Socioeconomic status as a predictor of melanoma survival in a series of 1083 cases from Brazil: just a marker of health services accessibility?

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Melanoma survival is determined by disease-related and patient-related factors; there is a growing body of evidence that other issues may play a role in this disease. In this study, the role of socioeconomic factors in the evolution of melanoma was evaluated. This was a retrospective study with incident cases of melanoma treated in an oncology center in Rio de Janeiro, Brazil, during the period of 1997-2004. The socioeconomic variable of choice was education (9 years or more vs. 8 years or less of school attendance). In this period, there were 1083 patients with primary melanoma of the skin, 58.1% with low school attendance. No difference was found in relation to the year of diagnosis with respect to overall survival. Five-year survival for the entire group was 67.0%. Men had worse survival [hazard ratio (HR) 1.91, 95% confidence interval (CI) 1.54-2.35]; a protective effect was found for whites (HR 0.64, 95% CI 0.49-0.84), higher educational level (HR 0.55, 95% CI 0.44-0.69), and upper limb lesions (HR 0.61, 95% CI 0.38-0.98). A higher risk of death was observed for patients with nodular melanoma (HR 1.96, 95% CI 1.49-2.58), acrolentiginous melanoma (HR 2.68, 95% CI 2.09-3.44), lesions in the soles and palms (HR 1.78, 95% CI

Introduction

Melanoma, the most lethal primary skin cancer, is responsible for more than 85% of the deaths attributable to cutaneous neoplasms [1]. The incidence of melanoma has increased during the last few decades, largely because of an increase in the diagnosis of thin lesions and stability in the diagnosis of thick lesions; melanoma mortality increased up to the 1990s and now it appears to have arrived at a plateau [2].

Prognostic factors for melanoma have been described, related to stage of the disease, age, and sex. In lesions restricted to the skin, the thickness of the lesion, presence of ulceration, or mitoses are the most important factors and in patients with regional spread of disease, the extension of lymph node involvement, and in metastatic disease, the involvement of viscera, and the levels of lactate dehydrogenase are the most important factors.

It has long been known that socioeconomic factors may have an impact on the incidence and survival of many malignant diseases. Poor socioeconomic status (SES) has shown an inverse association with the incidence of melanoma, probably because of more frequent recrea1.22–2.6), and increasing age (HR 1.02 for each year, 95% CI 1.01–1.02). In the multivariate analysis, after controlling for stage, age, sex, ethnicity, and clinical type, education remained a protective factor both for overall survival (HR 0.76, 95% CI 0.61–0.94) and for relapse-free survival (HR 0.76, 95% CI 0.61–0.94). In conclusion, socioeconomic status as measured by educational level represented an important factor related to melanoma clinical evolution in the cohort studied. *Melanoma Res* 23:199–205 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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tional sun exposure in more affluent groups [3-5]. However, there is some evidence that poor SES may have an adverse effect on the development of chronic diseases, including cancer [6], and on cancer survival including melanoma. Some ecological and populationbased case-control studies have found an association between lower SES and higher melanoma mortality [7–9]. This evidence comes from developed countries, with well-placed health systems and population with a higher educational background than observed in developing countries. Most of the studies deal with aggregate information of mortality and SES, as well as with many different measures of SES, such as characteristics of the neighborhood, income, occupation, housing tenure, and educational level (EL). One hospital-based study with patients with localized disease showed improved survival for patients with higher SES [10]. It seems that education is a good marker of SES in melanoma [11], as well as in other diseases [12]. It is possible that such variables have distinct behaviors in populations with lower socioeconomic indexes as a whole, lower prevalence of the disease, higher exposure to environmental ultraviolet irradiation exposure, and higher proportion of nonwhites.

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This study aimed to ascertain the survival of melanoma patients in a developing country and to evaluate the role of SES in time-dependent events.

Materials and methods Study population

A retrospective case series of patients with a diagnosis of melanoma between January 1997 and December 2004, treated at a reference oncology center in Rio de Janeiro, Brazil, was ascertained. This is a public institution where anyone can be cared for by the coverage of the SUS (National Health System). The treatment follows prespecified guidelines according to the Brazilian group of melanoma. Most of the patients referred to this center come from the town of Rio de Janeiro and its metropolitan region.

In this institution, all patients are required to either have the biopsy placed in the hospital or to bring histological material (slides and paraffin blocks) to be reviewed. In this way, cases were identified through the Pathology Database with the diagnosis of primary cutaneous malignant melanoma (ICD 10-C43, ICD-O 8720/3 to 8772/3, except 8728/3). Patients with melanoma in the mucosa, eye, or an unknown primary site were excluded. Information on demographic characteristics, characteristics of the lesion, therapeutic approach, and follow-up was collected from the patients' files. In this center, information on patient's EL, as measured by the highest degree attained, was requested in the initial evaluation of the patient, and was used as an SES surrogate. In Brazil, formal education is divided into three main courses: fundamental level (8 years), followed by secondary level (3 years) and superior level (4-6 years). Patients were initially categorized as illiterate, fundamental level, secondary level, and superior level; on further analysis, this variable was treated as a dichotomous variable, the categories illiterate and fundamental (comprising 8 years or less of school attendance) corresponding to low EL and the categories secondary and superior (9 years or more of school attendance) corresponding to high EL.

Every effort was made to localize patients.

For half of the patients, the initial diagnosis had been made at the oncology center, and for the remaining, the initial diagnosis was made at other health services. For follow-up purposes of this study, the date of patient inclusion in the Pathology Service registries at the Cancer Hospital was stated as the date of diagnosis.

According to the local Ethics Committee, an informed consent form was sent by mail to all patients thought to be alive. As only 27% of the informed consent forms were returned, and there were no refusals, the Ethics Committee allowed the inclusion of all cases in the study, with no further attempt to find the missing individuals.

Data analysis

Overall survival was ascertained considering the time elapsed between the registry in the Pathology Department and death of any cause; relapse-free survival was determined considering the interval between the registry in the Pathology Department and the first evidence of relapse, local, regional or systemic, or death. Patients without any reported event were censored at the last visit or contact. It is a policy of the hospital to maintain regular follow-up of up to 5 years after the treatment. For patients with missing data, their vital status was ascertained through the Death Registry Databank of the Rio de Janeiro State.

The year of enrollment in the cohort was analyzed as a discrete variable.

Descriptive analysis was carried out, t-tests were used for evaluating continuous variables, and χ^2 -tests were used for comparisons between proportions. Time to event curves were estimated by the Kaplan-Meier method, and the curves were compared by the log rank test. The median follow-up was calculated using the Kaplan-Meier method. Multiple regression analysis was further carried out using the proportional hazards method of Cox. The variables with *P*-values less than 0.2 were analyzed in the model for both overall and disease-free interval. The variables that were evaluated in the multiple regression model were EL, sex, age (in years), skin color, clinicalpathological type, topography of the lesion, place of diagnosis, and year of diagnosis. The choice of the model was guided by the analysis of deviance, and the evaluation of model adjustment; adequacy of the model was verified by analysis of Schoenfeld, Martingale, deviance, and score residues. Initially, staging was evaluated as a confounding variable, but on analyzing the residues, it was clear that this variable violated the proportionality of the model; a stratified analysis was carried out by staging. Statistical significance was set as P < 0.05. All of the analyses were carried out using the free software R 2.14.1 (http://www. r-project.org/).

Results

Between 1997 and 2004, 1191 patients were diagnosed with melanoma in the hospital, of whom 1131 had primary cutaneous lesions. The following exclusions were applied: 15 individuals had no follow-up information, 15 individuals were younger than 18 years of age, and 18 individuals had no information on school attainment, leaving 1083 individuals for analysis in this cohort (Table 1). Eleven patients had no information about relapse and were excluded from the relapse-free survival analysis. During this period, there was an increase in the number of cases that were diagnosed each year, with an annual increment of 8.5%. No changes in the distribution of demographical or clinical variables were found in the study population in this period. Most of these individuals

Table 1 Sociodemographic and clinical characteristics of melanoma patients diagnosed in 1997–2004, reference oncological center, Rio de Janeiro, Brazil

 Table 2
 Socio-demographic and clinical characteristics

 of melanoma patients diagnosed in 1997–2004 according

 to education, reference oncological center, Rio de Janeiro, Brazil

Variables	N (%)	
Median age (mean)	58 (56.7) years	
Sex M:F	524 (48.4)/559 (51.6)	
Ethnicity		
White	944 (87.2)	
Non-white	135 (12.5)	
Unknown	4 (0.4)	
Educational level		
Illiterate	96 (8.9)	
Fundamental (up to 8 years)	533 (49.2)	
Secondary (9-12 years)	266 (24.6)	
Superior (more than 12 years)	188 (17.4)	
Topography of the lesion	. ,	
Head and neck	125 (11.5)	
Trunk	368 (34.0)	
Upper limbs	148 (13.7)	
Lower limbs	224 (20.7)	
Nail bed	48 (4.4)	
Palms and soles	170 (15.7)	
Clinical-pathological type		
Superficial spreading melanoma	594 (54.8)	
Nodular melanoma	205 (18.9)	
Lentigo maligna melanoma	26 (2.4)	
Acral lentiginous melanoma	220 (20.3)	
Nonclassified	38 (3.5)	
Staging TNM (clinical)		
	481 (44.4)	
	361 (33.3)	
	161 (14.9)	
IV	42 (3.9)	
I and II non specified	38 (3.5)	
Breslow index (median) ^a	2.00 mm	
Ulceration (presence of) ^b	371 (53.1)	
Place of diagnosis		
Cancer Hospital	547 (50.5)	
Public Hospital	131 (12.1)	
Private facility	222 (20.5)	
Undefined	182 (16.9)	

TNM, tumor-node-metastases.

^aInformation available for 970 (89.6%) patients.

^bInformation available for 695 (64.2%) patients.

lived in Rio de Janeiro (51.4%) or in another metropolitan region (28.5%); most of the remaining lived in other areas of the State of Rio de Janeiro. In 2009, the Ministry of Health estimated 400 new cases of melanoma in the State of Rio de Janeiro [13]; it is possible that this cohort of patients represents 30–50% of all cases of melanoma diagnosed in this State.

Information about education was available from 1083 patients, of whom 629 (58%) had 8 years or less of education and 454 (42%) patients had 9 years or more of education. EL was associated with age, sex, ethnicity, stage of disease on diagnosis, type and topography of the lesion: patients with higher EL were younger, with a higher proportion of men and whites, and most presented with initial disease (stage I, median Breslow index 1.5 mm, minority of cases with ulceration), had a larger proportion of superficial spreading melanoma (SSM) and lesions in the trunk, whereas individuals with lower EL were older, included a larger proportion of women and non-whites, presented with more advanced lesions (stages II–IV, median Breslow index 3.0 mm, more cases

	Education		
	\leq 8 years	\ge 9 years	<i>P</i> -value
Sex (%)			
Male	52.7	47.3	< 0.001
Female	63.1	36.9	-
Age			
Mean	60.1	50.8	< 0.001
Median	63.0	50.0	-
Ethnicity (%)			
White	55.1	44.9	< 0.001
Non-white	77.8	22.2	-
Staging			
Stage I	48.0	52.0	< 0.001
Stage II	60.0	40.0	_
Stage III	75.2	26.2	_
Stage IV	73.8	26.2	_
Type	70.0	2012	
Superficial spreading	49.3	50.7	<i>P</i> <0.001
Nodular	60.0	40.0	-
Lentigo maligna	65.4	34.6	_
Acrolentiginous	81.4	18.6	_
Topography	01.4	10.0	
Head and neck	64.8	35.2	< 0.001
Trunk	48.1	51.9	<0.001
Upper limbs	49.3	50.7	
Lower limbs	49.3 53.6	46.4	
Nail beds	72.9	27.1	-
	72.9 84.1	15.9	-
Soles and palms Breslow index ^a	84.1	15.9	-
Mean	5.74	0.00	< 0.001
		2.66	< 0.001
Median Ulceration ^b	3.0	1.5	-
		00.0	<0.001
Yes	71.1	28.9	<0.001
No	48.6	51.4	-
Systemic therapy			
Yes	57.5	42.5	0.1212
No	63.0	37.0	-
Sentinel lymph node biop			
Yes	56.3	43.7	0.1235
No	53.5	46.5	-

^a10.4% of the patients had missing information on the Breslow index.

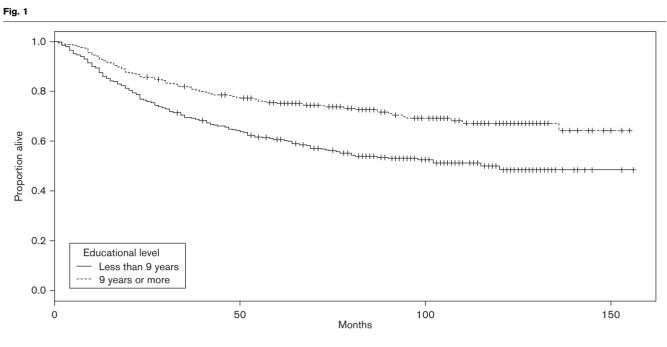
^b35.8% of the patients had missing information on ulceration.

^cFor stages I and II.

with ulceration), had more nodular melanoma (NM), lentigo maligna melanoma and acrolentiginous melanoma (ALM), and lesions at the head and neck, lower limbs, soles and palms, and nail beds (Table 2). No statistically significant differences were observed in EL among patients who underwent sentinel lymph node biopsy (P = 0.1235) or systemic therapy (P = 0.1212).

Patients were recruited into this study over a period of 8 years. As this is a long time period, it is possible that the clinical characteristics, standards of care or other nonmeasured factors pertaining to the patients could have changed. No association was found between year of diagnosis and overall survival, but there was an association with relapse-free survival.

The median follow-up was 74 months; median survival was not attained. 1-year survival was 89.9% and 5-year survival was 67.0%. Five-year overall survival was 90.2% for stage I, 58.0% for stage II, 29.1% for stage III, and



Overall survival of melanoma cases diagnosed in 1997–2004 according to the education level, reference oncology center, Rio de Janeiro, Brazil. Log rank $\chi^2 = 28$, 1 d.f., *P*<0.001. Dashed line represents a higher educational level and continuous line represents a lower educational level.

9.5% for stage IV. Seventy-nine patients were sentinel lymph node biopsy positive; the 5-year survival was 46.1% for those with microscopic stage III.

In the univariate analyses of overall survival, men had a worse survival [hazard ratio (HR) = 1.91, 95% confidence interval (CI) 1.54–2.35], a protective effect was found for whites (HR = 0.64, 95% CI 0.49-0.84) and in patients with higher EL (HR = 0.55, 95% CI 0.44–0.69) (Fig. 1). Survival differed according to clinical-pathological type, being SSM reference (5-year survival 77.3%), NM had 5-year survival 61.3% (HR = 1.96, 95% CI 1.49-2.58), and ALM had 5-year survival 47.7% (HR = 2.68, 95% CI 2.09–3.44); topography of the lesion, being head and neck lesions reference (5-year survival 69.0%), patients with upper limbs lesions had 5-year survival 80.8% (HR = 0.61, 95% CI 0.38-0.98) and palms and soles lesions 47.7% (HR = 1.78, 95% CI 1.22–2.60); and age (HR = 1.02, 95% CI 1.01-1.02) (Table 3). There was no difference in overall survival according to the year of diagnosis.

Overall survival was higher among the most educated: the 5-year overall survival was 76.5% for those with more than 12 years of education, 74.5% for those with 9–11 years of education, 62.4% for those with 8 years or less of education, and 50.8% for the illiterate. In multivariate analysis, illiterate individuals had survival and relapse-free survival very similar to those of individuals with 8 years or less of education (fundamental school attainment), and individuals with 9–11 years of education

(high school level) and 12 years or more of education (college level) had similar estimates.

In patients with localized disease (stages I and II), no statistically significant differences were found in overall survival according to sentinel lymph biopsy (HR = 0.96, 95% CI 0.81–1.15), but the positivity of the lymph nodes had a negative impact on this outcome (HR = 3.73, 95% CI 2.44–5.69).

For non-white patients, individuals with higher EL had improved survival (HR = 0.41, 95% CI 0.19–0.86), with a 5-year survival of 70.8% for higher EL and 47.7% for lower EL.

Information for relapse was available for 1072 patients. One-year relapse-free survival was 77.2% and 5-year free survival was 56.5%. In the univariate analyses, men (HR = 1.68, 95% CI 1.40–2.02) and non-whites (HR = 1.56, 95% CI 1.23–1.99) had a worse relapse-free survival; a protective effect was found for those with higher EL (HR = 0.56, 95% CI 0.46–0.68). For clinical-pathological type, with SSM the reference category, worse prognosis was observed for NM (HR = 2.21, 95% CI 1.74–2.80) and ALM (HR = 2.81, 95% CI 2.52–3.51). According to topography of the primary lesion, with head and neck lesions the reference, plantar and palmar lesions had a poorer outcome (HR = 1.95, 95% CI 1.40–2.72). Increasing age was found to be a moderate deleterious risk factor (HR = 1.02, 95% CI 1.01–1.02) (Table 3).

	Relapse-free survival		Overall survival	
	Univariate (95% CI)	Multivariate ^a (95% CI)	Univariate (95% CI)	Multivariate ^a (95% Cl
School education				
Illiterate	1.0	-	1.0	-
Fundamental	0.73 (0.55-0.98)	_	0.72 (0.52-1.00)	_
High school	0.44 (0.32-0.62)	-	0.44 (0.30-0.64)	-
College	0.40 (0.28-0.59)	_	0.40 (0.26-0.60)	_
<9 years	1.0	1.0	1.0	1.0
>8 years	0.56 (0.46-0.68)	0.76 (0.61-0.94)	0.55 (0.44-0.69)	0.76 (0.61-0.94)
Sex				
Female	1.0	1.0	1.0	1.0
Male	1.68 (1.40-2.02)	1.41 (1.17–1.71)	1.91 (1.54–2.35)	1.58 (1.27–1.97)
Age	1.02 (1.01-1.02)	1.01 (0.99–1.01)	1.02 (1.01-1.02)	1.01 (1.00-1.02)
Туре				
Superficial spreading	1.0	1.0	1.0	1.0
Nodular	2.21 (1.74-2.80)	1.17 (0.91–1.50)	1.96 (1.49-2.58)	0.99 (0.75–1.33)
Lentigo maligna	1.22 (0.63-2.39)	1.07 (0.54-2.11)	1.28 (0.60-2.73)	1.25 (0.58-2.69)
Acrolentiginous	2.81 (2.52-3.51)	1.18 (0.92–1.51)	2.68 (2.09-3.44)	1.05 (0.79-1.40)
Nonclassified	3.57 (2.27-5.62)	2.26 (1.40-3.66)	3.70 (2.28-5.98)	2.38 (1.44-3.94)
Place of diagnosis				. ,
Cancer Hospital	1.0	1.0	1.0	1.0
Public Hospital	0.73 (0.54-0.99)	0.77 (0.56-1.06)	0.86 (0.57-1.13)	0.88 (0.62-1.27)
Private facility	0.53 (0.40-0.70)	0.74 (0.55-0.98)	0.52 (0.38-0.73)	0.74 (0.53-1.04)
Undefined	1.42 (1.13-1.80)	1.23 (0.97-1.57)	1.70 (1.31-2.19)	1.52 (1.16-1.99)
Period	0.94 (0.90-0.98)	0.94 (0.91-0.98)	0.99 (0.95-1.04)	_
Ethnicity				
White	1.0	_	1.0	_
Non-white	1.56 (1.23-1.99)	_	1.52 (1.16-1.99)	_
Site				
Head and neck	1.0	_	1.0	_
Trunk	0.86 (0.63-1.20)	-	0.90 (0.63-1.31)	_
Upper limbs	0.69 (0.46–1.04)	_	0.61 (0.38–0.98)	_
Lower limbs	0.93 (0.66–1.32)	-	0.84 (0.57–1.26)	_
Palms and soles	1.95 (1.40–2.72)	_	1.78 (1.22–2.60)	_

Table 3 Overall survival and relapse-free survival, univariate and multiple regression analyses, melanoma cases diagnosed in 1997–2004, reference oncology center, Rio de Janeiro, Brazil

Cl, confidence interval.

^aCox proportional hazards model stratified by tumor-node-metastases staging.

In the multivariate analysis, higher EL remained a protective factor for overall survival, with an HR = 0.76 (95% CI 0.61–0.94), after adjusting for age, sex, clinical-pathological type, and place of diagnosis, stratified by tumor-node-metastases staging (Table 3). In relation to relapse-free survival, higher EL was a protective factor, with an HR = 0.76 (95% CI 0.61–0.94), adjusted for age, sex, clinical-pathological type, place of diagnosis, and year of diagnosis, stratified by tumor-node-metastases staging (Table 3).

Discussion

In this study, it was observed that SES as measured by school attainment was associated with the overall and disease-free survival in patients diagnosed with melanoma. The present study explored SES and the clinical evolution in the context of a large public tertiary care hospital in a developing country.

Overall survival and relapse-free survival of the entire cohort are comparable with that found in other tertiary cancer centers in other countries [14,15], reflecting the similarity of care as well as the homogeneous behavior of this disease in different countries. Socioeconomic inequalities have been associated with the incidence of many malignant diseases such as tobaccorelated neoplasms, and with a worse outcome for those patients with poorer social conditions [16]. Lower SES status is related to a more advanced stage of the tumor at the diagnosis.

Higher SES is associated with a higher incidence of melanoma; this has been attributed to more time spent in vacation in sunny places [3,4]. In Brazil, there is a larger proportion of whites among the more affluent population stratum. The 2000 demographic census in Brazil showed that 23% of the interviewed participants reported to have 9 years or more of school education, such estimates being 29% for white and 14% for non-white individuals [17]. However, higher SES is related to better survival from melanoma [8,9,18]. This finding could be related to diagnosis precocity, accessibility to treatment, smaller proportion of lesions in unfavorable topographies (soles and palms, back, scalp), and unfavorable types (ALM, NM). As a whole, these conditions may impact survival, but one cannot attribute to them the whole impact of SES.

In Brazil, the level of population schooling is relatively low compared with other industrialized countries.

Median schooling attendance is 6.5 years for the entire population and 8 years for the metropolitan region of Rio de Janeiro, where the study was carried out [19].

Because of many social and cultural factors, melanoma awareness in Brazil is much lower than that in countries with a high incidence of the disease such as Australia and New Zealand, and hence, a smaller proportion of diagnosis of early lesions can be expected. As a result, from 970 patients whose tumor thickness measurement (Breslow index) was available, the median value was 2.0 mm, in sharp contrast with American and European data [3,20], where most of the patients present with thinner lesions. In relation to melanoma prevention in Brazil, sun avoidance/protection behavior was reported by about 20% of individuals with higher ELs and in about 10% of individuals with lower EL [21].

In this study, patients with higher EL had a better prognosis as defined by lower thickness of the primary tumor, lower stage of disease on presentation, and less tumors presenting ulceration; however, these factors were insufficient to explain the effect of SES on the evolution of melanoma. Grouping individuals into two classes (8 years or less and 9 years or more of school education) improved the statistics and is in line with the literature on SES and cancer mortality. After modeling for all covariates, SES remained a strong factor related to both overall survival and disease-free survival, with HR = 0.76and 0.76, respectively. These findings are in agreement with those of other investigators who analyzed the relationship between melanoma survival and SES with different methods of evaluation of SES and study design [9,22], even taking into account different ethnic groups [23] and a hospital-based study [10].

Melanoma is a heterogeneous disease, and previous studies have suggested different pathways leading to this disease [24,25]. Melanomas may differ according to the patterns of sun exposure in clinical, biological, and epidemiological aspects. It has been reported that melanoma cases without chronic sun exposure have higher rates of mutations and amplifications in BRAF and NRAS, whereas those arising in individuals with chronic sun exposure, mucosal, and ALM had a higher frequency of deletions of CDKN2A and mutations in c-KIT [26-28]. Epidemiological studies have also shown that distinct topography, clinical type, age, and sex characteristics can comprise almost separate sets of disease [29,30]. These tumors may have different clinical behaviors and prognosis. In a given population, one can find particular proportions of these lesions. For example, in populations with a large proportion of dark-skinned individuals, one may find more cases of ALM. Melanomas that occur in younger individuals tend to occur in areas subject to intermittent exposure (lower limbs), predominantly SSM, whereas melanomas in older individuals tend to be related to chronic sun exposure and type lentigo maligna melanoma [28,29]. There is also a growing body of evidence relating sun exposure with improved survival for patients with melanoma [31,32].

In this study, some differences related to SES and characteristics of the individuals were observed. In the group of patients with higher EL predominate tumors in the trunk and upper limbs, clinical type SSM, and younger median age. However, these same characteristics are present in groups of patients with chronic intermittent sun exposure, a group with a better prognosis [30].

Keeping in mind that melanoma can be approached as a group of distinct diseases in molecular and epidemiological settings, it is possible that one of the reasons for the different outcomes currently attributed to SES may be related to the presence of a higher proportion of tumors with a better prognosis in the group of patients with higher EL.

No differences in access to treatment in this population can explain such a difference; considering that patients were treated at the same institution, no differences were found in relation to access to therapeutic interventions. In this cohort, no patient received adjuvant immunotherapy, and during the period of this study, drugs such as ipilimumab and vemurafenib were not available.

The Brazilian population is characterized by an intense admixture of ethnic groups [18], and 12.5% of patients in this cohort were classified as non-whites, a poorly studied group of melanoma patients. Overall survival was better for white patients with stage I and II disease, but for those with more advanced disease, there was no difference in relation to skin color.

This study has some weaknesses: this cohort represents a group of patients treated at a tertiary public cancer center; thus, it does not necessarily reflect the behavior of this disease in the entire population, considering that wealthier individuals are usually treated at private facilities; data were collected for clinical use during a period of 8 years and imperfections in sociodemographical variables collected during this period could have been introduced; in this period, there was a change in the American Joint Committee on Cancer staging, and missing information on microstaging predominate in the first years of the cohort; and the education level was chosen as the SES surrogate, because income is often under-reported, and other variables such as occupation were missing in a large proportion of patient records.

However, the study has some strengths, considering that all information was obtained on an individual basis from each patient, including issues related to the demography, tumor on diagnosis, treatment, and follow-up. The patients were treated in a single cancer center, by the same group of physicians, and following standardized

therapeutic procedures. In fact, the proportion of patients who underwent sentinel lymph node biopsy and received systemic therapy was the same in relation to estimated SES. The median follow-up time was long; thus, it was possible to detect relapses and deaths as most of them occur in the first years of follow-up. In the same vein, the results of treatment were similar to those observed in other countries [14,15], even with similar designs [10].

Conclusion

Higher SES as measured by reported EL in this cohort was associated with better survival of patients with melanoma, even after adjusting for clinical prognostic factors. Prospective studies evaluating sociodemographic factors may yield unrevealed issues associating SES and the prognosis of malignant melanoma.

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Conflicts of interest

There are no conflicts of interest.

References

- 1 Miller AJ, Mihm MC Jr. Melanoma. N Engl J Med 2006; 355:51-65.
- 2 Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. CA Cancer J Clin 2007; 57:43–66.
- 3 MacKie RM, Hauschil A, Eggermont MM. Epidemiology of cutaneous melanoma. *Ann Oncol* 2009; **20 (Suppl 6)**:v1–v7.
- 4 Pérez-Gomez P, Aragonés N, Gustavsson P, Lope V, López-Abente G, Pollán M. Socio-economic class, rurality and risk of cutaneous melanoma by site and gender in Sweden. *BMC Public Health* 2008; 8:33.
- 5 Shack L, Jordan C, Thomson CS, Mark V, Moller H. Variation in incidence of breast, lung and cervical cancer and malignant melanoma of skin by socioeconomic group in England. *BMC Cancer* 2008; 8:271.
- 6 Dalstra JAA, Knust AE, Borrell C, Breeze E, Cambois E, Costa G, et al. Socioeconomic differences in the prevalence of common chronic diseases: an overview of eight European countries. Int J Epidemiol 2005; 34: 316–326.
- 7 Beswick S, Affeck P, Elliott F, Gerry E, Boon A, Bale L, et al. Environmental risk factors for relapse of melanoma. Eur J Cancer 2008; 44:1717–1725.
- 8 Birch-Johansen F, Hvilsom G, Kjaer T, Storm H. Social inequality and incidence of and survival from malignant melanoma in a population-based study in Denmark, 1994–2003. *Eur J Cancer* 2008; 44:2043–2049.

- 9 Jeffreys M, Sarfati D, Stefanovic V, Tobias M, Lewis C, Pearce N, et al. Socioeconomic inequalities in cancer survival in New Zealand: the role of extent of disease at diagnosis. Cancer Epidemiol Biomarkers Prev 2009; 18:915–921.
- 10 Mandalá M, Imberti GL, Piazzalunga D, Belfiglio M, Lucisano G, Labianca R, et al. Association of socioeconomic status with Breslow thickness and disease-free and overall survival in stage I–II primary cutaneous melanoma. Mayo Clin Proc 2011; 86:113–119.
- 11 Eide MJ, Weinstock MA, Clark MA. Demographic and socioeconomic predictors of melanoma prognosis in the United States. J Health Care Poor Underserved 2009; 20:227–245.
- 12 Liberatos P, Link BG, Kelsey JL. The measurement of social class in epidemiology. *Epidemiol Rev* 1988; **10**:87–121.
- 13 National Cancer Institute of Brazil (INCA) Estimate 2010 Cancer Incidence in Brazil. Rio de Janeiro, 2009.
- 14 Balch CM, Gershenwald JE, Soong S-J, Thompson JF, Atkins MB, Byrd DR, et al. Final version of 2009 AJCC melanoma staging and classification. J Clin Oncol 2009; 27:6199–6206.
- 15 Livestro DP, Muzikansky A, Kaine EM, Flotte TJ, Sober AJ, Mihm MC, et al. Biology of desmoplastic melanoma: a case-control comparision with other melanomas. J Clin Oncol 2005; 23:6739–6746.
- 16 Clegg LX, Reichman ME, Miller BA, Hankey BF, Singh GK, Lin YD, et al. Impact of socioeconomic status on cancer incidence and stage at diagnosis: selected findings from the surveillance, epidemiology, and end results: national longitudinal mortality study. *Cancer Causes Control* 2009; 20:417–435.
- 17 Brazilian Institute of Geography and Statistics (IBGE), 2000 Demographic Census – Education: Results of the Sample. Available at http:// www.ibge.gov.br/home/estatistica/populacao/censo2000/educacao/ tabela_brasil.shtm [Accessed 26 June 2009].
- 18 Rachet B, Quinn MJ, Cooper N, Coleman MP. Survival of melanoma of the skin in England and Wales up to 2001. Br J Cancer 2008; 99:S47–S49.
- 19 Brazilian Institute of Geography and Statistics (IBGE), Synthesis of Social Indicators, 2006.
- 20 Lipsker D, Engel F, Cribier B, Velten M, Hedelin G. Trends in melanoma epidemiology suggest three different types of melanoma. *Br J Dermatol* 2007; **157**:338–343.
- 21 Szklo A, Almeida LM, Figueiredo V, Lozana JA, Mendonça GAS, Moura L, et al. Behaviors related to sunlight exposure versus protection in a random population sample from 15 Brazilian State capitals and the Federal District, 2002-2003. Cad Saude Publica 2007; 23:823–834.
- 22 Belloni-Fontini A, Piaserico S, Tonin E, Alaibac M. Melanoma and immunosupression. *Dermatology* 2009; **218**:88.
- 23 Zell JA, Cinar P, Obasher M, Ziogas A, Meyskens FL, Anton-Cuver H. Survival for patients with invasive cutaneous melanoma among ethnic groups: the effects of socioeconomic status and treatment. *J Clin Oncol* 2008; 26:66–75.
- 24 Mishima Y. Melanocytic and nevocytic malignant melanomas. Cancer 1967; 20:632-649.
- 25 Whiteman DC, Watt P, Purdie DM, Hughes MC, Hayward NK, Green AC. Melanocytic nevi, solar keratosis, and divergent pathways to cutaneous melanoma. J Natl Cancer Inst 2003; 95:806–812.
- 26 Curtin JA, Fridlyand J, Kageshita T, Patel HN, Busam KJ, Kutzner H, *et al.* Distinct sets of genetic alterations in melanoma. *N Engl J Med* 2005; 353:2135–2147.
- 27 Fecher LA, Cummings SD, Keefe MJ, Alani RM. Toward a molecular classification of melanoma. J Clin Oncol 2007; 25:1606–1620.
- 28 Saldanha G, Potter L, DaForno P, Pringle JH. Cutaneous melanoma subtypes show different BRAF and NRAS mutation frequencies. *Clin Cancer Res* 2006; 12:4499–4505.
- 29 Anderson WF, Pfeiffer RM, Tucker MA, Rosenberg PS. Divergent cancer pathways for early-onset and late-onset cutaneous malignant melanoma. *Cancer* 2009; **115**:4176–4185.
- 30 Lachiewicz AM, Berwick M, Wiggins CL, Thomas NE. Epidemiologic support for melanoma heterogeneity using the surveillance, epidemiology, and end results program. J Invest Dermatol 2008; 128:243–245.
- 31 Berwick M, Armstrong BK, Ben-Porat L, Fine J, Kricker A, Eberle C, et al. Sun exposure and mortality from melanoma. J Natl Cancer Inst 2005; 97:195–199.
- 32 Rosso S, Sera F, Segnan N, Zanetti R. Sun exposure prior to diagnosis is associated with improved survival in melanoma patients: results from a long-term follow-up study of Italian patients. *Eur J Cancer* 2008; 44:1275–1281.