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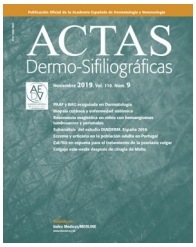

CASE AND RESEARCH LETTER

[Translated article] Cutaneous Melanoma and Sentinel Lymph Node Biopsy: A Single-Center Retrospective Study of 331 Patients in Argentina

Análisis retrospectivo de 331 pacientes con melanoma cutáneo estudiados con ganglio centinela en una sola institución en Argentina

To the Editor:

Cutaneous melanoma (CM) is the leading cause of death due to skin cancer.[1,2] Sentinel node biopsy (SNB) is a minimally invasive procedure that, following the Multicenter Selective Lymphadenectomy Trial (MSLT-1) protocol, is considered to be a prognostic element for MC.[1–5] Other factors associated with prognosis are tumor thickness, mitotic index, location, histologic subtype, ulceration, lymphovascular invasion, regression, lymphocyte infiltrate, age, and sex.[1,3]

Few representative studies exist in South America and our study therefore provides information to the region.[1,6,7] Our objective was to analyze disease-free survival (DFS) and overall survival (OS) in a cohort of patients with CM $\geq$ T1b, assessed using the sentinel node (SN) in a private institution in Argentina. The secondary objective was to identify the risk factors associated with a positive SN.

We performed a retrospective study that included all patients with CM in whom SNB was indicated, between 2006 and 2017. Table 1 summarizes the selection criteria and the variables analyzed. Unfortunately, the mitotic index (MI) was excluded from the analysis due to variability in the histopathology records over the years. Patients were classified by Breslow thickness into 4 groups, and location was divided into head and neck, upper member, lower member, and torso.

OS, DFS, and the statistical relationship between SN and the different factors were analyzed using Kaplan–Meier curves and a Cox regression. The statistical software package Stata® version 13.1, 2016, was used and significance was established for values of $p < .05$.

Of the 1505 patients diagnosed with CM in the study period, 345 were included; 192 (55.6%) were men and the median age was 61.5 years (range, 17–94 years). The median Breslow thickness was 1.88 mm (range, 0.63–12 mm). Table 2 shows a summary of the descriptive analysis.

Of the 345 patients included because they had undergone SNB, only 331 met all the inclusion criteria for the study. SNB was therefore performed only on those patients. Ninety-four (28.4%) were positive and 75 (81.5%) of these underwent lymphadenectomy, which, in 35.9% of cases, revealed additional positive lymph nodes. The median follow-up time was 45 months (range, 0–153 mo) and 58 patients were lost to follow-up. Furthermore, 86 (25%) patients presented a locoregional and/or distant recurrence. Of these, 37 patients had a positive SN. Estimated OS was 77.9% and 66.4% at 5 and 10 years, respectively, whereas estimated DFS was 70.7% and 63.5% at 5 and 10 years, respectively. The locoregional recurrence rate was 18.8%.

Table 3 shows the independent predictive factors for mortality and disease-free survival. Notable factors were Breslow thickness, ulceration, and positive SN.

Our study, while retrospective, provides epidemiologic value regarding CM in South America and confirms the prognostic value of SNB.

Although only patients with SNB were included, the distribution and frequencies were similar to published cases in terms of sex, age, and location.[1,7] The positive-SN rate was 28.4%, which was higher than in other series (15–23%).[2,4] Age was linked to OS and DFS only in the univariate analysis. Previous studies have found that the oldest patients had the worst outcome (>65 y).[8]

The multivariate analysis found that only Breslow thickness (intermediate and thick), ulceration, and positive SN were independent factors for OS and DFS. Inflammation was also significant for DFS only. The classic MSLT-1 protocol determined the importance of SNB for identifying hidden metastasis[2,4,5]; others also found that thickness, ulceration, location, histologic subtype, and SN status were independent factors.[3,8] Other studies also confirmed that ulceration was associated with worse OS and DFS[2–4,8,9]; today it is considered to be a factor associated with poor prognosis, which changes the staging in CM in which it presents.

Five-year OS was 77.8% (less than reported figures) and 72.7% with positive SNB.[2,9] For positive SNB, the multivariate

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Table 1 Characteristics of Patients and Histology.

Characteristics	Number	%
Age, y		
<65	195	56.4
>65	151	43.6
Sex		
Male	192	55.6
Female	153	44.4
Location		
Head and neck	33	9.6
Upper member	54	15.7
Lower member	150	43.5
Torso	105	30.4
Other	3	.8
Histologic classification		
Nodular	152	44.1
Surface spreading	150	43.5
Lentigo maligna	10	2.9
Others	33	9.5
Growth pattern		
Vertical and radial	185	53.6
Vertical	151	43.8
Radial	7	2
Not available	2	0.6
Breslow thickness		
T1 (0–1 mm)	90	26.1
T2 (1.01–2 mm)	108	31.3
T3 (2.01–4 mm)	71	20.6
T4 (>4.01 mm)	76	22
Clark level		
Level I	2	0.6
Level II	12	3.5
Level III	177	51.3
Level IV	140	40.6
Level V	14	4
Ulceration		
Yes	103	67.5
No	233	29.9
Not available	9	2.6
Perineural invasion		
Yes	9	2.6
No	241	69.9
Not available	95	27.5
Lymphovascular invasion		
Yes	25	7.3
No	230	66.7
Not available	90	26
Regression		
Yes	39	11.3
No	285	82.6
Not available	21	6.1
Inflammatory infiltrate		
Yes	186	53.9
No	138	40
Not available	21	6.1

Table 2 Characteristics of Patients and Histology.

Characteristics	Number	%
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Table 3 Predictive Factors for Disease-Free Survival and Overall Survival: Univariate and Multivariate Analyses.

	DFS						OS					
	Univariate			Multivariate			Univariate			Multivariate		
	HR	95% CI	*p*	HR	95% CI	*p*	HR	95% CI	*p*	HR	95% CI	*p*
Sex	0.7	0.4–1	.058	—	—	—	0.6	0.4–1	.056	—	—	—
Age >65 years	1.5	1–2.3	.048			NS	1.5	1–2.3	.048			NS
Primary tumor site	0.6	0.4–1	.058			—	1.1	0.8–1.4	.747	—	—	—
Tumor subtype: nodular	3.3	1.9–5.5	<.001			NS	3.6	1.9–6.8	<.001			NS
Breslow thickness, mm	2.6	2.1–3.4	<.001	1.8	1.1–3.2	0.042	2.6	1.9–3.4	<.001	1.6	1.2–2.5	.045
Clark Level	2.6	1.9–3.5	<.001			NS	2.7	1.9–3.9	<.001			NS
Ulceration	2.9	2.1–4.1	<.001			NS	3.8	2.3–6.2	<.001	2.1	1.1–3.9	.026
Regression	0.2	0.1–0.7	.135	—	—	—	0.1	0.2–0.8	.028			NS
Inflammatory infiltrate	0.5	0.3–0.9	.02	0.6	0.3–0.95	.03	0.5	0.3–0.9	.02			NS
Perineural invasion	0.8	0.7–1.1	.242	—	—	—	0.8	0.6–1.1	.311	—	—	—
Positive sentinel node	4.9	3.1–7.6	<.001	2.8	1.7–4.6	<.001	5.6	3.3–9.5	<.001	3.4	1.9–5.9	<.001
Extracapsular extension	2.4	1.3–4.3	.005			NS	3.4	1.7–6.6	<.001			NS

Abbreviations: CI indicates confidence interval; DFS, disease-free survival; HR, hazard Ratio; NS, not significant; OS, overall survival.

analysis only found Breslow thickness as a prognostic factor, similar to the findings of other studies.[9] The MI, while the subject of debate, may be linked to lymph-node metastasis. Tejera-Vaquerizo et al.[8] found that the MI directly affected OS, DFS and a positive SN. In our study, it was not possible to analyze the MI due to lack of data.

An interesting point of this study is that the inflammatory infiltrate, defined as the presence of intratumoral lymphocytes, is interpreted as a protective factor in the multivariate analysis for DFS. This continues to be the subject of debate, given that some studies have found that its presence improves survival, whereas others have found the opposite.[8,10]

Limitations of our study include its retrospective nature and the inability to analyze lymphovascular invasion, MI, and the rate of SN false negatives.

In conclusion, Breslow thickness and SN status are the main prognostic factors associated with OS and DFS. This cohort confirms the prognostic value of SNB and represents a new epidemiologic contribution for South America.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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