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Low educational attainment is still associated with late melanoma diagnosis: A cross-sectional study from a European setting with universal healthcare

Mercè Grau-Pérez[a,b,*], Camila Cabello[b], Jesús-María González-Martín[c], Leopoldo Borrego[a], Gregorio Carretero[b]

[a] Universidad de Las Palmas de Gran Canaria, Calle Juan de Quesada 30, 35001 Las Palmas de Gran Canaria, Spain
[b] Dermatology Department, Hospital Universitario de Gran Canaria Doctor Negrín, Barranco de la Ballena s/n, 35010 Las Palmas de Gran Canaria, Spain
[c] Research Unit, Hospital Universitario de Gran Canaria Doctor Negrín, Barranco de la Ballena s/n, 35010 Las Palmas de Gran Canaria, Spain

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ABSTRACT

Background: An early diagnosis of cutaneous melanoma remains determinant for improved survival. Low educational attainment has been associated with a late-stage diagnosis in settings where access to healthcare is restricted. Little evidence is available from regions with universal healthcare. We aimed at analysing whether educational attainment was associated with Breslow thickness at diagnosis in a peripheral European region with universal healthcare (in the Canary Islands, Spain).

Methods: We conducted a cross-sectional study with prospectively collected data (2010–2017). Patients were recruited at diagnosis, and information about Breslow thickness, age at diagnosis, gender, highest educational attainment and site of melanoma were registered. Univariate and multivariate linear regression analyses were performed.

Results: Low educational attainment was associated with thicker tumours at diagnosis. The association remained true after adjustment for age, gender and site of melanoma. In the multivariate analysis, tumours diagnosed in patients with low educational attainment were on average 1.08 mm thicker (95% confidence interval: 0.36–1.81; $p = 0.003$) than those diagnosed in patients with high educational attainment.

Conclusion: Public health strategies targeting this vulnerable group are currently needed in the Canary Islands (Spain).

1. Introduction

Despite the galloping progresses in the treatment of advanced melanoma, the prognosis of late-stage disease remains poor [1]. An early diagnosis keeps on being the most important determinant for survival. This emphasizes the need for a continuous research on determinants of late-stage diagnosis, that might change over time and across boundaries.

A systematic review of socioeconomic and lifestyle factors in melanoma established that patients of lower socioeconomic status (SES) are diagnosed with greater tumour thickness [2]. Nevertheless, most of the studies holding this evidence were conducted in the United States (U.S.) and in northern Europe, where high SES populations might be more likely to have access to a dermatologist and therefore might benefit from an earlier diagnosis [2]. Particularly in the U.S., differences in survival were found depending on the type of health insurance that patients had [3], or on the neighborhood they resided in [4,5], underlying the issue of differences in access to healthcare. Many studies assessing SES used educational attainment as the measurement tool [2].

Our country has a free public universal health coverage warranted to every resident regardless of their income, and the health area is assigned based on residence address. Our region (Canary Islands) is an archipelago with the status of outermost region of the European Union. It is located in the Atlantic Ocean and has many particularities that differentiate it from the mainland of Spain and from other European countries. It has a high ultraviolet exposure through the whole year and a low general educational attainment [6]. A better understanding of whether educational attainment has an important effect on stage of melanoma at diagnosis in our region could lead to a modification of public health strategies in the region and potentially decrease morbidity and mortality from melanoma [7].

Our objective was to evaluate whether in our setting the educational

* Corresponding author at: Dermatology Department, Hospital Universitario de Gran Canaria Doctor Negrín, Barranco de la Ballena s/n, 35010 Las Palmas de Gran Canaria, Spain.
E-mail address: merce.grau101@alu.ulpgc.es (M. Grau-Pérez).

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attainment had an impact on stage at diagnosis of cutaneous melanoma.

The study was conducted in the Melanoma Unit of a hospital of the Spanish public healthcare system located in the island of Gran Canaria.

2. Methods

2.1. Study population and data collection

From 2010, all patients evaluated in the Melanoma Unit of the Hospital Universitario de Gran Canaria Doctor Negrín were included in a prospective observational cohort. The hospital covers the north half of the island population (approx. 386 000 health cards). Once the diagnosis was confirmed, the patient automatically entered the protocol, and upon the first follow-up visit the patient was asked by the dermatologist about past medical and family history as well as sociodemographic data including the highest educational level attained. Histological data were included in the patient record. For the present study, we analyzed the clinical records of the patients diagnosed with invasive cutaneous melanoma evaluated in the Melanoma Unit of our center from January 2010 to June 2017. Data collected included gender, date of birth, date of diagnosis, Breslow thickness, body location, and educational attainment (highest educational level completed). This was classified as low (primary school, i.e. maximum period completed at 16 years of age, and $\leq$9 years of education), intermediate (when the patient had completed upper secondary education or high school, i.e. until 18 years of age, corresponding to 10–12 years of education) and high (the patient had attended college/university, i.e. $\geq$ 12 years of education). Site of melanoma was categorized into "head and neck", "limbs", "trunk (posterior)", "trunk (anterior)" acral (hand or feet) and "other". Patients with melanoma in situ, non-cutaneous and metastatic melanomas of unknown primary were excluded for comparative purposes. Patients with metastatic melanomas of known primaries were included and presented separately from non-metastatic melanomas. The decision to present the subgroup of patients with distant metastases separately was taken because of three reasons. First, in this minoritarian subgroup (and in opposition to non-metastatic melanoma) the presence of distant metastases has a considerable higher impact on survival than Breslow thickness. Second, in the presence of distant metastases, complete excision of the lesion allowing for accuracy of Breslow measurement is sometimes unfeasible, and it was expected that some values would be missing. Third, in case there were no missing data in this subgroup and patients were included in the main analyses, they could skew the results favoring an overestimation of the effect of low educational level. They were therefore excluded from the main analysis. The study was approved by the local ethics committee (Code GCH-MEL-2016-01).

2.2. Statistical analyses

Breslow thickness was considered a continuous variable and was measured in millimetres. The Shapiro-Wilk test was used to assess whether quantitative variables (Breslow thickness and age) followed a normal distribution and Kruskal-Wallis test to compare quantitative with qualitative variables. Because neither Breslow thickness nor age followed a normal distribution, the median and interquartile range (IQR) were used to describe quantitative variables. For qualitative variables (sex, educational attainment, type and site of melanoma), frequency and percentage were used. Simple linear regression was used for univariate analyses and multiple linear regression for multivariate ones (with Breslow thickness as outcome variable and age, gender, educational level and site of melanoma as explanatory variables). Educational attainment was our main exposure and we decided to include the variables age, gender and site of melanoma a priori in the multivariate model as according to previous literature they could be confounders of the association between educational attainment and Breslow thickness. Following conventions, an association was interpreted as being statistically significant if the probability of it being explained by chance was less than 1 in 20 ($p < 0.05$). Regression coefficients were also obtained with bootstrapping and genetic algorithms in order to assess the robustness of the multivariate model (Supplementary material, Table 4). Statistical analyses were performed with R Core Team 2018.

3. Results

235 patients were diagnosed with invasive cutaneous melanoma in the study period. Twelve patients lacked information about educational level and were excluded. Of those 12 patients with missing data, half were diagnosed with Breslow < 1 mm and half with deeper lesions, with three extreme values (8, 10 and 25 mm respectively). The overall median was 1.18 (IQR: 0.46–7.21). Three patients presented with metastatic melanoma of known primary. One of them lacked information about Breslow thickness and belonged to the intermediate educational attainment subgroup, while the other two presented with 1.5 mm and 55 mm of Breslow respectively, and were in the low educational attainment subgroup. The three were excluded from the overall analyses. The information about educational level in non-metastatic, cutaneous invasive melanoma was present in 220 patients (final sample). The demographic and histological characteristics of study participants are presented in Table 1. The median of Breslow thickness was 0.8 mm (IQR: 0.45-1.50) and the median age was 59 years (IQR: 45.75-70).

Patients with low educational level presented with thicker melanomas compared to patients with intermediate and high level in the univariate analysis, with a median of 1.02 mm (IQR: 0.5-3.12), 0.85 mm (IQR: 0.43-1.25) and 0.6 mm (IQR: 0.35-0.95) respectively ($p = 0.001$). No relevant differences in tumor thickness were found when comparing patients with high versus intermediate level. When stratifying by gender, the evidence of an association was stronger in men than in women (Kruskal-Wallis test $p = 0.002$ for men and $p = 0.10$ in women, respectively- Supplementary Table 3). The distribution of Breslow thickness per educational attainment category, stratified by gender is presented in Fig. 1.

In the multivariate analysis, we found strong evidence of an association between educational attainment category and Breslow thickness (Table 2). Considering the same gender, age and site of melanoma in a patient, the intermediate level of education accounted for 0.83 mm less of Breslow than low educational attainment (95% Confidence Interval

Table 1
Demographic, clinical and histological characteristics of cutaneous melanoma patients **(n = 220)**.

Breslow thickness*	0.8 (0.45–1.50)
Age*	59 (45.75–70.0)
Sex: Female	118 (53.64)
Education	
Low	92 (41.82)
Intermediate	67 (30.45)
High	61 (27.73)
Site	
Acral	16 (7,27)
Head & Neck	25 (11.36)
Limbs	74 (33.64)
Trunk (Posterior)	80 (36.36)
Trunk (Anterior)	25 (11.36)
Histological subtype (n = 200)	
SSM (Superficial Spreading Melanoma)	146 (73)
LMM (Lentigo Maligna Melanoma)	17 (8.5)
NM (Nodular Melanoma)	11 (5.5)
ALM (Acral Lentiginous Melanoma)	12 (6)
Unspecified and other	14 (7)

* Quantitative variables are presented as median (Interquartile range). Qualitative variables are presented as frequencies (%).

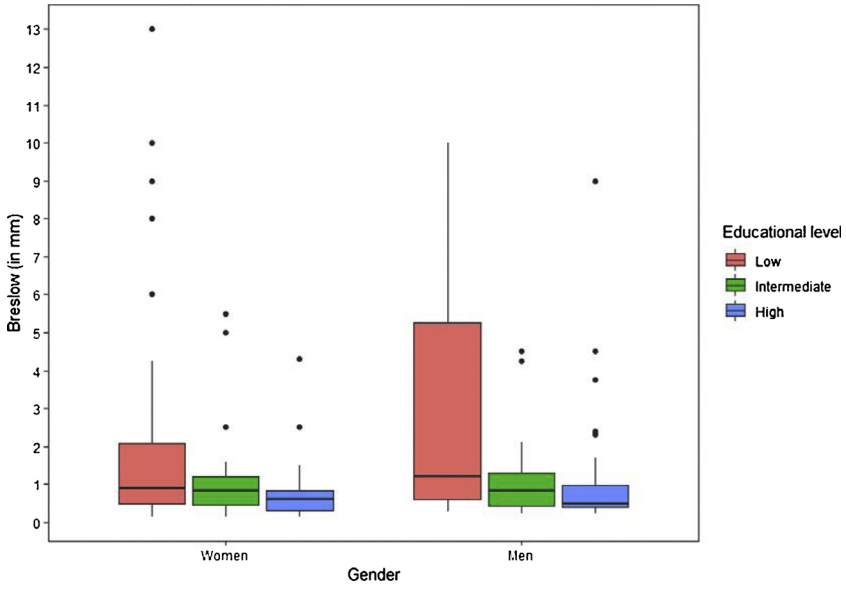

Fig. 1. Breslow thickness (median, IQR) stratified by education and gender.

Table 2
Univariate and Multivariate models, including age at presentation, gender, educational attainment and site of melanoma.

Variables	Univariate Model				Multivariate Model (Minimum Square)			
	Coef. b*	se	Confidence Interval (95%)	p-value	Coef. b*	se	Confidence Interval (95%)	p-value
Intercept					0.53	0.64	-0.74 – 1.79	0.41
Age	0.04	0.01	0.02 – 0.06	0.0001	0.02	0.01	0.00 – 0.04	0.03
Sex: Men	0.18	0.29	-0.38 – 0.75	0.52	0.56	0.29	-0.02 – 1.14	0.06
Education:								
Low	Ref				Ref			
Intermediate	-1.06	0.32	-1.70 - -0.42	0.001	-0.83	0.34	-1.51 - -0.15	0.02
High	-1.22	0.33	-1.87 - -0.56	0.0003	-1.08	0.37	-1.81 - -0.36	0.003
Site:								
Post Trunk	Ref				Ref			
Acral	1.92	0.57	0.80 – 3.03	0.001	1.82	0.55	0.74 – 2.91	0.001
Head & Neck	0.57	0.47	-0.37 – 1.50	0.23	0.21	0.46	-0.67 – 1.11	0.64
Limbs	0.33	0.33	-0.32 – 0.99	0.32	0.33	0.33	-0.32 – 0.99	0.31
Ant. trunk	-0.43	0.47	-1.34 – 0.5	0.36	-0.71	0.46	-1.61 – 0.19	0.12

*Coef. b= regression coefficient. se=Standard error.

CI: -1.51 – -0.15; p = 0.02), and a high level accounted for 1.08 mm less of Breslow at diagnosis (95% CI: -1.81 – -0.36; p = 0.003). Men presented with thicker tumours than women. For the same age, site of melanoma and educational attainment, men presented with 0.56 mm more of Breslow (95% CI: -0.02 – 1.14, p = 0.06, Table 2). Acral melanomas represented only 7.3% but were associated with a higher Breslow (1.82 mm more of Breslow than lesions on the posterior trunk, 95% CI: 0.74 – 2.91; p = 0.001).

4. Discussion

This study shows an association between educational attainment and melanoma thickness at diagnosis in our population and increases the available evidence of the relationship between melanoma thickness at diagnosis and educational level, in a new setting.

Our patients have a single way of access to the dermatologist, and this invariably takes place through the General Practitioner (GP), no matter the socioeconomic status. GPs are assigned upon geographic criteria and the possibility of upfront payment to accelerate consultation does not exist in our public system, where this study was based. Moreover, people from lower educational attainment in Spain have been found to attend more often the GP than people from higher attainment [8]. Despite this fact, patients of the lowest educational level were referred with significantly thicker melanomas. As other authors have suggested [9–11], the lack of awareness of the necessity of an early diagnosis might be the main reason behind this later diagnosis and would also explain a tendency to present at a more advanced age, when the neoplasia is more evident. Our results also underscore a failure of the public health campaigns in this vulnerable group.

Interestingly, the weight of the low educational level category in the distribution of patients diagnosed with melanoma was overall similar to that described in other populations with better human development index, like Sweden [12,13]. Eriksson et al obtained a proportion of 35,8% in the low educational level category vs 41,3% in our center. A study conducted in a public institution in Brazil [14] encountered a much higher proportion of patients in the low educational level subgroup (58,1%). Nevertheless, independently of the economics of the countries, in all three settings low educational level was associated with a higher Breslow.

Breslow thickness has been established as the single most important prognostic factor in the field of melanoma. Because the AJCC staging has changed twice in the last 10 years making comparisons based on stage of disease difficult, we focused on Breslow thickness as the measurement tool to assess disease burden at diagnosis. Still, we faced difficulties when willing to compare our results straightforward with other studies due to different categorizations of Breslow index into thin

and thick from other authors. Very few provided relative median or mean of each category. Youl et al, in a study conducted in Australia [15], dichotomized tumor thickness into thin and thick with a cutoff of 2 mm. Other cutoffs were used by other authors [16]. We categorized Breslow thickness into thin and thick with the cutoff of 2 mm to compare our results with the aforementioned study. We encountered almost the double proportion of thick melanomas in our population (10.8% vs 19.1%), with no differences in the categories of educational level compared to the distribution found by the Australian group. We hypothesize that the intensive melanoma prevention and early detection campaigns in Australia have been more effective than those driven in our region, maybe explaining those differences, at least partially.

The main limitation of our study is to have a limited sample and to have been conducted in a single center, thus potentially limiting its generalizability. Nevertheless, the main strengths are a prospective collection of data and an individual-based study cohort. The fact that access to healthcare is free in our country might limit its external validity, but it provides additional and updated evidence of the need to reinforce public health campaigns oriented to populations with low-educational attainment in any setting. It adds to the available international evidence that education has a high impact in the prognosis of melanoma, mainly linked to a late diagnosis. It also underscores the need in our region to modify and strengthen public health interventions in areas with low average educational attainment in order to achieve earlier diagnoses in this vulnerable subgroup. By making GPs in the region aware of these findings, earlier diagnoses could also probably be achieved in primary care at the individual-level. We are hoping that our findings will lead to effective changes in these directions to improve the morbidity and mortality from cutaneous melanoma in the region.

5. Conclusions

Patients with low educational attainment presented with the thickest tumors. Access to healthcare does not explain those differences in our population. This adds to the available evidence from other settings, that low educational attainment is importantly associated with a late diagnosis in melanoma. Furthermore, it underlines the unmet need to develop efficient public health strategies focusing on this more vulnerable population group.

Author contributions

MGP participated in the conceptualization of the study and was responsible for data interpretation and for the elaboration of the manuscript.

CCZ provided help with data interpretation and the revision of the manuscript.

JMGM was responsible for data analysis and provided help with data interpretation.

LB provided help with the design of the manuscript and with critical revision.

GC was responsible for the conceptualization of the study, data collection and supervision.

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Declaration of Competing Interest

We declare we do not have any conflict of interest with the present study.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2019.101576.

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