60 years (χ^2, simple correspondence analysis).

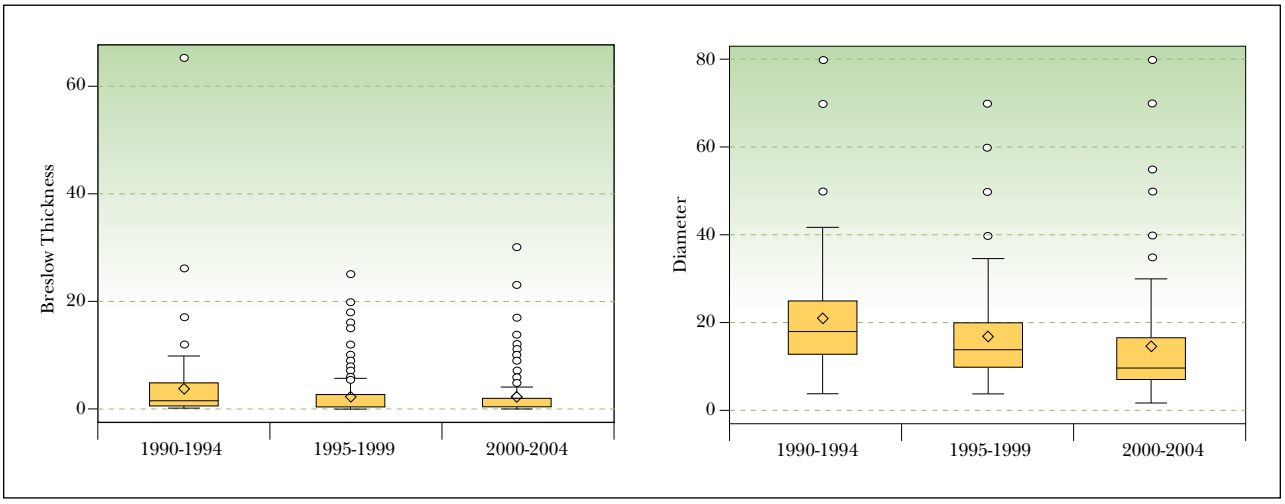

Figure 2. The thickness and size of the melanomas excised gradually decreased over the course of the period studied (15 years). Breslow thickness differed significantly from the first 5-year period to the following two, while size differed significantly between each of the 3 periods (analysis of variance, Duncan test).

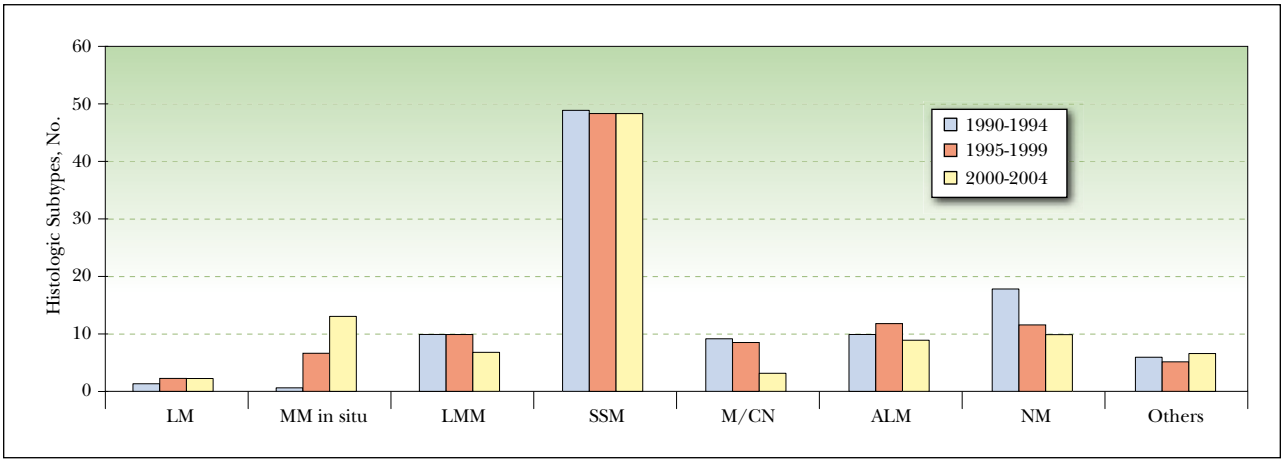

Figure 3. Changes in histologic subtypes of melanoma over time (percentage of total for period). We observed a gradual increase in melanomas in situ and a reduction in nodular melanomas (χ^2, simple correspondence analysis). LM indicates lentigo maligna; MM, malignant melanoma; M/CN, melanoma on congenital nevus; SSM, superficial spreading melanoma; ALM, acral lentiginous melanoma; NM, nodular melanoma; LMM, lentigo maligna melanoma.

Table 4. Characteristics of Melanomas in Successive Periods

	Period 1 (1990-1994)	*Period 2 (1995-1999)*	*Period 3 (2000-2004)*	*Statistical Significance*
Malignant melanomas, No.	124	185	217	
Mean (SD) age, y	57.8 (16.8)	56.5 (18.6)	56.0 (18.9)	NS
Breslow thickness, mm (SD)	3.80[a] (7.21)	2.45[a] (4.03)	2.19[a] (3.79)	*P*<.02
Median thickness, mm (range)	1.6 (0-65)	1.0 (0-25)	0.8 (0-30)	
Breslow thickness				*P*<.03
≤ 1 mm	44 (41.12%)[a]	92 (51.69%)[a]	122 (57.55%)[a]	
1.01-2 mm	16 (14.95%)	35 (19.66%)	38 (17.92%)	
2.01-4 mm	17 (15.89%)	23 (12.92%)	20 (9.43%)	
>4 mm	30 (28.04%)	28 (15.73%)	32 (15.09%)	
Clark level				*P*<.02
I	3 (2.80%)	17 (9.60%)	38 (18.54%)	
II	32 (29.91%)	46 (25.99%)	48 (23.41%)	
III	33 (30.84%)[a]	49 (27.68%)	57 (27.80%)[a]	
IV	30 (28.04%)	50 (28.25%)[a]	46 (22.44%)	
V	9 (8.41%)	15 (8.47%)	16 (7.80%)	
Mean (SD) diameter, mm	21.28[a] (13.09)	16.89[a] (11.72)	13.96[a] (11.21)	*P*<.0001
Median diameter, mm (range)	18 (4-80)	14 (4-70)	10 (2-80)	
Diameter				*P*<.0001
≤ 5 mm	3 (2.80%)	15 (8.15%)	33 (15.64%)	
5.01-10 mm	16 (14.95%)	54 (29.35%)	79 (37.44%)[a]	
10.01-20 mm	52 (48.60%)[a]	73 (39.67%)[a]	66 (31.28%)	
>20 mm	36 (33.64%)	42 (22.83%)	33 (15.64%)	
Location				NS
Head and neck	23 (24%)	34 (19.2%)	28 (13.7%)	
Arms	5 (5.2%)	18 (10.2%)	28 (13.7%)	
Trunk	32 (33.3%)[a]	62 (35%)[a]	93 (45.4%)[a]	
Legs	25 (26%)	42 (23.7%)	38 (18.5%)	
Acral sites	11 (11.5%)	21 (11.9%)	18 (8.8%)	
Histologic type, No. (% of total)				*P*<.0.02
Lentigo maligna	2 (1.61%)	6 (3.24%)	7 (3.23%)	
Melanoma in situ	1 (0.81%)	11 (5.95%)	30 (13.82%)	
Lentigo maligna melanoma	11 (8.87%)	18 (9.73%)	12 (5.53%)	
Superficial spreading melanoma	60 (48.39%)[a]	88 (47.57%)[a]	102 (47%)[a]	
Melanoma on congenital nevus	10 (8.06%)	12 (6.49%)	10 (4.61%)	
Acral lentiginous melanoma	11 (8.87%)	20 (10.81%)	19 (8.76%)	
Nodular melanoma	21 (16.94%)	20 (10.81%)	20 (9.22%)	
Other	8 (6.45%)	10 (5.41%)	17 (7.83%)	

Abbreviation: NS, not significant.
[a] Most common value in each analysis

legs, while men tended to present with advanced tumors located mainly on the trunk. It is generally accepted that these differences in Breslow thickness, which have been previously reported in Spain[13,16] and elsewhere,[18] are attributable to the fact that tumors are diagnosed earlier in women. Our results support this theory as the women in our study also had smaller-sized tumors than men at the time of diagnosis, regardless of histologic type.

On comparing groups by age, the most noteworthy finding was that patients aged over 60 years had the thickest and largest melanomas, an observation that is consistent with other findings from Spain and elsewhere.[12,13,18-20] These patients also had a greater percentage of malignant melanomas other than superficial spreading melanomas and a greater frequency of tumors on the head and neck and acral regions than patients under 60 years. A similar profile of tumor location has been reported in other

Spanish series,[12,13,15] contrasting with a lower number of tumors on the head in other countries.[1] This predilection for the head could be because Spanish patients have a greater proportion of lentigo maligna and lentigo maligna melanoma due to a greater level of chronic sun exposure in certain population groups for geographical and occupational reasons.

Changes Over Time

We found that the number of melanomas diagnosed at Hospital Universitario La Paz in Madrid and its catchment area increased from one 5-year period to the next. Based on data provided by the communications department of the hospital, the number of people in the health district studied increased from 550 242 in 1990 to 787 952 in 2004 (increase of 43%). In the same period, the number of malignant melanomas in our series increased by 75% (from 124 in the first period to 217 in the third).

We are aware that case reviews from individual centres cannot be used to draw conclusions on trends in disease incidence in the general population, basically because non-epidemiological factors can have an enormous influence in these centers. In our case, for example, we did not include malignant melanomas detected and excised from patients treated in our health district but in clinics or hospitals unrelated to Hospital Universitario La Paz, and we also know that more well-off patients might have consulted for malignant melanomas in private centers. Spain, however, does not have a national malignant melanoma registry, meaning that estimates of annual increases in overall incidence can only be made on the basis of data from limited series from just 1 or a few centers. The registry containing the largest number of malignant melanomas was created in 1997 by the Spanish Society for Dermatology and Venereology (AEDV).[21] This registry contains cases from all over Spain and is of unquestionable epidemiologic value but it cannot be used to draw accurate conclusions regarding incidence as it only includes cases that are voluntarily reported by certain dermatologists.

We observed a gradual decrease in both the thickness and size of malignant melanomas in Hospital La Paz and its catchment area. This trend, together with the growing number of cases detected, started to be observed at the end of the 1980s.[22] Similar analyses comparing changes in melanoma incidence in a single center have been conducted in other Spanish hospitals.[13-15,17,23,24] Almost all of these studies detected an increase in the number of melanomas diagnosed, together with, fortunately, a decrease in tumor thickness, level of invasion, and the relative proportion of nodular melanomas.

In our opinion, the fact that malignant melanomas are, generally speaking, being detected at an increasingly early stage has several explanations, including, in particular, a higher level of awareness among the general population, an improved level of training among the physicians involved in diagnosing and treating these tumors, and finally, technological advances. In recent decades, the monitoring of high-risk patients using photography and dermoscopy has become increasingly common in centers around the world hoping to promote an early suspicion of melanoma. Numerous studies have evaluated the usefulness of these 2 techniques and the conclusions reached to date suggest that they are both of value in identifying certain malignant melanomas that would otherwise go unnoticed. While photographs can reveal the unstable nature of new or pre-existing lesions,[25,26] suspect dermoscopic findings can complement clinical atypia.[27,28] The specialized pigmented lesion clinic at our hospital, opened in 1995, uses both methods as part of routine care. In this study, however, we have not analyzed how this clinic might have contributed to the decrease in Breslow thickness and the size of melanomas in each period.

In agreement with findings from other studies,[14,19,20,29,30] we found a reduction in the proportion but not in the number of tumors with a thickness of over 4 mm and of nodular melanomas over the 3 periods analyzed. It appears that a greater number of thinner tumors are being detected thanks to measures implemented to aid earlier diagnosis; this progress, however, has not been seen in terms of a reduction in the number of deep or nodular tumors, which are responsible for the bulk of health care expenditure and the majority of deaths due to melanoma.[31] It might seem as if many of the efforts have been made in vain; however, without them, we might have witnessed an even greater increase in the number of tumors that are thick at the time of diagnosis, leading to even greater expenditure and more deaths.

Breslow thickness is, unfortunately, not always associated with delayed consultation. Certain tumors are particularly aggressive and easily noticed by the patient; these tumors can reach a considerable thickness by the time of excision, even in patients who seek early medical advice. Other tumors, in contrast, detected by chance, may not reach any great thickness even if they go unnoticed and are not removed for some time. Breslow thickness is indeed associated with delayed consultation in uninformed patients but in patients familiar with melanoma, it is associated with tumor aggressiveness.[32,33]

In brief, given the increasing incidence of malignant melanoma and the lack of major advances in the treatment of advanced-stage tumors, primary prevention and early diagnosis are currently the best strategies for reducing melanoma-related deaths. Malignant melanoma is being detected at increasingly early stages thanks to improved

awareness of the disease among the general population, improved access to clinics, and improved diagnostic skills among physicians. Based on our analysis of melanoma incidence by sex and age, it can be deduced that messages about melanoma and the importance of early diagnosis are not effectively reaching men or elderly patients, who still occasionally consult for locally advanced tumors. The fact that the number of malignant melanomas over 4 mm in thickness and nodular melanomas has remained constant suggests the existence of a subset of biologically highly aggressive malignant melanomas that differ epidemiologically from thinner melanomas and whose incidence does not seem to have decreased despite the measures taken so far to establish an early diagnosis.

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Conflicts of Interest
The authors declare no conflicts of interest.

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