Dermatology Practical & Conceptual

Cutaneous Malignant Melanoma in Chile: Differences in Tumor Thickness and Overall Survival Between Patients From Public and Private Health Care Centers

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ABSTRACT

Introduction: A low socioeconomic status (SES) is associated with lower survival rates in cutaneous malignant melanoma (CMM). In South America, there are few studies that analyze CMM data according to SES.

Objectives: To determine the differences in microstaging and overall survival in CMM between public and private health care centers.

Methods: Retrospective cohort study. Histopathological reports with a diagnosis of CMM from two public hospitals (PuH) and one private health care center (PrH) in Santiago from 2008 to 2018 were included. Patients' death certificates were obtained to estimate overall survival.

Results: 1014 MMC were found. The mean age was 58.6 ± 16.8 years and 59.9% corresponded to

female patients. Of these, 33.9% received treatment at PuH and 66.1% at PrH. Patients from PuH had an increased risk of having an invasive CMM and a >1 mm thickness melanoma compared to PrH (odds ratio 2.77 and 6.06, respectively). Patients with invasive CMM from the PuH were 6.29-fold more likely to die than a patient from the PrH.

Conclusions: We observed a great disparity in tumor thickness between the socioeconomic status, reflecting a later detection and lower survival rate in PuH. Our results highlight a gap on which National Public Health should focus.

Introduction

Cutaneous malignant melanoma (CMM) is the most frequent cause of skin cancer-related deaths, its incidence has globally increased, and it has been estimated to further grow [1]. Due to its high prevalence in a younger population, it has great epidemiological relevance and repercussions for public health [2,3].

In Chile, the incidence varies significantly by geographic location, with an average of 2.4 to 3 cases for 100000 inhabitants and an increasing mortality rate between 1997 and 2015 [4,5].

The survival for CMM varies according to the tumoral depth at the time of diagnosis, with higher mortality rates in advanced stages [2]. Observational studies have demonstrated differing mortality rates depending on an individual´s socioeconomic status (SES) [6-9]. Rutherford et al showed that a reduction in socioeconomic inequality was associated with a significant reduction in melanoma mortality rate 5 years from diagnosis [9].

The Chilean health care system includes both private (PrH) and public (PuH) health care centers. Public hospitals mostly benefit those patients with lower SES, and for those individuals of higher SES, PrH is their main health care provider [4,10]

In Chile there is a lack of data on the differences in tumor thickness and survival in CMM according to the SES, making it challenging to establish prognostic differences among these patients.

Objectives

The objective of this study is to determine differences in tumoral thickness at the time of diagnosis and survival rates among patients diagnosed with CMM based on their health care provider.

Methods

This is a retrospective cohort study, which included all histopathologic reports found with the diagnosis of CMM between January 2008 and December 2018 at two public hospitals (Hospital San José and Hospital Barros Luco Trudeau) and one private health care center (Laboratorio Histodiagnóstico Málaga) in Santiago, Chile.

The exclusion criteria considered recurrent tumors, biopsies of extracutaneous melanoma, CMM metastasis, and incisional biopsies. Transected CMM (positive inferior margins) with a depth ≤4 mm (<T4 according to American Joint Committee on Cancer (AJCC) 8th edition) were also excluded due to the risk of underestimating tumoral depth.

Death certificates were used to calculate the overall survival rates of invasive CMM. Two research ethics committees (North and South Metropolitan Health care Chilean Services) approved this study as the patients' anonymity was safeguarded during the statistical analysis.

Statistical Analysis

The Shapiro-Wilk test was used to determine data distribution. The inferential analysis was performed by Fisher exact test and T student. Performed a logistic regression with an odds ratio (OR) and confidence interval of 95%.

Survival analysis was performed by Kaplan-Meier method. Log-Rank was used to compare different chances of survival and Cox regression was used to assess different variables, estimating hazard ratio (HR) and confidence interval (CI) of 95%.

The level of significance was defined as $P < 0.05$. The statistical analysis was performed using the statistical software STATA 13® (StataCorp).

Results

A total of 1014 melanomas were identified in both PuH and PrH. The gender distribution was 59.9% (N = 607) women and 40.1% (N = 407) men. The mean age at the time of diagnosis was 58.6 ± 16.8 years (range: 12-98 years).

In the PuH patients, tumors were located on the head and neck (29.9%), trunk (20.3%), palms and soles (16.9%), lower extremities (16.6%), upper extremities (12.5%) and perineal area (1.4%). On the other hand, in the PrH it was more frequent to find melanomas in the trunk (24.8%), followed by lower extremities (22.7%), head and neck (20.7%), upper extremities (18.5%), palms and soles (3.7%) and perineal area (0.9%). There were statistically significant differences in tumor location between these two groups (P < 0.001).

Distribution by health care provider showed that 33.9% of cases (N = 344) were diagnosed in PuH, while 66.1% (N = 670) were diagnosed in PrH. There was a statistically significant difference (P < 0.001) in the mean age at the time of diagnosis, with patients in PuH being older with a mean age of 64.2 ± 15.7 years (range: 20-98) compared to PrH patients with a mean age of 55.6 ± 26.6 years (range: 12-92). There was no statistically significant difference by gender, with 63.1% of women and 36.9% of men in the PuH and 58.2% of women and 41.8% of men in PrH (Table 1).

About the degree of infiltration, there was a statistically significant difference between public and private health care centers (P < 0.001). In PuH, 34.9% of melanomas were in situ and 65.1% were invasive, while in PrH, 56.1% were in situ and 43.9% were invasive. There was a statistically significant difference in the depth of infiltration of invasive CMM between the PuH and PrH (P < 0.001) (Table 1).

Using multivariable logistic regression analysis (adjusted for age and gender), being diagnosed with CMM in a PuH would increase the risk of having an invasive tumor by 2.77-fold (OR 2.77; CI 2.08-3.68). It also increases the risk of having an invasive melanoma with an infiltration greater than 1mm in depth by 6.06-fold (OR 6.06; CI 4.03-9.11), adjusted by age and sex when compared with patients seen at PrH.

Overall survival rates at the 5-year were 82.4%, with a significant difference between PuH (65.6%) and PrH (94%) (P < 0.001). Patients with invasive CMM in PuH had 6.29-fold higher risk of dying than those on PrH (HR 6.29; P < 0.001; CI 3.91-10.14) (Table 2).

5-year overall survival curves according to tumoral depth are shown in Figure 1 for PuH and in Figure 2 for PrH.

Table 1. Characteristics of patients with primary cutaneous melanoma stratified by public hospital (PuH) and private health care center (PrH)[a].

	PuH[a]	PrH[a]	P
Gender Female Male	 217 (63.1) 127 (36.9)	 390 (58.2) 280 (21.8)	 0.134
Age (years)[b]	64.2 ± 15.7	55.6 ± 16.6	<0.001
Infiltration In situ Invasive	 120 (34.9) 224 (65.1)	 376 (56.1) 294 (43.9)	 <0.001
Thickness T1 T2 T3 T4	 70 (31.5) 43 (19.4) 57 (25.7) 52 (23.4)	 223 (76.9) 35 (12.1) 19 (6.5) 13 (4.5)	 <0.001

[a] *Data are provided as number (percentage), unless otherwise indicated.*

[b] *Age in years ± Standard deviation*

Thickness as T1≤ 1 mm, T2 >1.0–2.0 mm, T3 >2.0–4.0 mm and T4 >4.00 mm.

Table 2. 5-year overall survival by health care center according to thickness.

	5-year OS	CI 95%
Public Hospital	65.6%	57.9%- 72.1%
T1	86.7%	74.9%- 93.1%
T2	81.5%	63.2%- 91.3%
T3	54.9%	38.7%- 68.5%
T4	28.5%	14.1%- 44.7%
Private health care center	94%	90.2%- 96.4%
T1	95.6%	91.4%- 97.8%
T2	95.2%	70.7%- 99.3%
T3	94.4%	66.6%- 99.2%
T4	75%	40.8%- 91.2%

CI = confidence interval; OS = overall survival.
Thickness as T1≤ 1 mm, T2 >1.0–2.0 mm, T3 >2.0–4.0 mm and T4 >4.00 mm

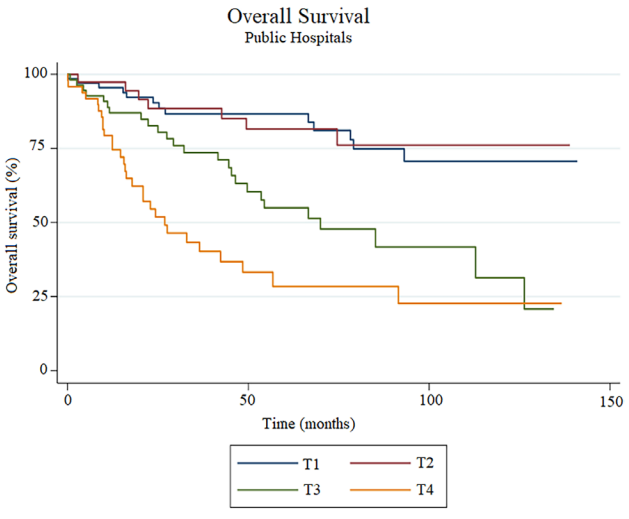

Figure 1. Overall survival curves according to tumoral depth in public hospitals (PuH).

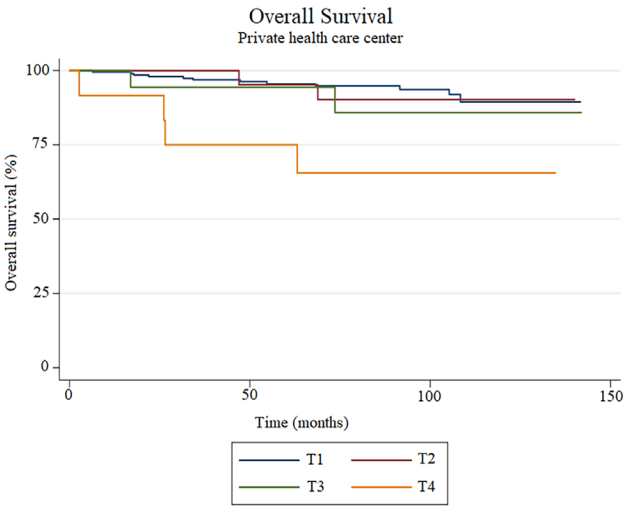

Figure 2. Overall survival curves according to tumoral depth in the private health care center (PrH).

Conclusions

In recent years, there has been an increasing focus on the influence of socioeconomic status (SES) on melanoma outcomes. Most studies show that SES is a strong predictor of CMM-specific mortality [11-14]. In Chile and South America, the influence of socioeconomic status on CMM has been rarely studied. Our study revealed a significant difference in the degree of infiltration between PuH and PrH, with 34.9% of in situ melanomas in PuH versus 56.1% in PrH. This difference was confirmed in the multivariable analysis, indicating a 2.77-fold higher risk of invasive CMM in patients treated at PuH.

Several studies have demonstrated significant disparities in tumoral depth and survival rates between individuals with high and low SES (6,15). Mandalá et al reported that 27.5% of patients with low SES had a Breslow >3 mm at diagnosis, compared to 9.41% for those patients with higher SES [15]. In our study, 68.5% of PuH tumors had a Breslow >1mm, compared to 23.1% for those in PrH. Reflecting an increased risk of thick melanoma in PuH by 6.06-fold.

Multiple studies have attempted to explain the gap between different SES groups. Education has been proposed as a relevant factor [16-18]. Lower education levels are associated with thicker tumors and more advanced stages at the time of diagnosis, while patients with higher education levels attend more frequently for skin checks and therefore tend to be diagnosed at earlier stages [17,18]. However, the literature shows that even after adjusting for education level, a low SES remained an independent predictor for advanced stages [19]. Individuals with high SES have greater access to dermatologists and therefore to an early diagnosis [8]. On the other hand, lower SES populations may have a lower recognition of early signs of skin cancer [20].

Overall survival rate at 5 years in our study was 82.4%, and there were differences between PrH and PuH. Patients with invasive CMM in PuH had 6.29-fold more mortality risk than patients in PrH, as shown by clear discrepancies in the Kaplan-Meier curve. These findings are consistent with international studies, which have shown that patients with higher SES have more favorable odds of survival [6,19,21-23].

When analyzing the possible causes of these survival differences, besides education and access to dermatologists, insurance, and therefore treatment access, are evident factors to consider. Recently, Rosenthal et al published an article comparing two forms of health insurance in the United States, one with an integrated health care system and the second group including other private insurances [11]. This study showed that patients in non-integrated private insurances that had lower income, had a 70% increased risk of dying from CMM compared to those with higher income, while in the integrated health care system, there was no increased risk between SES groups.

The location of CMM in the SPu and SPr exhibited statistically significant differences, with a greater prevalence of head and neck melanomas and acral melanomas in the SPu compared to the SPr. However, due to the focus of our study on identifying disparities in tumor thickness and overall survival between healthcare systems, we did not extensively explore the analysis of location. Nevertheless, it is worth noting that location could be an important factor to investigate in future studies.

Despite its contributions, our study has some limitations. For instance, being a retrospective study may have limitations in data collection and analysis. Also, even though we obtained data from two PuH, we had more patients from PrH than PuH, which may not reflect the national distribution of melanoma patients. Additionally, histopathological analysis was performed by different pathologists. However, given the multicentric nature of the study, it was not feasible to have all the data analyzed by a single specialist. Moreover, this study did not include other confounding factors, such as comorbidities or smoking, and did not assess the impact of patient-specific melanoma treatments.

The results in the present study have significant clinical relevance. Specifically, the greater tumoral depth in PuH, reflects that lower-income patients probably have a delay in the detection of CMM and consequently a reduced survival rate. Public health strategies should focus on this gap, in order to benefit the population at risk, for example by considering both clinical-pathologic features and nevus count which represents an easy to access prognostic factor and pathologic ones (in patients with previous melanoma) [(24,25]. This can be achieved by creating targeted prevention and early detection programs that are accessible and effective for patients

from lower socioeconomic backgrounds. In conclusion, future strategies should consider the impact of specific prevention campaigns and early detection programs for people from lower SES to reduce disparities in melanoma outcomes.

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