Original Article

# Retrospective study of patients with cutaneous melanoma treated at the Federal University of São Paulo.

## Estudo retrospectivo dos pacientes portadores de melanoma cutâneo atendidos na Universidade Federal de São Paulo.

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### ABSTRACT

**Objective:** to evaluate the characteristics of the patients with cutaneous melanoma treated at the São Paulo Hospital - UNIFESP. **Methods:** we conducted a retrospective study of 184 cases of cutaneous melanoma. We analyzed information on gender, age, tumor characteristics, histological characteristics and staging. **Results:** mean age at diagnosis was 58.7 years, with homogeneous age distribution between genders and predominance in white individuals (70.6%). There was a predominance of trunk involvement in men (36.7%) and lower limbs in women (42%). Sun exposure, with sunburns, was more common among males (31.2%) than among females (23.5%). There was an approximately three-fold increase in lymph node involvement when the mitotic index rose from zero (11.9%) to one or more mitosis per field (36.2%). In addition, the greater the Breslow thickness, the greater the lymph node involvement and poor the outcomes: 10.2% when less than 1mm and 59.2% when greater than 4mm. **Conclusion:** the characteristics of patients with cutaneous melanoma treated at Hospital São Paulo are similar to those found in the literature.

**Keywords:** Melanoma. Skin Neoplasms. Mitosis. Risk Factors. Melanoma/epidemiology.

## INTRODUCTION

Skin cancer is the most common form of cancer, accounting for about 40-50% of all neoplasias diagnosed in the United States according to the World Health Organization[1-3]. Skin cancers are primarily classified as non-melanoma and melanoma (Figure 1). Melanoma represents a small percentage of skin cancers diagnosed annually (about 3%), but accounts for most of the deaths caused by skin tumors, reaching 65% per year[4-6]. The incidence of melanoma continues to increase progressively, with an approximate increase of 33% in men and 26% in women in the period from 2002 to 2006[7], and about 90,000 new cases and 10,000 deaths in the United States in 2017, according to the American Cancer Society statistics.

The main risk factors related to the patient are skin phototype, personal and family history of



**Figure 1.** *Malignant lentigo melanoma, a subtype of melanoma, on the left face of a patient with phototype I.*

melanoma, presence of multiple atypical or dysplastic nevi and genetic factors. In addition, environmental factors such as intense or sporadic sun exposure,

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blistering, and UVB tanning play an important role in the development of melanoma[8-19]. Unfortunately, many patients receive diagnose at an advanced stage, or even experience disease progression, despite the established treatments. Melanoma evolves from several well-defined precursor lesions before it becomes invasive and metastatic[20,21]. Several studies have analyzed the predictive factors of prognosis related to melanoma, including tumor-related, factors such as Breslow thickness, presence of ulceration and mitotic index, which were identified as the three most independent factors important in the analysis of patients' outcomes[22-34].

Therefore, knowledge of the epidemiology and risk factors of cutaneous melanoma is of interest to all those studying and working with melanoma, including surgeons, dermatologists, oncologists and primary care physicians, for the development of new prevention campaigns, expansion of existing knowledge and publication of data to reach professionals who are not yet familiar with the disease[35].

Numerous studies have investigated the characteristics of melanoma patients and their prognostic factors. However, records from Latin America and Brazil remain scarce[36]. Thus, through this study, we seek to better understand the epidemiological and pathological profile of patients with melanoma treated in Brazil and thus improve the strategies of care in our country.

## METHODS

We conducted a retrospective study of epidemiological data collected from the Department of Skin Tumors of the Discipline of Plastic Surgery of the University Hospital of the Federal University of São Paulo (UNIFESP). The study was approved by the Ethics and Research Committee of UNIFESP under number 0986/11. We performed an analysis of the hospital and outpatient records of 184 patients with cutaneous melanoma treated at the Service from January 2005 to December 2010, based on a protocol that contained information about gender, color, age, occupation, sun exposure, tumor characteristics, location of the lesion, histological characteristics, staging and follow-up until the end of this work. Regarding the location of the lesions, we divided then into macroregions: head and neck, trunk, upper limbs, lower limbs or of unknown location.

We submitted the collected data to statistical analysis, in which we used non-parametric tests. We set the level of rejection of the null hypothesis at 5%, considering a significant value of p=0.05. We then compared the results to national and international epidemiological studies.

## RESULTS

Of the 184 patients, 103 (66%) were female and 81 (44%), male. Regarding skin color, 130 (70.6%) were classified as whites and 51 (27.7%) were non-whites (brown, blacks and natives). Three (1.6%) patients had no information on skin color. The mean patient's age was 58.7 years at the time of diagnosis. Of the patients analyzed, 49 (26.6%) worked exposed to the sun, 133 (72.2%) worked without sun exposure, and two (1.2%) did not report on their professions.

Regarding the histological aspects, 116 (63.1%) had at least one mitosis per field (mitotic index), 42 (22.8%) had a mitotic index equal to zero and in 26 (14.1%) we did not have access to histopathological examination. Of the patients analyzed, 125 (67.9%) did not present lymph node metastases, 58 (31.5%) presented lymph node involvement; one (0.6%) patient's record lacked this information.

The analysis showed no significant difference between genders, with calculated $X^2$ equal to 0.93 (p=0.6086). When we analyzed the

affected region in relation to the gender, we found statistically significant differences. Head, neck and trunk involvement was more common in men, and the upper and lower limbs were more common and women: calculated $X^2$ = 11.12 (p=0.0111) (Table 1).

**Table 1.** *Distribution of gender according to the regions involved.*

| Region | Female | | Male | |
|---|---|---|---|---|
| | N | % | N | % |
| Head and neck | 17 | 17.0 | 23 | 29.1 |
| Trunk | 24 | 24.0 | 29 | 36.7 |
| Upper limbs | 17 | 17.0 | 9 | 11.3 |
| Lower limbs | 42 | 42.0 | 18 | 22.9 |
| Total | 100 | 100 | 79 | 100 |

When comparing the exposure with the affected region, the results suggest a relation between the profession with sun exposure and the occurrence of head and neck melanoma, evidencing the role of sun exposure in the genesis of this neoplasm: calculated $X^2$=8.821 (p=0.0318) (Table 2). We excluded seven patients (3.8%) with no information to make the comparison from this analysis.

**Table 2.** *Distribution of the exposure risk factor according to the regions involved.*

| Region | Exposure | | Total | % of Yes |
|---|---|---|---|---|
| | Yes | No | | |
| Head and neck | 14 | 26 | 40 | 35.0 |
| Trunk | 18 | 34 | 52 | 34.6 |
| Upper limbs | 9 | 17 | 26 | 34.6 |
| Lower limbs | 8 | 51 | 59 | 13.6 |
| Total | 49 | 128 | 177 | 27.6 |

When we compared the risk factor incidence of the sunburn with the affected region, the percentage of sunburn of the head and neck was significantly higher than in the other regions, and the presence of burns in patients with melanoma of the lower limbs was lower: calculated $X^2$=12.59

(p=0.0056) (Table 3). We excluded fifteen patients (8.2%) with no information to make the comparison from this analysis.

**Table 3.** *Distribution of the sunburn risk factor according to the regions involved.*

| Region | Sunburn | | Total | % of Yes |
|---|---|---|---|---|
| | Yes | No | | |
| Head and neck | 20 | 19 | 39 | 51.2 |
| Trunk | 20 | 31 | 53 | 37.7 |
| Upper limbs | 9 | 17 | 24 | 37.5 |
| Lower limbs | 9 | 44 | 53 | 16.9 |
| Total | 58 | 111 | 169 | 34 |

We noticed that the more cephalic the region the greater the rate of patients within it that present sunburn as a risk factor, evidencing the low influence of this risk factor on the genesis of melanomas in lower and less exposed regions. When comparing the presence of the risk factor "exposure" with the gender, we did not obtain a statistically significant difference: calculated $X^2$=1.35 (p=0.2438) (Table 4). We excluded two patients (1.2%) who had no exposure information from this analysis.

**Table 4.** *Distribution of exposure risk factor according to gender.*

| Gender | Exposure | | Total | % of Yes |
|---|---|---|---|---|
| | Yes | No | | |
| Male | 25 | 55 | 80 | 31.2 |
| Female | 24 | 78 | 102 | 23.5 |
| Total | 49 | 133 | 182 | 30.2 |

When comparing the mitotic index of melanoma with lymph node involvement during follow-up, the analysis showed a significant association between the presence of one or more mitoses and the occurrence of lymph node metastasis, increasing the risk of metastases by 3.2 times: calculated $X^2$=8.71 (p=0.0032) (Table 5).

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**Table 5.** Distribution of lymph node involvement according to the presence of mitosis.

| Mitosis | Lymph node | | Total | % positive |
|---|---|---|---|---|
| | Positive | Negative | | |
| Present | 42 | 74 | 116 | 36.2 |
| Absent | 5 | 37 | 42 | 11.9 |
| Total | 47 | 111 | 125 | 37.6 |

Breslow thickness obtained through anatomopathological study was significantly associated lymph node involvement during follow-up: calculated $X^2$=38.56 (p<0.0001) (Table 6).

**Table 6.** Distribution of lymph node involvement according to the Breslow thickness.

| Breslow | Lymph node | | Total | % positive |
|---|---|---|---|---|
| | Positive | Negative | | |
| *In situ* (0) | 0 | 17 | 17 | 0.0 |
| <1 | 4 | 35 | 39 | 10.2 |
| 1.01 to 2 | 8 | 24 | 32 | 25.0 |
| 2.01 to 4 | 5 | 20 | 25 | 25.0 |
| >4 | 32 | 22 | 54 | 59.2 |
| Total | 58 | 126 | 184 | 31.5 |

## DISCUSSION

It is important to note that the collection of data was hampered by the deficiency of the institution's records, as it usually occurs in Brazil[36]. We found a prevalence of women in relation to men, a situation commonly described for all skin diseases. The reasons for this disparity remain unknown, but it is probably multifactorial, including differences in the skin layers and their physiology, sex hormones, age, ethnicity, lifestyle, occupation, among others[37-39]. As with other data found in the literature, there was no significant difference between genders within the most affected age groups[40-43]. Regarding the age at diagnosis, we noticed a higher incidence in patients over 50 years.

When analyzing the known risk factors for the development of melanoma, 70.6% of the patients were considered white, of which 49.4% had skin type I or II and 27.1% had light hair and eyes colors, thus predisposed to melanoma due to their phenotype. The most prevalent risk factor was skin type I or II, followed by sunburn with blisters during life. When comparing the regions affected with the sunburn history, we observed that more exposed regions, such as head and neck and trunk, are more related to patients who presented burns compared with patients without them. As described by other authors[20,44-46], the most affected regions were head and neck and trunk, accounting for 50.1%.

We found that men are more affected in regions such as head, neck and trunk, which can be explained by a greater sun exposure in men's work in relation to women. In addition, we observed a statistical difference when we compared the presence of sun exposure with the affected area, evidencing the role of exposure in head and neck and trunk melanomas and its low relation with less exposed regions[43].

The most important information that the study detected in relation to the prognosis of the patients arose through the analysis of the relationship between the presence of mitoses and the Breslow thickness with the metastatic involvement of lymph nodes. We verified that the presence of only one mitosis per field in the histopathological evaluation is associated with lymph node metastasis, taking the patient to stage III, with poor prognosis. These patients have an indication of adjuvant treatment for the spread of the disease, in agreement with several international studies[44-47]. Likewise, when we compared Breslow thickness with lymph node involvement, we noticed that the larger

the Breslow, the greater the risk of metastasis. Our study confirms this important information, published in the international review on prognostic factors and staging of cutaneous melanoma conducted by the American Joint Committee on Cancer[48,49].

In our study, we found plenty information that reaffirms the literature to date on risk factors more incident to the development of melanoma, such as light skin and eyes, sun exposure and sunburn, placing risk factors in two categories: phenotypic and non-preventable factors, and external factors, such as solar radiation, that can be prevented[49,50].

With this, we stimulate measures of melanoma prevention, such as campaigns to reduce sun exposure and encourage the use of sunscreens, as well as the identification of poor prognostic factors, to obtain better patient follow-up.

## R E S U M O

*Objetivo:* avaliar as características dos pacientes portadores de melanoma cutâneo atendidos no Hospital São Paulo - UNIFESP. *Métodos:* estudo retrospectivo de 184 casos de melanoma cutâneo. Foram analisadas as informações sobre sexo, idade, características do tumor, características histológicas e estadiamento. *Resultados:* a média de idade ao diagnóstico foi de 58,7 anos, com distribuição etária homogênea entre os sexos e predominância em indivíduos brancos (70,6%). Observou-se acometimento predominante de tronco, em homens (36,7%), e de membros inferiores, em mulheres (42%). A exposição solar, com queimaduras, foi mais comum entre homens (31,2%) do que entre mulheres (23,5%). Houve aumento de aproximadamente três vezes no acometimento linfonodal quando o índice mitótico subia de zero (11,9%) para uma ou mais mitoses por campo (36,2%), e aumento progressivo do acometimento linfonodal e de desfechos ruins quanto maior a espessura de Breslow: 10,2% quando menor do que 1mm e 59,2% quando maior do que 4mm. *Conclusão:* as características dos pacientes portadores de melanoma cutâneo atendidos no Hospital São Paulo são semelhantes às encontradas na literatura.

*Descritores:* Melanoma. Neoplasias Cutâneas. Mitose. Fatores de Risco. Melanoma/epidemiologia.

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