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# Primary cutaneous melanoma in hidden sites is associated with thicker tumours — a study of 829 patients

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**Abstract**

The aim of this study was to determine if primary cutaneous melanomas in hidden anatomical sites were associated with thicker tumours. Retrospective medical data of 829 patients with melanomas diagnosed at our centre between January 1976 and July 1998 were recorded from our database. Three groups were defined according to the anatomical site of the primary melanoma: (1) visible areas (group 1: 493 patients); (2) visible areas only to the patients or to their partners in privacy (group 2: 281 patients); and (3) hidden areas (group 3: 55 patients). Univariate analysis indicated that patients with melanoma in hidden regions presented significantly thicker tumours (median for group 3: 2.25 versus 1.17 for group 1 and 1.42 for group 2). This group were also more commonly males (group 3: 58% men versus group 1: 38% and group 2: 51%), in a more advanced stage (metastatic disease at diagnosis in 16% of patients in group 3 versus 6% in groups 1 and 2) and at a more advanced age (median group 3: 66 years versus group 1: 59 years and group 2: 51 years), than patients in the other two groups. The association between tumour thickness and body site remained statistically significant after a multivariate analysis. As a delay in diagnosis may be responsible for the thicker size of melanoma in the hidden areas, preventive programmes should stress the importance of not forgetting these locations in self-examination and screening. Special attention should be given to educating elderly men. © 2001 Elsevier Science Ltd. All rights reserved.

*Keywords:* Melanoma; Breslow thickness; Location; Site; Hidden

## 1. Introduction

The vertical thickness (Breslow thickness) is the most important pathological prognostic feature of a primary cutaneous melanoma [1–5]. Different clinical and histological characteristics have been reported to have some influence on tumour thickness, i.e. acral lentiginous melanoma (ALM) and nodular melanoma (NM), aged patients and men, which partly explains their worse survival [6,7]. Location of a primary tumour has been suggested to be an independent prognostic factor [4]. Less attention has been paid to the relationship between different areas and Breslow thickness. Only one recent study has shown that more occult areas are associated with thicker tumours [8].

Public awareness about melanoma has resulted in an increasing number of patients who are diagnosed at an early stage [6]. Better knowledge about the association of different clinical characteristics with thicker tumours could help to improve public education and screening programmes.

The aim of the present study was to determine if the tumour thickness correlates with a different degree of visibility in a location of primary cutaneous melanoma and to identify the specific clinical characteristics associated with tumours in more hidden areas.

## 2. Patients and methods

This study comprised 829 consecutive patients diagnosed with a cutaneous malignant melanoma at the Department of Dermatology of the Hospital General Universitario, Valencia, between January 1976 and July 1998. All the clinical data on the disease are from the database of cutaneous malignant melanoma of the above mentioned institution. Patients with incomplete records on their primary tumour or those with multiple primary tumours at diagnosis were excluded.

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The variables collected were: gender; age at diagnosis (patients were also classified as $<60$ and $\geqslant 60$ years); anatomical site; staging according to the American Joint Committee on Cancer Staging of Melanoma, TNM; histological type, classified as superficial spreading melanoma (SSM), NM, ALM, lentigo malignant melanoma (LMM) and others; Breslow thickness and Breslow thickness categories, in which cut-offs were in mm: $<0.75$, 0.76–1.50, 1.51–3.0, $>3.0$. The skin's surface was divided into three categories. The first category referred to those body regions visible to the patients during normal activities and included the face and anterior aspect of the neck, the chest and abdomen, the thigh (including medial and lateral aspects), the anterior aspect of the calf and foot (dorsum), arm (ventral), the forearm, and the hand. The second category included those body regions visible to the patients or to their partners in privacy: the posterior aspect of the neck, the back, the pubis, the buttocks, the groin, the posterior aspect of the legs and the penis. The third category was defined as hidden body regions to the patients and to their partners, and the scalp, the buttock fold, the soles and the oral cavity were then considered. Data were analysed using the Statistical Package for the Social Sciences (SPSS) for Windows version 7.5 software (SPSS Inc., IL, USA). Statistical procedures included the Chi-square test and Fisher's exact test for the univariate analysis and multinomial logistic regression for the multivariate analysis (for this purpose, Breslow thickness was reduced to two variables by grouping categories 1 and 2 together as a thin Breslow group, and 3 and 4 together as a thick Breslow group).

The level of significance was set at 0.05.

## 3. Results

The characteristics of the 829 patients are shown in Table 1. Because the number of patients was too low in some groups, stages were gathered into two categories: localised (stages I and II) and metastatic (stages III and IV). There were statistically significant differences

Table 1
Patient characteristics

| | Overall population | Group 1 | Group 2 | Group 3 | Group 2+3 | *P* value* | *P* value 1 versus 2+3 |
|---|---|---|---|---|---|---|---|
| Patients (%)[a] | 829 (100) | 493 (59) | 281 (34) | 55 (7) | 336 (41) | – | – |
| Age (years) | | | | | | | |
| Mean (S.D.) | 55 (17.70) | 57 (17.71) | 50 (17.33) | 62 (14.25) | 53 (17.39) | $<0.001$ | $<0.001$ |
| Median (range) | 57 (14–99) | 59 (15–99) | 51 (14–92) | 66 (32–83) | 53 (14–92) | | |
| Group of age (%)[b] | | | | | | | |
| $<60$ years | 469 (57) | 257 (52) | 190 (68) | 22 (40) | 212 (63) | $<0.001$ | 0.002 |
| $\geqslant 60$ years | 360 (43) | 236 (48) | 91 (32) | 33 (60) | 124 (37) | | |
| Sex | | | | | | | |
| Female | 468 (56) | 308 (62) | 137 (49) | 23 (42) | 160 (48) | $<0.001$ | $<0.001$ |
| Male | 361 (44) | 185 (38) | 144 (51) | 32 (58) | 176 (52) | | |
| Breslow (mm) | | | | | | | |
| Mean (S.D.) | 2.16 (2.47) | 2.02 (2.44) | 2.24 (2.47) | 3.06 (2.56) | 2.37 (2.50) | 0.01 | 0.04 |
| Median (range) | 1.30 (0.02–18) | 1.17 (0.02–18) | 1.42 (0.09–17) | 2.25 (0.06–11.5) | 1.64 (0.06–17) | | |
| Breslow categories (mm) | | | | | | | |
| I: 0–0.75 (%)[b] | 284 (34) | 193 (39) | 84 (30) | 7 (13) | 91 (27) | $<0.001$ | 0.003 |
| II: 0.76–1.50 | 168 (20) | 98 (20) | 62 (22) | 8 (15) | 70 (21) | | |
| III: 1.51–3.0 | 184 (22) | 98 (20) | 68 (24) | 18 (33) | 86 (26) | | |
| IV: $>3.0$ | 193 (23) | 104 (21) | 67 (24) | 22 (40) | 89 (26) | | |
| Histological type | | | | | | | |
| LMM (%)[b] | 130 (16) | 119 (24) | 7 (2) | 4 (7) | 11 (3) | $<0.001$ | $<0.001$ |
| SSM | 499 (60) | 266 (54) | 222 (79) | 11 (20) | 233 (69) | | |
| NM | 136 (16) | 83 (17) | 48 (17) | 5 (9) | 53 (16) | | |
| ALM | 54 (7) | 22 (4) | 0 (0) | 32 (58) | 32 (10) | | |
| Others | 10 (1) | 3 (1) | 4 (1) | 3 (5) | 7 (2) | | |
| Stage (%)[b] | | | | | | | |
| I+II | 774 (93) | 463 (94) | 265 (94) | 46 (84) | 311 (93) | 0.014 | 0.585 |
| III+IV | 55 (7) | 30 (6) | 16 (6) | 9 (16) | 25 (7) | | |

* Comparing the three groups. S.D., standard deviation; LMM, lentigo maligno melanoma; SSM, superficial spreading melanoma; NM, nodular melanoma; ALM, acral lentiginous melanoma.

[a] Percentage of the overall population.

[b] Percentage in the group.

Table 2
Results of the multivariate study

| Variable | B (SEM) | Significance |
|---|---|---|
| Histological type | | <0.0001 |
| LMM | −4.0959 (0.4117) | <0.0001 |
| SSM | −2.9185 (0.3458) | <0.0001 |
| ALM | −2.8687 (0.5150) | <0.0001 |
| Site of tumour | | 0.0079 |
| Group 1 | −1.2495 (0.4164) | 0.0027 |
| Group 2 | −1.0438 (0.4381) | 0.0172 |
| Sex (female) | −0.3925 (0.1678) | 0.0193 |
| Age (<60 years) | −0.6980 (0.1807) | 0.0001 |
| Constant | 4.2576 (0.5485) | <0.0001 |

Multinomial logistic regression study for Breslow thickness (dependent variable) related to all the characteristics (independent variables). Reference categories are: nodular melanoma (NM), Group 3, male gender and patients aged 60 and over. SEM, standard error of the mean; LMM, lentigo maligno melanoma; SSM, superficial spreading melanoma; ALM, acral lentiginous melanoma.

among the three groups relating to age, sex, histological type, Breslow thickness, Breslow categories and stage. *P* values are shown in Table 1. Group 3 tended to have thicker melanomas, presented a higher percentage of ALM and had a high proportion of older men.

In multivariate analysis, after adjustment for gender, age and histological type, the tumour site still remained an independent factor affecting Breslow thickness (Table 2). Histological type, gender and age were also statistically significant independent factors in this analysis. To make our results comparable with the only previous related study that has been reported [8], we gathered groups 2 and 3 into a new group (group 2 + 3), which was then compared with group 1. Characteristics of this new group 2 + 3 and *P* values of differences are also included in Table 1. There were statistically significant differences regarding age, sex, histological type, stage, Breslow category and Breslow thickness.

## 4. Discussion

Our study demonstrates that hidden body regions have a larger Breslow thickness and a higher rate of metastatic disease than visible regions. One previous report in a series of 178 patients also showed that tumours in less visible areas were significantly thicker at the time of diagnosis than those occurring in more visible areas [8]. However, the design of this study differs from ours because they considered only two location types — hidden areas and exposed areas — and their study was focused exclusively on the tumour thickness and its relationship with the different location types. Our group 2 + 3, which combined group 2 and 3, was comparable with their group of hidden areas. We also found that this new group presented a statistically significant greater thickness (in univariate analyses) than group 1, but this difference was most strongly associated with group 3 patients because they tended to have thicker tumours (median: 2.25 versus 1.17 in group 1 and 1.42 in group 2). These results could mean that the more hidden the location is, the thicker the tumour is, and it might be due to a delay in the diagnosis because melanomas in more hidden locations could more easily go unnoticed. However, the design of this study does not allow us to discern if the greater thickness is due to a particular different biological behaviour associated with these locations or to a delay in the diagnosis. Future screening programmes will probably show if there are different thickness as related to locations. Histological type could be a confounding factor because Breslow thicknesses has been demonstrated to be larger in NM and, to a lesser extent, in ALM [5]. The greater thickness showed in the group 3 could be explained by the high proportion of ALM (mainly because the plantar region was included in this group), but the multivariate analysis showed that the anatomical site had an independent statistically significant influence on the tumour thickness.

Patients that constituted the hidden site group represented 7% of the overall population of melanoma patients and were mainly elderly men. Although some controversy still remains concerning age and gender as prognostic factors [4,9], men seem to have a worse prognosis than women [9]. Increasing age is inversely related to survival and is considered an independent prognostic variable [10]. Therefore, patients with melanoma located in hidden areas in our series have two clinical characteristics, age and gender, which could worsen their prognosis.

The rising melanoma mortality rates underscore the need for early detection [11]. Several skin cancer educational programmes have enabled the detection of more melanoma cases at an early stage and with a thin thickness [11–14]. In theory, the early detection should increase melanoma cure rates (long-term survival figures of 92% for localised melanoma decline sharply to lower than 5% for metastatic disease [15]), although its efficacy, in survival terms, needs definitively to be confirmed. Nevertheless, screening and public education programmes are currently considered two important ways of fighting against melanoma. Thanks to these programmes, many people are aware of sun danger and avoid intense sun exposure and burns. However, many melanomas arise in sun-protected areas [16]. Our results are a useful reminder that all those programmes should stress the importance of not forgetting the more hidden body regions, with special attention being given to educating elderly men.

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