Histopathological predictive factors of sentinel node positivity in melanoma in the Blumenau-SC Brazilian region

Histopatologické prediktivní faktory pozitivity sentinelové uzliny u melanomu v brazilské oblasti Blumenau-SC

Kraft Rovere R., de Almeida V. D., de Freitas C.H., Costa Câmara P., Danesi Pinto R.

Department of Medicine, Regional University of Blumenau, Brazil

Summary

Background: This study aims to evaluate the relationship between sentinel lymph node positivity and risk factors associated with cutaneous melanoma, as well as the epidemiological data of patients diagnosed with this condition in the Blumenau-SC region. ***Material and methods:*** This is a cross-sectional study analyzing medical records of patients diagnosed with melanoma who underwent sentinel lymph node biopsy at a nuclear medicine service in Blumenau, Santa Catarina. The variables analyzed included Breslow classification, Clark classification, regression, ulceration, histological subtype, age, and sex. Patients were divided into two groups: those with a positive diagnosis and those with a negative diagnosis. ***Results:*** The variables with the highest statistical significance were: histological subtype, with nodular melanomas associated with positivity ($P < 0.001$); ulceration, which was more prevalent in the positive group ($P = 0.0018$); Breslow classification, which showed a significantly higher mean in the positive group ($P = 0.0002$, Mann-Whitney test); and Clark level, which was significant in patients with higher classifications. Other variables analyzed did not show statistical significance. ***Study limitations:*** The mitotic index was not analyzed as a variable; this study was based on the 7th edition of the American Joint Committee on Cancer (AJCC) cancer staging manual. ***Conclusion:*** This study presented results consistent with current literature, confirming the predictive values of sentinel lymph node positivity, aiding in better patient selection for this invasive procedure, and avoiding unnecessary analyses that may lead to irreversible adverse effects.

Souhrn

Východiska: Cílem této studie je vyhodnotit vztah mezi pozitivitou sentinelových lymfatických uzlin a rizikovými faktory spojenými s kožním melanomem, a rovněž epidemiologické údaje o pacientech s touto diagnózou v regionu Blumenau-SC. ***Materiál a metody:*** Jedná se o průřezovou studii, která analyzuje lékařské záznamy pacientů s diagnózou melanomu, kteří podstoupili biopsii sentinelové lymfatické uzliny v centru nukleární medicíny v Blumenau, Santa Catarina. Mezi analyzované proměnné patřila Breslowova klasifikaci, Clarkova klasifikace, regrese, ulcerace, histologický podtyp, věk a pohlaví. Pacienti byli rozděleni do dvou skupin: pacienti s pozitivní diagnózou a pacienti s negativní diagnózou. ***Výsledky:*** Proměnné s nejvyšší statistickou významností byly: histologický podtyp, přičemž nodulární melanomy byly spojeny s pozitivitou ($p < 0,001$), ulcerace, která byla častější ve skupině s pozitivní diagnózou ($p = 0,0018$), Breslowova klasifikace, která vykazovala významně vyšší průměr ve skupině s pozitivní diagnózou ($p = 0,0002$, Mann-Whitneyův test), a stupeň dle Clarka, který byl významný u pacientů s vyšší klasifikací. Ostatní analyzované proměnné nebyly statisticky významné. ***Limity studie:*** Mitotický index nebyl analyzován jako proměnná; tato studie byla založena na 7. vydání příručky American Joint Committee on Cancer (AJCC) pro staging nádorů. ***Závěr:*** Tato studie prezentovala výsledky v souladu s aktuální literaturou, přičemž potvrdila prediktivní hodnotu pozitivity sentinelové lymfatické uzliny, napomohla lepšímu výběru pacientů pro tento invazivní zákrok a vyloučila zbytečná vyšetření, které mohou vést k nevratným nežádoucím účinkům.

Klíčová slova

melanom – sentinelová lymfatická uzlina – prediktivní hodnota

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Patrícia Costa Câmara
Rua Frederico Guilherme Busch
288 – APTO 701
Jardim Blumenau, Blumenau-SC
Brazil
e-mail: drapatriciacamara@gmail.com

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Introduction

Cutaneous melanoma is a malignant neoplasm originating from melanocytes (cells that produce melanin, the substance responsible for skin color). Skin cancer accounts for 30% of malignant tumors registered in Brazil, with melanoma representing 3% of malignant skin neoplasms. It is considered the most severe due to its high metastatic potential [1].

Currently, the incidence of melanoma has been increasing significantly. In Blumenau, melanoma morbidity has risen from 4.4 to 22.4 cases per 100,000 inhabitants, corresponding to an incidence approximately three times higher than that of Santa Catarina state and ten times higher than the national average [2].

The Brazilian Melanoma Guideline recommends sentinel lymph node biopsy (SLNB) for patients with primary tumor thickness ≥ 1.00 mm; < 1.00 mm when ulceration or angiovascular invasion is present; or between ≥ 0.75 mm and < 1.00 mm with one or more mitoses per field. For patients with thickness ≥ 4.00 mm, SLNB is also recommended for regional disease control. When the thickness is less than 0.75 mm, even with mitoses present, the SLNB positivity rate is < 5%, making the procedure's indication questionable [3].

However, the multicenter MLST-1 study showed no significant increase in survival for patients with thick melanomas (> 4.00 mm) who underwent SLNB compared to those who were only observed, highlighting controversies regarding its indications. Despite this, SLNB demonstrated improved locoregional disease control, provided more accurate staging, and avoided extensive lymphadenectomies [4].

The sentinel lymph node positivity rate in stage I tumors (T1N0M0) ranges from 5% to 8%. However, if criteria such as age, tumor size ≥ 0.8 mm, location on the trunk or extremities, or minimal/absent lymphocytic infiltrate are present, positivity rates can reach 30% [5].

Another study identified that lesions with ulceration, Breslow ≥ 0.75 mm, and Clark IV had positivity rates of 6.3–11%, while neoplasms without these characteristics had positivity rates below 5% [6].

A retrospective study from the years 1999–2007 concluded that nodular histological type and Breslow thickness were significant predictors of positivity. Specifically, 52% of nodular melanomas had positive SLNB, and each unit increase in Breslow thickness represented a 13% increased chance of positivity. Clark classification and ulceration were not significant in that study [7].

In a systematic review and meta-analysis of thin melanomas, across 60 studies including 10,928 patients in total, the overall positivity rate for lymph nodes ≤ 1 mm was 4.5%. For lymph nodes with Breslow ≥ 0.75 mm, Clark IV/V, and mitoses ≥ 1/mm², rates increased to 8.8%, 7.3%, and 26.6%, respectively [8].

The high melanoma rates in Blumenau have attracted the interest of several researchers. This study complements a previously published study of 62 patients who underwent SLNB, aiming to identify those most likely to benefit from the procedure [9].

Thus, this study aims to evaluate risk factors related to the pathological analysis of the primary lesion and to assess the epidemiological profile of melanoma patients in the Blumenau region.

Tab. 1. Distribution of absolute and relative frequencies, means, and 95% confidence estimates of patients' sociodemographic characteristics.

Characteristics	Number of Patients (N = 135)	95% CI
Sex		
male	68 (50.4%)	(41.94–58.8)
female	67 (49.6%)	(41.2–58.06)
Age (years)		
20–30	12 (8.9%)	(4.09–13.69)
30–40	12 (8.9%)	(4.09–13.69)
40–50	27 (20%)	(13.25–26.75)
50–60	33 (24.4%)	(17.2–31.69)
60–70	32 (23.7%)	(16.53–30.88)
70–80	14 (10.4%)	(5.23–15.51)
80–90	5 (3.7%)	(Raw data)
	Mean ± SD	**95% CI**
age (male) (N = 68)	(54.84 ± 12.75)	(51.81–57.87)
age (female) (N = 67)	(51.7 ± 16.58)	(47.73–55.67)
age (both) (N = 135)	(53.28 ± 14.8)	(50.78–55.78)

CI – confidence interval, SD – standard deviation

Methodology

Study design

This is a retrospective cross-sectional study.

Population/sample

Medical records of all patients diagnosed with cutaneous melanoma in Blumenau, referred for sentinel lymph node biopsy at the Cintilus nuclear medicine service from 2008 to June 2017, were analyzed.

Inclusion criteria

Patients over 18 years old who signed the informed consent form, diagnosed with cutaneous melanoma, and indi-

cated for biopsy at the nuclear medicine service.

Exclusion criteria

Patients with incomplete or illegible medical records.

Data collection

The variables analyzed were: Breslow classification, Clark classification, regression, ulceration, histological subtype of the primary tumor, and sex.

Pathological data, including Breslow classification, Clark classification, regression, ulceration, and histological subtype, were obtained from pathology laboratory records.

The **Breslow classification** consists of five grades: In situ (Tis); ≤ 1.00 mm (T1); > 1 and ≤ 2 (T2); > 2 and ≤ 4 (T3); > 4 (T4). The **Clark classification** comprises five levels: In situ (I); papillary dermis (II); papillary dermis up to the papillary-reticular dermis boundary (III); reticular dermis up to the hypodermis (IV); hypodermis (V) [10].

Regression is the reduction of tumor volume due to the host's immune response. Clinically, regression may manifest as total or partial volume reduction, depigmentation, division of the original lesion into multiple smaller lesions, depression, or atrophy at the site. In this study, only histological regression, identified from the pathologist's report, was evaluated. Regression was classified as present or absent.

Ulceration is described as a biological event characterized by the absence of epidermis over the tumor. The presence or absence of ulceration was determined from the pathological report.

Location refers to the origin of the primary lesion, categorized as head and neck, upper limbs, lower limbs, or trunk.

Histological subtype was classified as nodular, lentigo maligna, acrolentiginous, superficial spreading, or desmoplastic.

Sex was determined from the patient's medical record.

Data analysis

Patients were divided into two groups: those with a positive SLNB diagnosis and those with a negative diagnosis. Data analysis was conducted using specific statistical methods to identify predictive factors associated with sentinel lymph node positivity. Data were organized into descriptive tables containing absolute and relative frequencies, means, standard deviations, and 95% confidence interval estimates.

For associations, patients were allocated into positive and negative SLNB groups, and the Chi-square test of independence was used. For quantitative variables, the Shapiro-Wilk test was applied to assess normality. The Student's t-test (parametric) and Mann-Whitney test (non-parametric) were used for group comparisons. Statistical significance was considered when $P < 0.05$. Data were entered into a spreadsheet and analyzed using Microsoft Excel 2016 and Statistica version 7, 2004 (StatSoft, Inc.).

Ethical considerations

This project was submitted to Plataforma Brasil and approved by the Ethics and Research Committee of FURB. CAAE: 67388717.5.0000.5370.

Results

Of the 201 patients referred to the nuclear medicine service, 66 were excluded due to incorrect diagnosis, missing medical records, or records lacking necessary information.

From the analysis of medical records of 135 patients diagnosed with cutaneous melanoma who underwent sentinel lymph node biopsy, eight variables were evaluated: sex, age, histological subtype, presence or absence of ulceration, presence or absence of regression, location, and Breslow and Clark classifications. However, 15 patients lacked complete information, reducing the sample size for positive and negative groups to N = 120.

The mean age of the sample was 53.2 years. Of the patients, 68 were male (50.4%) and 67 were female (49.6%), as shown in Tab. 1. Despite a male predominance in the positive SLNB subgroup (58.8%, N = 10), there was no statistically significant correlation. Similarly, no significant association was found between age and exam positivity, with a Student's t-test yielding P = 0.8691.

Tab. 2 shows the distribution of absolute and relative frequencies, means, and 95% confidence estimates of specific patient characteristics.

Tab. 3 shows the associations between characteristics and exam results using the Chi-square test of independence. Only the positive and negative groups (N = 120) were considered, excluding 15 unclassified cases. There were 17 positive cases and 103 negative cases.

The following statistical significances were observed:

1. **Type:** superficial spreading was more frequent in negatives, and nodular was more frequent in positives ($P < 0.001$);
2. **Ulceration:** more prevalent in the positive group ($P = 0.0018$);
3. **Breslow:** higher mean classification in the positive group ($P = 0.0002$, Mann-Whitney test);
4. **Clark:** higher classification in positives, lower in negatives ($P = 0.0153$).

Regarding histological subtype, the most frequent subtypes were superficial spreading melanoma (66.7%, N = 80) and nodular (14.2%, N = 17). Among positive SLNB cases, 41.2% (N = 7) were nodular, indicating an association with positivity ($P < 0.001$, Chi-square test). In the negative group, superficial spreading was predominant (72.8%, N = 75), associated with negativity ($P < 0.001$).

Ulceration was statistically significant, with a higher prevalence in the positive group ($P = 0.0018$, Chi-square test).

For regression, all positive SLNB patients showed regression, as did 85.4% (N = 88) of negative patients, with no statistical significance.

Location showed a predominance in the back (32.5%, N = 39), followed by lower limbs (20%), upper limbs, and trunk (15% each). In positive SLNB cases, the trunk was preferred, but no statistical significance was found.

By Breslow classification, all patients with lesions < 1 mm had negative SLNB (24.3%, N = 25). Positive cases were predominantly in the $1 \leq b \leq 4$ range (58.8%, N = 10). Positive SLNB patients had a higher mean Breslow classification (4.25) compared to negatives (2.2), with an association ($P < 0.0002$, Mann-Whitney test).

Tab. 2. Distribution of absolute and relative frequencies, means, and 95% confidence estimates of specific patient characteristics.

Characteristics	Number of patients (N = 135)	95% CI
Type		
superficial spreading	90 (66.7%)	(58.71–74.62)
nodular	20 (14.8%)	(8.82–20.81)
in situ	5 (3.7%)	(0.52–6.89)
lentiginous/acral	5 (3.7%)	(0.52–6.89)
lentigo	2 (1.5%)	(0–3.52)
microinvasive	1 (0.7%)	(0–2.19)
desmoplastic	1 (0.7%)	(0–2.19)
not reported	11 (8.1%)	(3.53–12.76)
Ulceration		
positive	31 (23%)	(15.87–30.06)
negative	104 (77%)	(69.94–84.13)
Regression		
positive	17 (12.6%)	(7–18.19)
negative	118 (87.4%)	(81.81–93)
Location		
back	44 (32.6%)	(24.69–40.5)
lower limbs	28 (20.7%)	(13.9–27.58)
upper limbs	20 (14.8%)	(8.82–20.81)
trunk	19 (14.1%)	(8.21–19.94)
head/neck	19 (14.1%)	(8.21–19.94)
inguinal	1 (0.7%)	(0–2.19)
back and upper limbs	1 (0.7%)	(0–2.19)
not reported	3 (2.2%)	(0–4.71)
Breslow (classification 1)		
< 1	27 (20%)	(13.25–26.75)
1 ≤ b ≤ 4	76 (56.3%)	(47.93–64.66)
> 4	17 (12.6%)	(7–18.19)
not reported	15 (11.1%)	(5.81–16.41)

Characteristics	Number of patients (N = 135)	95% CI
Breslow (classification 2)		
< 0.75	16 (11.9%)	(6.4–17.3)
0.75 ≤ b ≤ 1.00	16 (11.9%)	(6.4–17.3)
1.00 < b ≤ 2.00	10 (7.4%)	(2.99–11.83)
> 2.00	78 (57.8%)	(49.45–66.11)
not reported	15 (11.1%)	(5.81–16.41)
	Mean ± SD	**95% CI**
Breslow (male) (N = 62)	(2.84 ± 2.94)	(2.11–3.57)
Breslow (female) (N = 58)	(2.19 ± 2.82)	(1.47–2.92)
Breslow (both) (N = 120)	(2.53 ± 2.89)	(2.01–3.04)
Clark		
I	4 (3%)	(0.1–5.82)
II	28 (20.7%)	(13.9–27.58)
III	41 (30.4%)	(22.61–38.13)
IV	45 (33.3%)	(25.38–41.29)
V	5 (3.7%)	(0.52–6.89)
II and III	1 (0.7%)	(0–2.19)
not reported	11 (8.1%)	(3.53–12.76)
AP		
negative	63 (46.7%)	(38.25–55.08)
positive	10 (7.4%)	(2.99–11.83)
not reported	62 (45.9%)	(37.52–54.33)
IHC		
negative	101 (74.8%)	(67.49–82.14)
positive	7 (5.2%)	(1.44–8.93)
not reported	27 (20%)	(13.25–26.75)
Results		
negative	103 (76.3%)	(69.12–83.47)
positive	17 (12.6%)	(7–18.19)
not classified	15 (11.1%)	(5.81–16.41)

CI – confidence interval, IHC – immunohistochemistry, SD – standard deviation

Clark classification also showed statistical significance. Among positive SLNB patients, none had Clark I or II, with a predominance of Clark IV (52.9%, N = 9), followed by Clark III (23.5%, N = 4) and Clark V (5.9%, N = 1), with P = 0.0153 (Chi-square test).

Tab. 4 presents the results of the Shapiro-Wilk normality test for quantitative variables. Age showed a normal distribution, while Breslow did not (P < 0.05), suggesting the use of the non-parametric Mann-Whitney test (see the results in Tab. 3).

Tab. 3. Association between characteristics and exam results.

Characteristics	Positive (N = 17)	Negative (N = 103)	Total (N = 120)	P
Sex				
male	10 (58.8%)	51 (49.5%)	61 (50.8%)	0.4769
female	7 (41.2%)	52 (50.5%)	59 (49.2%)	
	(Mean ± SD)	**(Mean ± SD)**	**(Mean ± SD)**	
Age (years)	(53.35 ± 15.25)	(52.73 ± 14.32)	(52.82 ± 14.39)	0.8691(*)
Type				
superficial spreading	5 (29.4%)	75 (72.8%)	80 (66.7%)	**< 0.001(a)**
nodular	7 (41.2%)	10 (9.7%)	17 (14.2%)	
in situ	0 (0%)	3 (2.9%)	3 (2.5%)	
lentiginous/acral	1 (5.9%)	4 (3.9%)	5 (4.2%)	
lentigo	0 (0%)	2 (1.9%)	2 (1.7%)	
microinvasive	0 (0%)	1 (1%)	1 (0.8%)	
desmoplastic	0 (0%)	1 (1%)	1 (0.8%)	
not reported	4 (23.5%)	7 (6.8%)	11 (9.2%)	
Ulceration				
negative	8 (47.1%)	84 (81.6%)	92 (76.7%)	**0.0018**
positive	9 (52.9%)	19 (18.4%)	28 (23.3%)	
Regression				
positive	17 (100%)	88 (85.4%)	105 (87.5%)	0.0926
negative	0 (0%)	15 (14.6%)	15 (12.5%)	
Location				
back	7 (41.2%)	32 (31.1%)	39 (32.5%)	0.1210(b)
lower limbs	3 (17.6%)	21 (20.4%)	24 (20%)	
upper limbs	0 (0%)	18 (17.5%)	18 (15%)	
trunk	5 (29.4%)	13 (12.6%)	18 (15%)	
head/neck	1 (5.9%)	16 (15.5%)	17 (14.2%)	
inguinal	1 (5.9%)	0 (0%)	1 (0.8%)	
back and upper limbs	0 (0%)	1 (1%)	1 (0.8%)	
not reported	0 (0%)	2 (1.9%)	2 (1.7%)	

P – the value from Chi-square test of independence. If $P < 0.05$, then significant association.

() P-value from Student's t-test for independent samples (parametric test).

* If $P < 0.05$, then significant differences.

**P-value from Mann-Whitney test for independent samples (non-parametric test). If $P < 0.05$, then significant differences.

(a) For the Chi-square test, only "superficial spreading" and "nodular" types were considered due to their higher frequency (limitation of the Chi-square test, which cannot have more than 25% of expected frequencies below 5).

(b) For location, only the most frequent locations (back, lower limbs, upper limbs, trunk) were used due to Chi-square test limitations. The result was not significant.

(c) For Breslow, the Chi-square test excluded patients without classification.

(d) For Clark association with exam positivity, the Chi-square test grouped levels I and II, and IV and V. Patients without classification and one with dual classification (II and III) were excluded (the same reason as above).

Tab. 3 – continuing. Association between characteristics and exam results.

	(Mean ± SD)	(Mean ± SD)	(Mean ± SD)	
Breslow (classification 1)				
< 1	0 (0%)	25 (24.3%)	25 (20.8%)	**0.0319(c)**
1 ≤ b ≤ 4	10 (58.8%)	59 (57.3%)	69 (57.5%)	
> 4	4 (23.5%)	10 (9.7%)	14 (11.7%)	
not reported	3 (17.6%)	9 (8.7%)	12 (10%)	
Breslow (classification 2)				
< 0.75	0 (0%)	15 (14.6%)	15 (12.5%)	0.1196
0.75 ≤ b ≤ 1.00	0 (0%)	14 (13.6%)	14 (11.7%)	
1.00 < b ≤ 2.00	1 (5.9%)	9 (8.7%)	10 (8.3%)	
> 2.00	13 (76.5%)	56 (54.4%)	69 (57.5%)	
not reported	3 (17.6%)	9 (8.7%)	12 (10%)	
	(Mean ± SD)	**(Mean ± SD)**	**(Mean ± SD)**	
Breslow	(4.25 ± 3.11)	(2.2 ± 2.79)	(2.46 ± 2.9)	**0.0002()****
Clark				
I	0 (0%)	2 (1.9%)	2 (1.7%)	**0.0153(d)**
II	0 (0%)	26 (25.2%)	26 (21.7%)	
III	4 (23.5%)	33 (32%)	37 (30.8%)	
IV	9 (52.9%)	31 (30.1%)	40 (33.3%)	
V	1 (5.9%)	2 (1.9%)	3 (2.5%)	
II and III	0 (0%)	1 (1%)	1 (0.8%)	
not reported	3 (17.6%)	8 (7.8%)	11 (9.2%)	

P – the value from Chi-square test of independence. If P < 0.05, then significant association.

() P-value from Student's t-test for independent samples (parametric test).

* If P < 0.05, then significant differences.

**P-value from Mann-Whitney test for independent samples (non-parametric test). If P < 0.05, then significant differences.

(a) For the Chi-square test, only "superficial spreading" and "nodular" types were considered due to their higher frequency (limitation of the Chi-square test, which cannot have more than 25% of expected frequencies below 5).

(b) For location, only the most frequent locations (back, lower limbs, upper limbs, trunk) were used due to Chi-square test limitations. The result was not significant.

(c) For Breslow, the Chi-square test excluded patients without classification.

(d) For Clark association with exam positivity, the Chi-square test grouped levels I and II, and IV and V. Patients without classification and one with dual classification (II and III) were excluded (the same reason as above).

Tab. 4. Results of the Shapiro-Wilk normality test. Quantitative variables.

Variables (exam result N/P)	N	Range	Mean ± SD	95% CI	(Median ± IQR)	P	Normal?
age (negative)	103	(20–81)	(52.73 ± 14.32)	(49.96–55.49)	(54 ± 9.5)	0.2485	yes
age (positive)	17	(28–85)	(53.35 ± 15.25)	(45.51–61.19)	(53 ± 6.5)	0.5363	yes
Breslow (negative)	94	(0.2–20)	(2.2 ± 2.79)	(1.63–2.76)	(1.23 ± 0.74)	< 0.001	no
Breslow (positive)	14	(1.5–11)	(4.25 ± 3.11)	(2.45–6.05)	(2.95 ± 2.13)	0.0047	no

IQR – interquartile range, P – the value from Shapiro-Wilk test; if P < 0.05, then non-normal distribution

Discussion

A clinical study in the United States, involving 70 major centers, identified ulceration and age > 60 years as predictors of sentinel lymph node (SLN) positivity [11]. Conversely, another U.S. study found that advanced age (> 65 years) was associated with a particularly low SLN positivity rate [12]. A study in southern Brazil, while not evaluating age, found significance for ulceration (P = 0.059). A literature review from Silva et al. concluded that ulceration is associated with positive sentinel lymph nodes [13]. Regarding age, this study diverged due to lack of statistical significance, but ulceration was consistent with other studies, as it is a significant marker of aggressiveness in cutaneous melanoma, even affecting tumor staging [10].

In a study from northeastern Brazil, the predominant histological subtype in positive SLNB cases was nodular, followed by superficial spreading [14]. An international study involving 1,250 melanoma patients found superficial spreading as the predominant histological pattern in positive SLNB cases, followed by nodular [6]. A similar study found nodular histology predominant in 62.5% of positive biopsy cases [9]. A European study suggested that patients with nodular melanomas had a higher risk of SLNB positivity compared to those with superficial spreading melanomas (P = 0.02) [15]. This study identified significance for superficial spreading in negative cases and nodular histology in positive cases. This association with nodular subtype may be due to its rapid vertical growth, unlike superficial spreading, which tends to grow radially.

Breslow thickness and SLN metastasis size were significantly associated with positive tumors [16]. Lesion thickness > 2 mm was an independent prognostic factor for SLN positivity[17]. The importance of Breslow thickness for SLN positivity is widely recognized in both international and national literature and is a primary recommendation in the Brazilian Melanoma Guideline published in *Anais de Dermatologia* in 2016 [3]. This study confirmed that patients with positive biopsies had a significantly higher mean Breslow level compared to negatives. Regarding the epidemiological profile, most patients had TNM stages T3 and T4, consistent with current literature.

Clark levels are frequently reported as associated with SLN positivity [12]. A British study found a strong correlation between high Clark levels and Breslow thickness [15]. A meta-analysis also considered Clark level significantly associated with SLN positivity [18]. However, another study found a relationship with Clark level but not with other variables [19]. Clark level is a weak predictor of positivity when analyzed alone but becomes significant when combined with other predictive factors [20]. Despite recent studies suggesting Clark levels are weak predictors, this study found significance for Clark IV/V in the positive group.

Although the 2016 Brazilian Melanoma Guideline considers the mitotic index an important prognostic factor, incorporating it as a criterion for SLNB in melanomas with thickness ≥ 0.75 mm and <1 mm, this variable was not analyzed in this study due to inconsistent measurement units, which prevented accurate analysis. However, this variable will be reviewed for future publications.

This study was based on the 7th edition of the AJCC cancer staging manual. During the study, a new edition was published, altering some melanoma staging factors, notably the Breslow thickness threshold, which changed from 0.75 mm to 0.8 mm, representing a limitation of this study.

Conclusion

The findings of this study align with most recent literature. This work serves to guide future research to identify methods that assist both researchers and clinicians in safely indicating invasive procedures, ensuring patients do not undergo unnecessary procedures from which they will not benefit.

This study will also contribute to deepening knowledge about the patterns of melanocytic lesions in the studied region, fostering new research for more in-depth discussions on the topic.

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