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ORIGINAL ARTICLE

Sentinel Lymph Node Biopsy in Patients With Melanoma

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KEYWORDS
Melanoma;
Sentinel lymph node biopsy;
Prognostic value

Abstract
Introduction and objectives: The incidence of melanoma is currently increasing worldwide. One of the factors influencing disease prognosis is the presence of regional lymph node metastases. Sentinel lymph node biopsy attempts to identify subclinical lymph node metastasis as a prognostic factor in the disease. The aim of this study was to analyze differences between patients with melanoma for whom positive or negative results were obtained in sentinel lymph node biopsy and to assess the impact of the technique on disease prognosis.
Material and methods: Sentinel lymph node biopsy was carried out in patients with melanoma of the following characteristics: Breslow thickness ≥1mm, Breslow thickness <1mm with ulceration, Clark level IV-V, or regression. Lymphadenectomy was performed in patients with positive sentinel node biopsy. Data were also collected on the following variables: sex, age, skin phototype, site and type of melanoma, Breslow thickness, Clark level, ulceration, regression, cancer stage at diagnosis, TNM classification, change in cancer stage during follow-up, and death due to melanoma.
Results: Positive sentinel node biopsies were recorded in 19.44% of patients. Positive results were associated with the following variables: nodular melanoma (crude odds ratio [ORc] compared with superficial spreading melanoma, 3.44; 95% confidence interval [CI], 1.33–8.90); Breslow thickness >2.0, for a thickness of 2.1–4.0 (ORc, 21.12; 95% CI, 2.60–172.03) and for a thickness >4.0 (ORc, 23.25; 95% CI, 2.44–221.73); Clark level IV (ORc, 8.73; 95% CI, 1.03–74.12); ulceration (ORc, 4.86; 95% CI, 1.58–14.90); T3 (ORc, 4.20; 95% CI, 1.52–11.63) and T4 (ORc, 4.67; 95% CI, 1.27–17.15) in the TNM

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classification; change in cancer stage during follow-up (ORc, 7.20; 95% CI, 2.25-22.99); and death due to melanoma (ORc, 8.67; 95% CI, 3.62-96.15).

Conclusions: These results confirm the prognostic importance of sentinel lymph node biopsy, which facilitates identification of patients with a greater tendency towards disease progression and death due to melanoma.

PALABRAS CLAVE
Melanoma;
Biopsia del ganglio centinela;
Valor pronóstico

La técnica del ganglio centinela en pacientes con melanoma

Resumen

Introducción y objetivos: Actualmente existe un aumento mundial de la incidencia de melanoma. Su pronóstico depende entre otros factores de la existencia de metástasis en los ganglios linfáticos regionales. La realización de la biopsia del ganglio centinela persigue la identificación de metástasis ganglionares subclínicas como factor pronóstico de la enfermedad. El presente estudio tiene por objetivo estudiar las diferencias entre los pacientes con melanoma, positivos y negativos a la biopsia del ganglio centinela, y analizar el impacto de esta técnica en su pronóstico.

Material y métodos: Se realizó biopsia del ganglio centinela a los pacientes con melanomas de espesor Breslow ≥ 1 mm o con Breslow < 1 mm y ulceración, nivel de Clark IV-V o regresión. Aquellos con biopsia positiva fueron sometidos a linfadenectomía.

Además, se recogieron las siguientes variables: sexo, edad, fototipo, localización y tipo de melanoma, niveles Breslow y Clark, ulceración, regresión, estadio inicial, TNM, cambio de estadio y fallecimiento por melanoma.

Resultados: El 19,44% de los pacientes presentó ganglios positivos. Esta positividad se presentó asociada con el melanoma nodular (odds ratio cruda [ORc]: 3,44; intervalo de confianza al 95% [IC 95%]: 1,33-8,90) con respecto al melanoma de extensión superficial Breslow superior a 2,0 (nivel 2,1-4,0: ORc: 21,14; IC 95%: 2,60-172,03, nivel > 4,0: ORc: 23,25; IC 95%: 2,44-221,73), nivel Clark IV (ORc: 8,73; IC 95% 1,03-74,12), ulceración (ORc: 4,86; IC 95%: 1,58-14,90), estadios T3 y T4 (T3: ORc: 4,20; IC 95%: 1,52-11,63; T4: ORc: 4,67; IC 95% 1,27-17,15), cambio de estadio (ORc: 7,20; IC 95%: 2,25-22,99) y fallecimiento por melanoma (ORc: 8,67; IC 95%: 3,62-96,15).

Conclusiones: Estos resultados confirman la importancia pronóstica de la biopsia del ganglio centinela, que permite identificar a los pacientes con mayor tendencia a la progresión de la enfermedad y fallecimiento por melanoma.

Introduction

The epidemiology of melanoma differs from that of any other tumor.[1] The incidence of melanoma increases by between 3% and 7% annually in countries where the population is predominantly white.[2] On this basis, it is estimated that the incidence will double every 10 to 20 years. This increase has led to the classification of melanoma as a worldwide epidemic[3] and makes it a significant public health concern throughout the world.[4]

The continent with the highest incidence of melanoma is Oceania; in Australia and New Zealand, it is the fourth most common cancer in men and the third most common in women.[5] The second-highest incidence is found in North America, with Europe in third place.[5]

In Europe, approximately 60 000 new cases are diagnosed each year (26 100 in men and 33 300 in women), which accounts for 1% of all cancers diagnosed. The incidence of melanoma in Europe is slightly higher in women than men, with 7 and 6 cases per 100 000 population per year, respectively. This is in contrast to the trend in other parts of the world with a higher incidence, such as Australia, New Zealand, and the United States, where the incidence is higher in men than women. The rates also follow a North-South gradient. The highest incidences are found in Scandinavia—with approximately 15 cases per 100 000 population per year[5]—and Mediterranean countries have the lowest rates—between 5 and 7 cases per 100 000 population per year in Spain.[6] Recent years have, nevertheless, also seen a substantial increase in these countries.[7]

Alongside this increase in the incidence of melanoma, recent years have seen a growth in research effort aimed at understanding this aggressive tumor. The biological behavior of malignant melanoma is determined by a series of different factors that will influence the prognosis and, consequently, the management of the disease. Significant advances have been made in our understanding of the genetics of this tumor in an effort to determine its molecular basis,[8] although molecular, chromosomal, immunohistochemical, or histologic markers that could predict its behavior remain unavailable.[9] Experts agree, however, that the prognosis of patients diagnosed with malignant melanoma depends

essentially on 2 factors: the depth of the primary tumor (Breslow thickness) and the presence or absence of regional lymph node metastases.[10]

Sentinel lymph node biopsy (SLNB) has become the most accurate diagnostic technique with which to determine the histologic stage of regional lymph nodes. It is a recently introduced diagnostic technique designed to facilitate the identification of subclinical lymph node metastases with minimal morbidity.[11] The technique has superseded other conventional noninvasive techniques such as lymph node ultrasound or positron emission tomography, which require greater tumor volume in order to detect metastasis and are therefore associated with delayed diagnosis. Currently, the histologic stage of sentinel lymph nodes (SLN) is the most important prognostic factor for survival, and it has been widely used to standardize the criteria applied and results obtained among different working groups.[12] Furthermore, some studies have confirmed the prognostic value of SLNB for the survival of patients with melanoma.[13,14]

The aim of this study was to compare the characteristics of patients with melanoma in whom SLNB had detected positive lymph nodes with those in whom a negative result was obtained and to analyze the prognostic value of the technique.

Materials and Methods

Study Population

This descriptive study included patients attending the Department of Dermatology at Hospital Universitario Dr. Peset in Valencia, Spain, with a diagnosis of melanoma including a pathology report and in whom SLNB was performed between 1998 and 2008 (144 patients).

Methodology

Sentinel Lymph Node Biopsy

SLNB was performed in all patients in whom melanoma with a Breslow thickness of at least 1 mm had been excised and in whom no palpable enlarged lymph nodes had been present at diagnosis. In addition, given that a notable proportion of patients (6%) with melanomas less than 1 mm thick have been shown to have subclinical metastasis following SLNB,[15] patients were also included on a case-by-case basis if they had melanoma less than 1 mm thick along with additional risk factors such as ulceration, Clark level IV or V, or histologic signs of regression, as indicated in the latest guidelines for the prevention and treatment of melanoma.[10,16]

Biopsy was performed by first identifying the SLN by labeling with radioactive isotopes; regional lymph nodes were identified and labeled by isotope lymphography following perilesional intradermal injection of contrast agent (0.5-1 mCi of ^{99m}Tc-labeled antimony sulfide colloid), with the dose divided into 2 to 4 injections. The SLNs were then identified and biopsied.

A pathology study was then done to identify tumor cells. The nodes were fixed in 5% formaldehyde and embedded in paraffin for routine histologic analysis with hematoxylin-eosin and immunohistochemistry with S100 and HMB45. Serial sections were taken through the entire specimen.

In those patients with positive SLNB, regional lymph node dissection was performed in a second surgical intervention to remove the affected lymph node chain.

Follow-up was performed using established protocols for melanoma according to the TNM stage of the tumor.[17]

In parallel, a retrospective study was performed to obtain information from the patient's clinical history according to a defined protocol. Data were collected on sex, age at diagnosis (≤ 25, 26–45, 46–65, >65 years), skin phototype (I, II, or III), melanoma site (head, trunk, upper limb, lower limb, mucosa), histologic type of the melanoma (superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma, acral lentiginous melanoma, polypoid melanoma, amelanotic melanoma), Breslow thickness (≤ 1.0, 1.1–2.0, 2.1–4.0, >4.0 mm), Clark level (I, II, III, IV, V), histologic ulceration (yes/no), histologic regression (yes/no), initial stage (IA, IB, IIA, IIB, IIC, III), TNM (T1, T2, T3, T4), change in melanoma stage (yes/no), and death due to melanoma (yes/no).

Statistical Analysis

Quantitative variables were presented as means (SD) and qualitative variables as absolute and relative frequencies. The study variables were compared by Pearson χ^2 test for qualitative variables and *t* test for quantitative variables. In the event that cells contained n<5, the Fisher exact test was used. The cutoff for statistical significance was $P<.05$.

Results

A total of 144 patients diagnosed with melanoma between 1998 and 2008 underwent SLNB and were included in the study. The mean follow-up was 58.45 months. Table 1 shows the general characteristics of the patients. Male patients accounted for 58.33% of the group and most patients were older than 45 years (mean age, 55.10 [15.89] years). The most common skin phototype was type II and there were no patients with a type IV skin phototype in the study population. In most cases, the melanoma was located on the trunk (54.17%), followed by the upper limb (29.86%) and then the lower limb (13.89%). There were only 2 cases of melanoma on the head and 1 case of melanoma on the genital mucosa of the vulva. More than 90% of melanomas corresponded to nodular melanoma (45.14%) or superficial spreading melanoma (45.14%). Most tumors had a Breslow thickness between 1.1 and 2.0 mm (mean depth, 2.16 [1.66] mm). Most of the melanomas had a Clark level of III (54.86%) or IV (26.39%). Ulceration was present in 60.42% of the melanomas studied. There was no reference to regression in the histories of 119 out of 144 cases; in 15 of the 25 patients in whom regression was mentioned, histologic regression was present (60%). The most common initial stage was IB (31.25%) and the most common tumor stage in the TNM classification was T2 (38.89%). In the majority of patients, the initial stage did not change during

Table 1 General and Clinical Characteristics of the Study Population (n = 144)

	N	Percentage (95% CI)	*P*[a]
Sex			
Male	84	58.33 (50.15-66.18)	.005
Female	60	41.67 (33.82-49.85)	
Age			
≤25 y	9	6.25 (3.09-11.16)	<.001
26-45 y	30	20.83 (14.79-28.04)	
46-65 y	60	41.67 (33.82-49.85)	
>65 y	45	31.25 (24.08-39.17)	
Skin phototype			
I	10	6.94 (3.58-12.03)	<.001
II	87	60.42 (52.26-68.16)	
III	47	32.64 (25.36-40.61)	
Site of the melanoma			
Head	2	1.39 (0.23-4.51)	<.001
Trunk	78	54.17 (45.98-62.18)	
Upper limb	20	13.89 (8.94-20.28)	
Lower limb	43	29.86 (22.81-37.71)	
Mucosa	1	0,69 (0.003-3.38)	
Histologic type of the melanoma			
SSM	65	45.14 (37.15-53.32)	<.001
Nodular	65	45.14 (37.15-53.32)	
LMM	4	2.78 (0.89-6.56)	
ALM	4	2.78 (0.89-6.56)	
Polypoid	4	2.78 (0.89-6.56)	
Amelanotic	2	1.39 (0.23-4.51)	
Breslow thickness, mm			
≤1.0	33	22.92 (16.60-30.31)	<.001
1.1-2.0	56	38.89 (31.18-47.04)	
2.1-4.0	38	26.39 (19.68-34.04)	
>4.0	14	9.72 (5.64-15.41)	
Clark level			
I	0	—	<.001
II	13	9.03 (5.11-14.58)	
III	79	54.86 (46.68-62.85)	
IV	38	26.39 (19.68-34.04)	
V	1	0.69 (0.003-3.38)	
Histologic ulceration			
No	57	39.58 (31.84-47.74)	<.001
Yes	87	60.42 (52.26-68.16)	
Histologic regression[b]			
No	10	40.00 (22.41-59.79)	.157
Yes	15	60.00 (40.21-77.59)	
Initial stage			
IA	14	9.72 (5.64-15.41)	<.001
IB	45	31.25 (24.08-39.17)	
IIA	28	19.44 (13.59-26.52)	
IIB	24	16.67 (11.24-23.43)	
IIC	5	3.47 (1.28-7.53)	
III	28	19.44 (13.59-26.52)	
TNM Classification			
T1	32	22.22 (15.99-29.56)	<.001
T2	56	38.89 (31.18-47.04)	

Table 1 *(continued)*

	N	Percentage (95% CI)	*P*[a]
T3	41	28.47 (21.55-36.25)	
T4	15	10.42 (6.18-16.24)	
Change in stage			
No	130	90.28 (84.59-94.36)	<.001
Yes	14	9.72 (5.64-15.41)	
Death due to melanoma			
No	135	93.75 (88.84-96.91)	<.001
Yes	9	6.25 (3.09-11.16)	

Abbreviations: ALM, acral lentiginous melanoma; LMM, lentigo maligna melanoma; SSM, superficial spreading melanoma; TNM, tumor, node, metastasis.
[a]χ^2 test.
[b]Only referred to in 25 of the clinical histories reviewed.

the follow-up period (90.28%); a change in stage only occurred in 14 patients (9.72%). Nine patients (6.25%) died due to melanoma.

A SLN was identified in 142 out of 144 patients (98.61%). In the 2 remaining patients (1.39%), the contrast agent did not migrate and the location of the SLN could not be determined. Table 2 shows the characteristics of the SLNs identified in the 142 patients. The SLN was located in a single lymphatic chain in 84.03% of patients. SLNs were identified in 2 different lymphatic chains in 13.19% and in 3 lymphatic chains in only 1.39% of patients. The majority of patients (72.92%) only had a single SLN.

Micrometastasis (detected by histology and immunohistochemistry) was observed in 28 out of 142 patients (19.44%), and in 85.71% of those, only a single lymph node was affected. In 5 (17.86%) of the 28 patients undergoing elective lymph node dissection to remove the affected lymph node station, further lymph nodes containing melanoma metastases were identified.

Table 3 shows the characteristics of the patients with positive (28) and negative (114) lymph nodes.

We did not observe a statistically significant association between sex, age, skin phototype, or tumor site and the presence of positive lymph nodes. We did, however, observe an association between the presence of positive lymph nodes and the histologic type of the melanoma. Specifically, there was an association between nodular melanoma and the presence of positive lymph nodes (crude odds ratio [cOR], 3.44; 95% confidence interval [CI], 1.33-8.90 compared with superficial spreading melanoma). We also found an association between tumor thickness and the presence of positive lymph nodes. Breslow thickness of 2.1-4.0 (cOR, 21.14; 95% CI, 2.60-172.03) and >4.0 (cOR, 23.25; 95% CI, 2.44-221.73) were associated with the presence of positive lymph nodes. Likewise, Clark level IV was associated with the presence of positive lymph nodes (cOR, 8.73; 95% CI, 1.03-74.12). A potential association with Clark level V could not be assessed because only 1 patient fell into this category. Ulceration was also associated with the presence of positive SLNs; the likelihood of identifying positive lymph nodes was 4 times greater in patients with ulcerated melanoma (cOR, 4.86; 95% CI, 1.58-14.90). Histologic regression was only reported for 25 patients, none of whom had positive lymph nodes; the association between regression and positive SLNs could therefore not be assessed. No statistically significant association was observed between initial melanoma stage and the presence of positive lymph nodes. However, 28 patients with positive lymph nodes had stage III melanoma, whereas 114 patients without positive lymph nodes had stage I or II melanoma. The tumor stage of the TNM classification also appeared to be associated with the presence of positive lymph nodes. Stage T3 (cOR, 4.20; 95% CI, 1.52-11.63) and T4 (cOR, 4.67; 95% CI, 1.27-17.15) were both associated with greater positivity. Patients with positive SLNs had a greater tendency towards progression of the disease and, therefore, change in melanoma stage (cOR, 7.20; 95% CI, 2.25-22.99). Finally, an association was observed between death due to melanoma and the presence of positive SLNs (cOR, 8.67; 95% CI, 3.62-9).

Discussion

This retrospective study covers a 10-year period. SLNB was introduced for use in cutaneous melanoma in 1992,[18] and most retrospective studies therefore cover a shorter time period. For instance, Avilés-Izquierdo et al[19] analyzed the results obtained over a 7-year period in 155 patients.

Our study included 144 patients with melanoma. Patients with a Breslow thickness of at least 1 mm were automatically included and those with a Breslow thickness less than 1 mm were included if they also had ulceration or a Clark level IV or V (33 patients, 22.92%). Although some of the inclusion criteria for SLNB have changed over the years, they remain clearly defined. If we consider the new National Comprehensive Cancer Network (NCCN) criteria[10] for the management of melanoma (Breslow thickness of at least 1 mm, high mitotic index or Breslow thickness of at least 0.75 mm with a Clark level of IV/V),[20,21] all of our patients would meet the criteria for SLNB.

Table 2 Characteristics of Sentinel Lymph Nodes (n=142)

	N	Percentage (95% CI)	*P*[a]
Site			
1 lymph node station	121	84.03 (77.35-89.34)	<.001
2 lymph node stations	19	13.19 (8.38-19.48)	
3 lymph node stations	2	1.39 (0.23-4.51)	
Number of sentinel lymph nodes identified			
1	105	72.92 (65.22-79.70)	<.001
2	25	17.36 (11.82-24.20)	
3	11	7.64 (4.08-12.89)	
4	1	0.69 (0.03-3.78)	
Micrometastasis			
No	114	79.17 (71.96-85.21)	<.001
Yes	28	19.44 (13.59-26.52)	
Number of sentinel lymph nodes with micrometastasis			
0	114	79.17 (71.96-85.21)	<.001
1	24	16.67 (11.24-23.43)	
2	3	2.08 (0.53-5.56)	
3	1	0.69 (0.03-3.78)	
Lymph node dissection			
No	114	79.17 (71.96-85.21)	<.001
Yes	28	19.44 (13.59-26.52)	
Negative	23	82.14 (64.76-93.15)[*]	<.001
Positive	5	17.86 (6.85-35.24)[b]	

[a]χ^2 test.
[b]Calculated based on the total number of lymph node dissections performed (n=28).

The standardized rates for melanoma worldwide are slightly higher for women than men (5.50 and 5.30 per 100 000 population, respectively).[22] In our study we found a predominance of men. It should be remembered, however, that the group of patients included in this study will be skewed by the inclusion only of higher grade melanomas, which are less common in women.[23]

The most common site of the primary tumor in our study was the trunk. This is consistent with the notable increase in the frequency of melanomas on the trunk observed in other studies, particularly in countries with a high incidence of melanoma.[23]

Unlike in other studies, analysis of histologic type showed nodular melanoma to be as common as superficial spreading melanoma in our patients. Avilés-Izquierdo et al[19] reported a much higher frequency of superficial spreading melanoma (44.7%) than nodular melanoma (18.8%).

The mean Breslow thickness in our patients was 2.16 (1.66) mm, similar to that found in other studies.[19]

Of the 144 patients in whom SLNB was performed, melanoma micrometastases were detected in 28 (19.44%). This proportion is similar to the findings of Morton et al[20] (16%) and Avilés-Izquierdo et al[19] (21.30%).

Analysis of the characteristics of the primary melanoma revealed a predominance of nodular and polypoid melanoma in patients with positive SLNs. In contrast, no positive SLNs were observed in cases of lentigo maligna melanoma or acral lentiginous melanoma. This finding contrasts with the results obtained by Avilés-Izquierdo et al,[19] who found that, along with nodular melanoma, acral lentiginous melanoma was the most common histologic type in patients with positive SLNs. This difference may be due to the small number of patients with acral lentiginous melanoma in our study (only 4 out of 144 patients).

We also observed an association between greater Breslow thickness (>2.0) and positive SLNB. Only 1 patient with a tumor thickness ≤1 mm had positive SLNs, a finding that is consistent with the study by Cuéllar et al.[13] This confirms that SLNB is of limited use in patients with melanomas less than 1 mm thick.

It should also be noted that the association between positive SLNB and nodular melanoma may be skewed by the greater Breslow thickness normally found in these tumors at the time of diagnosis.

Increasing Clark level was also associated with a greater proportion of melanomas with positive SLNB for levels II, III, and IV. The only patient with a Clark level V melanoma in our study had a negative result in SLNB, possibly due to a failure in the technique or because the tumor did not display lymphatic spread, since the patient had numerous in-transit skin metastases without enlarged lymph nodes 12 months after diagnosis.

Table 3 Patients With Positive or Negative Sentinel Lymph Nodes (N=144)

	No positive lymph nodes (n=114)		Positive lymph nodes (n=28)			*P*
	N	Percentage (95% CI)	N	Percentage (95% CI)	cOR (95% CI)	
Sex						
Male	67	80.72 (71.18-88.15)	16	19.28 (11.85-28.82)	1 (ref)	.875
Female	47	79.66 (67.98-88.49)	12	20.34 (11.51-32.01)	1.07 (0.46-2.47)	
Age						
≤25 y	9	100.00 (71.69-100.00)	0	0.00 (0.00-28.31)	–	.237
26-45 y	25	86.21 (70.00-95.46)	4	13.79 (4.54-30.00)	1 (Ref)	
46-65 y	47	79.66 (67.98-88.49)	12	20.34 (11.51-32.01)	1.60 (0.47-5.47)	
>65 y	33	73.33 (59.07-84.68)	12	26.67 (15.32-40.93)	2.27 (0.65-7.89)	
Skin phototype						
III	38	82.61 (69.64-91.58)	8	17.39 (8.42-30.36)	1 (ref)	.244
II	70	81.39 (72.13-88.58)	16	18.60 (11.42-27.87)	1.09 (0.43-2.77)	
I	6	60.00 (29.11-85.77)	4	40.00 (14.23-70.89)	3.17 (0.72-13.87)	
Site of the melanoma						
Head	2	100.00 (22.36-100.00)	0	0.00 (0.00-77.64)	–	.691
Mucosa	1	100.00 (5.00-100.00)	0	0.00 (0.00-77.64)	–	
Upper limb	17	85.00 (64.39-96.04)	3	15.00 (3.96-35.61)	1 (ref)	
Trunk	63	81.82 (72.02-89.26)	14	18.18 (10.74-27.98)	1.26 (0.2-4.89)	
Lower limb	31	73.81 (59.04-85.39)	11	26.19 (14.61-40.95)	2.01 (0.49-8.21)	
Histologic type of the melanoma						
LMM	4	100.00 (47.29-100.00)	0	0,00 (0.00-52.71)	–	.036
ALM	4	100.00 (47.29-100.00)	0	0.00 (0.00-52.71)	–	
Amelanotic	2	100.00 (22.36-100.00)	0	0.00 (0.00-77.64)	–	
SSM	57	89.06 (79.56-95.09)	7	10.94 (4.91-20.44)	1 (ref)	
Nodular	45	70.31 (58.30-80.52)	19	29.69 (19.48-41.69)	3.44 (1.33-8.90)	
Polypoid	2	50.00 (9.43-90.57)	2	50.00 (9.43-90.57)	8.14 (0.99-67.25)	
Breslow thickness, mm						
≤1.0	31	96.87 (85.54-99.84)	1	3.12 (0.16-14.46)	1 (ref)	<.001
1.1-2.0	50	89.29 (79.04-95.54)	6	10.71 (4.46-20.95)	3.72 (0.43-32.38)	
2.1-4.0	22	59.46 (43.21-74.28)	15	40.54 (25.72-56.79)	21.14 (2.60-172.03)	
>4.0	8	57.14 (31.14-80.44)	6	42.86 (19.56-68.85)	23.25 (2.44-221.73)	
Clark level						
I	0	–	0	–	–	.002
II	12	92.31 (67.52-99.61)	1	7.69 (0.38-32.48)	1 (ref)	
III	67	87.01 (78.07-93.21)	10	12.99 (6.79-21.93)	1.79 (0.21-15.31)	
IV	22	57.89 (41.90-72.73)	16	42.10 (27.27-58.10)	8.73 (1.03-74.12)	
V	1	100.00 (5.00-100.00)	0	0.00 (0.00-95.00)	-	
Histologic ulceration						
No	51	92.73 (83.38-97.65)	4	7.27 (2.35-16.62)	1 (ref)	.003
Yes	63	72.41 (62.33-81.02)	24	27.59 (18.98-37.67)	4.86 (1.58-14.90)	
Histologic regression[b]						
No	10	100.00 (74.11-100.00)	0	0.00 (0.00-25.89)	–	–
Yes	15	100.00 (81.90-100.00)	0	0.00 (0.00-18.10)	–	
Initial stage						
IA	13	100.00 (79.42-100.00)	0	0.00 (0.00-20.58)	–	<.001
IB	45	100.00 (93.56-100.00)	0	0.00 (0.00-6.44)	–	
IIA	27	100.00 (89.50-100.00)	0	0.00 (0.00-10.50)	–	
IIB	24	100.00 (88.26-100.00)	0	0.00 (0.00-11.73)	–	
IIC	5	100.00 (54.93-100.00)	0	0.00 (0.00-45.07)	–	
III	0	0.00 (0.00-10.15)	28	100.00 (89.85-100.00)	–	
TNM Classification						
T1	31	100.00 (90.79-100.00)	0	0.00 (0.00-9.21)	–	<.001
T2	49	87.50 (76.83-94.37)	7	12.50 (5.63-23.17)	1 (ref)	
T3	25	62.50 (46.86-76.39)	15	37.50 (23.61-53.14)	4.20 (1.52-11.63)	
T4	9	60.00 (34.54-81.91)	6	40.00 (18.09-65.46)	4.67 (1.27-17.15)	

Table 3 *(continued)*

	No positive lymph nodes (n=114)		Positive lymph nodes (n=28)			*P*
	N	Percentage (95% CI)	N	Percentage (95% CI)	cOR (95% CI)	
Change in stage						
No	108	84.37 (77.30-89.91)	20	15.62 (10.09-22.70)	1 (ref)	<.001
Yes	6	42.86 (19.56-68.85)	8	57 (14-80.44)	7.20 (2.25-22.99)	
Death due to melanoma						
No	112	84.21 (77.26-89.68)	21	15.79 (10.32-22.74)	1 (ref)	<.001
Yes	2	22.22 (3.91-56.21)	7	77.79 (43.79-96.09)	8.67 (3.62-96.15)	

Abbreviations: ALM, acral lentiginous melanoma; LMM, lentigo maligna melanoma; Ref, reference level; SSM, superficial-spreading melanoma; TNM, tumor, node, metastasis.

[a] χ^2 test.

[b] Only referred to in 25 of the clinical histories reviewed.

The presence of ulceration in patients with positive SLNB was significantly more frequent than in those with negative sentinel nodes, and ulcerated melanoma had a 4.86 times higher risk of being associated with positive SLNB than did nonulcerated melanomas.

T3 and T4 stages in the TNM classification for melanoma (which encompasses Breslow thickness and ulceration) were also associated with positive SLNB.

In terms of survival and vital status of patients at the end of the study, we found an association between the presence of positive SLNB and change in melanoma stage. We also confirmed the association between positive SLNB and death due to melanoma reported previously.[14] Our study confirms the prognostic importance of SLNB for the survival of patients with melanoma. Taken together, our results indicate that, in patients with melanoma with a Breslow thickness >1 mm, positive SLNB identifies those patients with a greater tendency towards disease progression and death due to melanoma. Thus, as shown in previous studies,[14] our data indicate that this technique has clear prognostic value.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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