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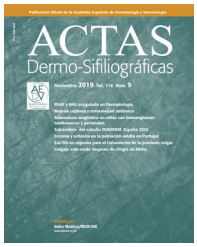

CASE AND RESEARCH LETTER

Sentinel Lymph Node Biopsy in Elderly Melanoma Patients: A Real Practice Cohort

Biopsia del ganglio centinela en pacientes mayores con melanoma: cohorte en la práctica real

To the Editor:

Melanomas in the elderly account for 40% of diagnosed melanomas and account for 60.2% of deaths.[1] Sentinel lymph node biopsy (SLNB) is currently recommended as a staging method for intermediate-thickness melanoma (Breslow thickness, ≥0.8 mm). The ASCO guidelines state that SLNB may be recommended at all ages after discussion of the potential benefits and risks of harm.[2]

Data from the Surveillance, Epidemiology and End Results Program (SEER) suggest that the incidence of thick melanoma is significantly higher in patients over 60 years of age and that mortality is higher than in other age groups. The age group with the highest percentage of death from melanoma is patients aged 75–84 years. In addition, a study analysing 3 different cohorts – including the SEER cohort – with more than 300,000 patients found that age predicts a worse melanoma-specific survival.[3,4] SLNB remains controversial and the peculiarities in the elderly have not been thoroughly studied.

The primary objective of our study was to determine if there is a difference in SLNB status predictors in two different age groups, younger and older than 75 years old. A secondary objective was to describe the difference in complications in both groups.

A cohort, retrospective, single centre, longitudinal, observational study was performed with all the patients that have underwent SNLB from January 2008 to December 2020. Inclusion criteria were the following: All consecutive adult patients with cutaneous melanoma that underwent SLNB. The cohort was divided in two age groups for age related analysis, younger and older than 75 years old. The study protocol was approved by institutional review board and informed consent was obtained from all patients.

The following clinical and histologic characteristics were selected as independent variables: sex, age, anatomic location, histologic subtype, Breslow thickness, ulceration, regression, lymphovascular invasion, mitosis, SLNB location, and SLNB complications.

Statistical analyses were performed using SPSS software ver. 22.0 (IBM®, Armonk, NY, USA). Group comparisons were performed using the Fisher test or Mann–Whitney *U*-test, Pearson chi-square test or independent samples *T* test as necessary. Multivariate logistic regression analysis with backward stepwise selection was performed to assess associations ($p < 0.1$).

Patient characteristics are summarized in Table 1. The sample includes a total of 150 patients who have underwent SLNB. The SLNB was identified in 146 patients (97.3%). The mean age of the participants was 70.6 years old. Positive SLNB was more frequent in ≥75-year-old group (29.3% vs. 18.3%). Although this result was not statistically significant ($p = 0.114$).

Bivariate and multivariate analysis are summarized in Tables 2 and 3. The logistic regression multivariate analysis showed that for the ≥75-year-old group, ulceration was associated with SNLB positivity with an Odds Ratio of 13.3 (95%CI 2.7–65.0). Also, the risk grows when age increases, specifically the odds increase by 19% for each year over 82-year-old on the stepwise selection model. As secondary objective regarding complications, 86% of the patients did not experience any, and seroma, affecting 9.6% of the patients was the commonest with no difference among both age groups.

Many reports have found age-dependent prognostic factors on SLNB status but most randomized trials and major studies have excluded patients older than 70–75 years.[5,6] Consequently, data on the feasibility and diagnostic accuracy of the method in this patient group are so far lacking. Also, there are some existing models to predict SN status in melanoma patients that combine clinicopathologic factors depending on the primary tumour, but they do not take age into account or are not specific for the elderly.[7] It has been postulated that SLNB is a poor predictor of prognosis in older patients because its positivity declines with increasing age.[8] In a large study ($n = 858$), the frequency of sentinel node (SN) metastases decreased with increasing age from 18 to 70 years, despite an increase in other poor prognostic factors. Whether this represents a lower sensitivity of the procedure or a different biological behaviour of melanomas in older patients remains unanswered.[9] In our cohort, posi-

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Table 1 Clinical and histopathological characteristic of study patients.

	Cohort		<75 years-old		≥75 years-old		
Variable	*N*	%	*N*	%	*N*	%	*p*
Sex							
Male	85	56.7	40	53.3	45	60	0.410
Female	65	43.3	35	46.7	30	40	
Location							
Trunk	61	40.7	28	37.3	33	44	0.337
Head and neck	18	12	10	13.3	8	10.7	
Upper limb	30	20	19	25.3	11	14.7	
Lower limb	41	27.3	18	24	23	30.7	
Histologic subtype							
Lentigo maligno	5	3.5	0	0	5	6.9	0.006
Superficial spreading melanoma	76	53.5	40	57.1	36	50	
Nodular melanoma	5	3.5	5	7.1	0	0	
Acral lentiginous melanoma	8	5.6	6	8.6	2	2.8	
Other	48	33.8	19	27.1	29	40.3	
Lymphovascular invasion							
Absent	147	98.7	74	98.7	73	98.6	1.000
Present	2	1.3	1	1.3	1	1.4	
Ulceration							
Absent	119	79.3	57	76	62	82.7	0.313
Present	31	20.7	18	24	13	17.3	
Regression							
Absent	144	96	72	96	72	96	1.000
Present	6	4	3	4	3	4	
SLNB location							
Axillar	73	50.7	36	52.2	37	49.3	0.753
Cervical	13	9	6	8.7	7	9.3	
Inguinal	52	36.1	23	33.3	29	38.7	
Other	6	4.2	4	5.8	2	2.7	
SLNB result							
Negative	111	76	58	81.7	53	70.7	0.119
Positive	35	24	13	18.3	22	29.3	
Lymphadenectomy result							
Negative	21	63.6	10	71.4	11	57.9	0.424
Positive	12	36.4	4	28.6	8	42.1	
Nodal metastases on follow-up							
Absent	127	84.7	69	92	58	77.3	0.013
Present	23	15.3	6	8	17	22.7	
Visceral metastases on follow-up							
Absent	132	88	69	92	63	84	0.132
Present	18	12	6	8	12	16	
Complications SLNB							
No	129	86	64	85.3	65	86.7	0.201
Seroma	14	9.3	6	8	8	10.7	
Paresthesia	3	2	1	1.3	2	2.7	
SLNB not found	4	2.7	4	5.3	0	0	
Desenlace complicación BSGC							
Complete remission	16	94.1	7	100	9	90	1.000
Persistence	1	5.9	0	0	1	10	

Table 1 (*Continued*)

	Cohort		<75 years-old		≥75 years-old		
Variable	*N*	%	*N*	%	*N*	%	*p*
Exitus							
No	133	88.7	70	93.3	63	84	0.071
Yes	17	11.3	5	6.7	12	16	
	Mean	St. dev.	Mean	St. dev.	Mean	St. dev	*p*
Age	70.6	15.9	58.4	13.2	82.8	5.6	**(<0.001)**
Breslow index	2.6	2.1	2.6	2.1	2.6	2.0	0.914
Mitosis	3.8	6.1	4.0	5.7	3.6	6.4	0.707

SLNB: sentinel node biopsy, St. dev: standard deviation.

Table 2 Superior: Bivariate studies between study category and outcome using X^2, Fisher, Mann–Whitney *U* or independent samples *T* test as necessary.

	<75yo					*≥75yo*				
	−SLNB −58		*+SLNB −13*			*−SLNB −53*		*+SLNB −22*		
Variable	*N*	%	*N*	%	*p*	*N*	%	*N*	%	*p*
Sex										
Male	30	51.7%	7	53.8%	0.89	33	62.3%	12	54.5%	0.534
Female	28	48.3%	6	46.2%		20	37.7%	10	45.5%	
Sí	1	1.7%	1	7.7%		2	3.8%	0	0%	
Location										
Trunk	23	39.7%	3	23.1%	0.725	25	47.2%	8	36.4%	0.102
Head and neck	6	10.3%	2	15.4%		8	15.1%	0	0%	
Upper limb	15	25.9%	4	30.8%		7	13.2%	4	18.2%	
Lower limb	14	24.1%	4	30.8%		13	24.5%	10	45.5%	
Histologic subtype										
Lentigo maligno	32	59.3%	5	41.7%	0.642	5	9.6%	0	0%	***0.002***
Superficial spreading melanoma	4	7.4%	1	8.3%		31	59.6%	5	25.00%	
Nodular melanoma	5	9.3%	1	8.3%		2	3.8%	0	0%	
Acral lentiginous melanoma	13	24.1%	5	41.7%		14	26.9%	15	75.00%	
Lymphovascular invasion										
Absent	57	98.3%	13	100.00%	1	52	98.1%	21	100.00%	1
Present	1	1.7%	0	0%		1	1.9%	0	0%	
Ulceration										
Absent	45	77.6%	9	69.2%	0.496	49	92.5%	13	59.1%	***0.001***
Present	13	22.4%	4	30.8%		4	7.5%	9	40.9%	
Regression										
Absent	55	94.8%	13	100.00%	1	51	96.2%	21	95.5%	1
Present	3	5.2%	0	0%		2	3.8%	1	4.5%	
SLNB location										
Axillar	30	53.6%	6	46.2%	0.574	28	52.8%	9	40.9%	***0.056***
Cervical	4	7.1%	2	15.4%		7	13.2%	0	0%	
Inguinal	18	32.1%	5	38.5%		16	30.2%	13	59.1%	
Other	4	7.1%	0	0%		2	3.8%	0	0%	
Lymphadenectomy result										
Negative	3	60.00%	7	77.8%	0.58	0	0%	11	57.9%	–
Positive	2	40.00%	2	22.2%		0	0%	8	42.1%	

Table 2 (*Continued*)

	<75yo					≥75yo				
	−SLNB −58		+SLNB −13			−SLNB −53		+SLNB −22		
Variable	*N*	%	*N*	%	*p*	*N*	%	*N*	%	*p*
Exitus due to melanoma										
Si	4	100%	1	100%	–	6	100%	6	100%	–
SNLB complication										
No	53	91.4%	11	84.6%	0.553	44	83.00%	21	95.5%	0.333
Seroma	4	6.9%	2	15.4%		7	13.2%	1	4.5%	
Paraesthesia	1	1.7%	0	0%		2	3.8%	0	0%	
Complication outcome										
Complete remission	5	100%	2	100%	–	8	88.9%	1	100.00%	1

	−SLNB			+SLNB				
Variable	*N*	Media	DT	*N*	Media	DT	*t*	*p*
Age	53	81.55	4.66	22	85.86	6.61	***−2.788***	***0.009***
Breslow index	52	2.25	1.98	20	3.37	1.98	*−2.148*	*0.035*
Mitosis	53	3.19	5.74	22	4.50	7.89	−0.804	0.424

SLNB: sentinel node biopsy. Inferior: Bivariate studies between study category and outcome using independent samples *T* test for quantitative variables in the ≥75 year old group. The *p* values < 0.1 were considered statistically significant and become part of the logistic regression model.

Table 3 Logistic regression model the behaviour of the variables is studied using a backward stepwise selection model. The variables selected to perform the study are chosen among the ones that showed statistical significance on the regression model.

	Variable forced introduction						Backward stepwise selection					
					CI95%	OR					CI95%	OR
	B	ET(*B*)	Sig.	OR	Inferior	Superior	*B*	ET(*B*)	Sig.	OR	Inferior	Superior
Ulceration	1.046	1.139	0.359	2.846	0.305	26.556	1.945	0.869	0.025	6.997	1.275	38.404
Age ≥ 82	.277	0.092	0.003	1.32	1.101	1.581	1.418	0.801	0.077	4.127	0.859	1.834

Includes all variables that $p < 0.1$ on bivariate analysis. $\chi^2 = 24.41$; gl = 3; $p \leq 0.001$; $R^2_L = 0.287$; $R^2_{Cox\&Snell} = 0.288$; $R^2_{Nagalkerke} = 0.415$.

tivity was 11 points higher in the ≥75-year-old group (29.3% vs 18.3%).

Patients in the ≥75-year-old group, with ulcerated melanoma, older than 82 years-old have the higher likelihood of positivity in SLNB in our cohort. The present study focuses on elderly patients aged 75 years or older. As it is retrospective, bias may exist. The study confirms that SLNB might be recommended in the elder safely. Although SLNB remains controversial due to its lack of impact on survival, it is still the best staging system for micrometastases. It is the authors opinion that it should be offered in elderly patients.

Conflict of interest

The authors declare they have no conflict of interest.

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