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ORIGINAL ARTICLE

Sentinel lymph node biopsy for cutaneous melanoma: A propos of 144 cases

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Summary

Purpose: *The aim of this study was to identify the predictive factors of a positive sentinel lymph node (SLN) in patients with cutaneous malignant melanomas and tumor progression.*

Methods: *From October of 2000 to January of 2006, 144 patients with cutaneous malignant melanoma underwent SLN biopsy. Patients were divided into two groups according to the SLN status (positive vs negative) which were compared with regards to patient demographics and primary tumor characteristics.*

Results: *In 37 (25.69%) patients SLN biopsy was positive . Nodular melanomas (p=0.047), blood (p=0.010) and lymph (p<0.001) vessel infiltration, mitotic rate (p=0.019) and Breslow thickness (p=0.012) were predictive of a positive SLN biopsy. The overall recurrence, mortality and the overall disease free survival (DFS) rates were 6.25, 1.4 and 93.75, respectively.*

Conclusion: *SLN biopsy is the most important predictor of early disease recurrence and survival in patients with cutaneous malignant melanoma. Considering all the examined factors, a positive SLN biopsy is related with Breslow thickness and lymph vessel infiltration.*

Key words: *melanoma, predisposition to sentinel lymph node positivity, recurrence, sentinel lymph node biopsy, survival*

Introduction

SLN biopsy has become a widely accepted method for staging regional lymph nodes in patients with malignant melanoma. In 1992, Morton et al. [1] proposed the concept of the SLN in malignant melanoma according to which the pathological status of the SLN reflects the entire pathological status of all the other nodes of the regional nodal basin; consequently, if the SLN is pathologically negative, all the other nodes of the same area are cancer-free [1-3].

Today, technetium 99m-labelled radioisotope and a hand-held gamma probe in combination with a blue dye are utilized in most centers for SLN identification. The reliability of the SLN biopsy as an accurate staging procedure is dependent on the ability to identify the true SLN and the extent of its histopathological examination. Both are instrumental in limiting the false negative rate of the SLN biopsy [4].

The reported rates of SLN identification with this technique range from 82 to 100%. The rate of SLNs positive for micrometastases ranges from 15 to 26% of the patients [5]. Detection of micrometastasis by this technique has been shown to be highly predictive of the further disease course [6-8]. A positive SLN is also used as an indicator to decide which patients should be considered for additional surgery [9], adjuvant treatment or various research protocols.

The identification of risk factors for melanoma progression remains critical for the management of this disease. At present, there is no consensus on the factors that may predict patients at higher or lower risk of having a positive SLN and to iden-

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tify higher risk patients while potentially sparing lower risk patients from undergoing SLN biopsy. Several clinical and histological characteristics of the primary melanoma have been examined with regard to their potential role in predicting SLN positivity [10-14].

The aim of this study was to analyse our own series of patients with malignant melanoma subjected to SLN biopsy in order to determine if those with negative SLN fared better than those with positive SLN biopsy, who subsequently underwent radical lymphadenectomy. We also tried to investigate if age, sex, tumor location and type, Breslow thickness, Clark level, ulceration, blood and lymph vessel infiltration and mitotic rate of the melanotic lesion might predispose to SLN positivity and tumor progression.

Methods

Patient population

From October of 2000 to January of 2006, 144 patients with histologically confirmed cutaneous malignant melanoma underwent SLN biopsy. All of the patients were referred to the 2nd Department of Propedeutic Surgery of Athens University and to the Department of Plastic Surgery of 'A Sygros' Hospital. The epidemiologic characteristics of the patient population according to sex are summarized in Table 1.

Inclusion criteria for SLN biopsy were as follows: 1) Age ≥ 18 years; 2) Breslow thickness of the primary lesion ≥ 0.6 mm; and 3) No evidence of palpable adenopathies.

The overall mean time between excision of the primary lesion and SLN biopsy was 1.4 months ±1.12 standard deviation (SD). This time was 1.3 months±1.02 SD in males and 1.4 months±1.22 in females.

Preoperative evaluation

This consisted of a detailed medical history, physical examination and imaging studies (CT scan of the head-neck, chest and abdomen), together with determination of serum alkaline phosphatase, lactate dehydrogenase (LDH) and S-100 serum levels.

Lymphoscintigraphy

Dynamic lymphoscintigraphy was performed on the morning, 2–4 h before the operation, with a total dose of 40–60MBq of 99m Technetium (Tc) -radiolabelled sulphur colloid in a total volume of 0.6 ml of normal saline injected intradermally at 4 points around the biopsy site. The acquisition of dynamic images began as soon as the intradermal injection had been given. The drainage of the radioactive material was detected by scintigraphy and the location of the SLN, or if

Table 1. Patient baseline characteristics according to sex

Characteristics	*Male (N=72)*	*Female (N=72)*	*Total*
Age, years ± SD	57.1 ± 14.6	53.9 ± 16.2	55.5 ± 15.4
Location			
1	14	11	25
2	37	21	58
3	5	17	22
4	16	23	39
Melanoma type			
ALM	2	3	5
LMM	-	1	1
NM	52	51	103
SSM	18	17	35
Clark level			
II	7	6	13
III	22	21	43
IV	35	40	75
V	8	5	13
Breslow thickness (mm) ± SD	2.9 ± 2.1	2.6 ± 1.8	2.7 ± 1.9
Ulceration			
Yes	29	29	58
No	43	43	86
Blood vessel infiltration			
Yes	7	8	15
No	65	64	129
Lymph vessel infiltration			
0	19	13	32
1	21	14	35
2	29	32	61
3	3	13	16
Mitoses			
1	21	24	45
2	35	33	68
3	16	15	31
Follow up (mos) ± SD	32.4 ± 17.2	35.7 ± 18.7	34.1 ± 18

ALM: Acral lentiginous maligna melanoma, LMM: Lentigo maligna melanoma, SSM: Superficial spreading melanoma, NM: Nodular melanoma. Location of the melanoma: 1: Head and neck, 2: Trunk, 3: Upper extremity, 4: Lower extremity. Lymph vessel infiltration: 1: Mild, 2: Moderate, 3: Dense. Mitoses: 1: Mild, 2: Moderate, 3: Dense. SD: standard deviation, mos: months.

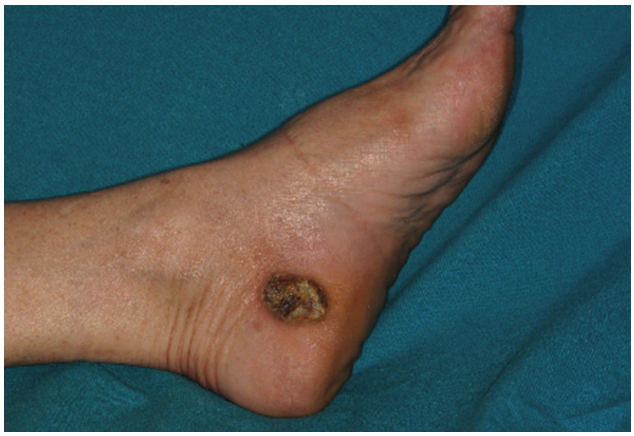

Figure 1. a: A 74-year-old female with ulcerated nodular melanoma, Clark V and Breslow 3.4 mm.

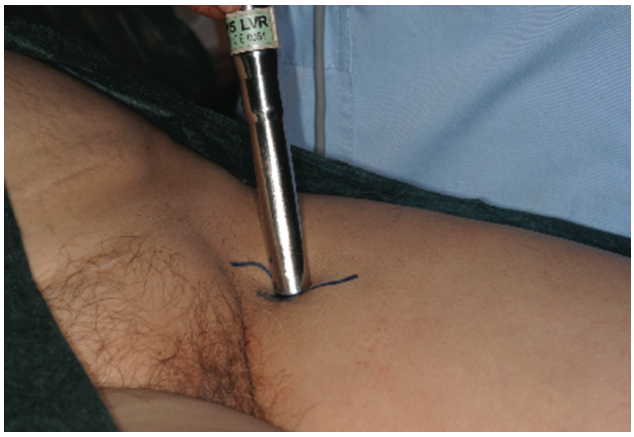

Figure 1. b: Preoperative lymphoscintigraphy for determination of the SLN.

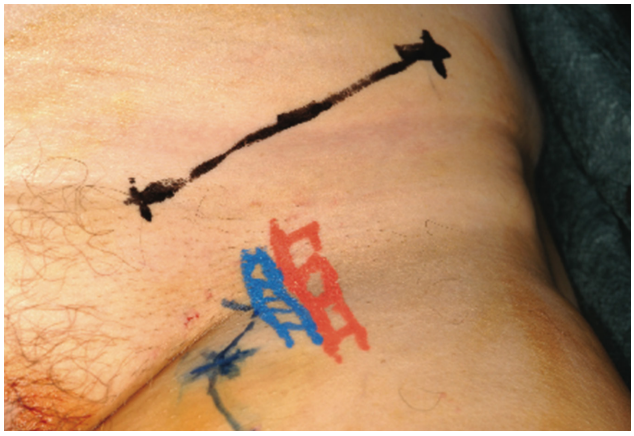

Figure 1. c: The surgical approach.

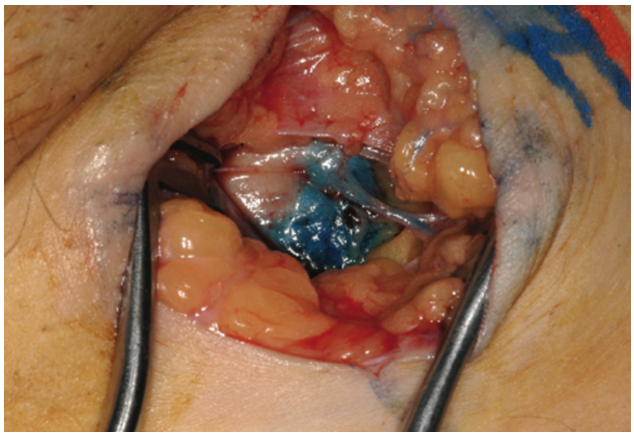

Figure 1. d: The identified SLN marked with lymphozurin.

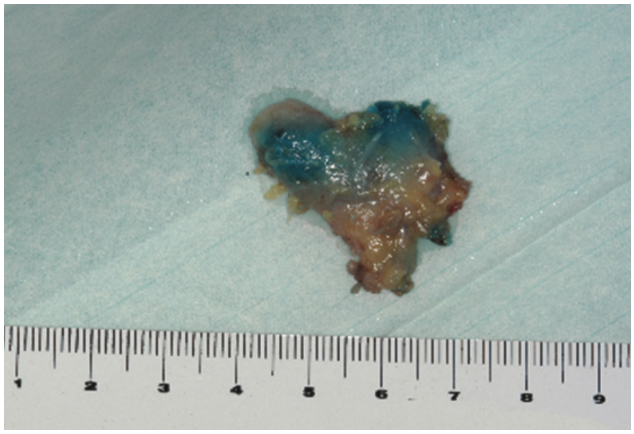

Figure 1. e: The surgical specimen.

there was drainage to more than one SLN or more than one basin were marked on the skin of the patient with indelible ink and static scintigrams were produced.

Surgical technique

SLN biopsy was performed under local anesthesia, 1–2 h after lymphoscintigraphy. Shortly before the operation 0.5–1 ml of lymphazurin blue dye was injected intradermally at the same points as the 99mTc-radiolabelled sulphur colloid. Care was taken not to inject the solution into the subcutaneous tissue. The injection sites were massaged and the primary site was elevated, if possible, to allow the solution to be taken up by the cutaneous lymphatics.

Surgical exploration was undertaken through a 2 -4 cm S-incision, oriented to facilitate completion of the dissection if necessary. Surgical dissection was guided by a hand-held gamma probe and by the visualization of the blue-stained afferent lymphatic channel. The identified SLN was then excised and measured for ex vivo radioactivity. Additional hot nodes were removed until the ratio of the background radioactivity to the hottest ex vivo SLN was less than 10% (Figures 1a, b, c, d, e). A wide local excision of the primary tumor site was then carried out using the generally accepted margins [15].

Pathological examination

All excised SLNs were submitted to the pathology laboratory. The lymph nodes were, firstly, separated from the surrounding fat and connective tissue. Then,

Table 2. Distribution of the SLNs according to the nodal sites

Nodal sites involved	*Location*	*SLN (+)*	*SLN (-)*	*Total*
1	1	5	29	34
	2	25	56	81
	3	11	57	68
≥ 2	1 + 1	10	34	44
	1 + 2	-	2	2
	2 + 2	-	3	3
	2 + 3	-	3	3
Total		51	184	235

Location of the nodal sites involved: 1: Neck area, 2: Axilla, 3: Inguinal area. 1+1: neck area+neck area, 1+2: neck area+axilla, 2+2: axilla+axilla, 2+3: axilla+inguinal area. SLN: sentinel lymph node.

Table 3. Lymph node dissection

Patients, N	*Nodal site*	*SLN (+)*	*SLN (-)*
6	Cervical (N=6)	4	2
25	Axillary (N=30)	24	1
9	Inguinal (N=9)	9	-
Total 40	45	37	3

SLN: sentinel lymph node.

the SLNs were step-sectioned and stained with haematoxylin and eosin (H&E) (1st section) and S-100 protein (2nd section). If the initial review of these sections was negative, 6 additional consecutive sections were made (sections 3–8). Sections 3, 5 and 7 were stained with H&E, sections 4 and 8 with S-100 protein and section 6 with human melanoma black 45 (HMB-45) 45. All SLNs containing any cell compatible with melanoma cell morphology (and immunophenotype) were considered metastasis-positive.

Follow-up and further treatment

If the SLN biopsy was positive for metastasis, a formal lymphadenectomy was performed at a later date. After lymphadenectomy, adjuvant treatment was administered. Patients with negative SLN had no further treatment.

All patients were advised to inform us about any suspicious observations as quickly as possible. Postoperative follow-up consisted of physical examination, chest radiography and CT scans, together with determination of serum alkaline phosphatase, lactate dehydrogenase and S-100 serum levels. Each melanoma patient was followed up for 5 years according to our protocol.

Statistics

Patients were divided into two groups according to the SLN status. The event of interest was the presence of a positive SLN. To determine the association between the event of interest and each clinical or pathologic factor, chi-square test was used; proportions and odds ratios with 95% confidence interval (CI) were also carried out. To derive a model for the occurrence of positive SLN, a multivariate model was fitted by using a stepwise variable selection method. Factors entered into the model if they were independently significant at the 0.1 level, but were dropped if they were not significant at the 0.1 level when adjusted for variables already in the model. In the final model, the possibility (logit) of a positive SLN was calculated by the formula: logit (positive SLN)=3.5365+1.8547 (lymph vessel infiltration)+0.3087 (Breslow thickness). The recurrence curve of melanoma for each factor groups was compared by log-rank test. All reported p values were two-sided at a significance level of 5%. Analyses were performed with SAS 9.1.3 software (SAS Institute Inc., Cary, NC).

Results

In 37 out of 144 patients (25.69%) SLN biopsy was positive for metastasis from the primary melanotic lesion and in 107 (74.31%) patients SLN biopsy was negative. A total of 235 SLNs was identified, with a ratio of 1.6319 SLN per patient. Fifty one (21.71%) SLNs were positive from the primary melanotic lesion and 184 SLNs (78.29%) were negative. A single SLN was found in 86 (59.73%) out of 144 patients. In 39 out of 144 patients 2 (27.08%) SLNs were identified and in 19 (13.19%) two or more SLNs were identified. In 124 out of 144 patients (86.12%), SLN was identified in one nodal site and in 20 (13.88%) SLNs were located in two nodal sites (Table 2).

A total of 45 radical lymph node dissections were performed in 40 patients. In 3 of them, lymph node dissection was performed due to recurrence of the primary tumor although SLN biopsy was negative. Lymph node dissections are summarized in Table 3.

Complications

The complication rate associated with SLN

Table 4. Univariate analysis of SLN positive and negative groups

Characteristics	*SLN negative N (%)*	*SLN positive N (%)*	*Total N (%)*	*p-value*
Sex				0.095
Male	49 (34.1)	23 (15.9)	72 (50.0)	
Female	58 (40.3)	14 (9.7)	72 (50.0)	
Age, years ± SD	56.4 ± 15.7	53.2 ± 14.5	55.5 ± 15.4	0.283
Melanoma type				0.047
ALM	3 (2.1)	2 (1.3)	5 (3.4)	
LMM	1 (0.6)	0 (0.0)	1 (0.6)	
NM	71 (49.5)	32 (22.2)	103 (71.7)	
SSM	32 (22.2)	3 (2.1)	35 (24.3)	
Location				0.150
1	22 (15.3)	3 (2.1)	25 (17.4)	
2	40 (27.8)	18 (12.5)	58 (40.3)	
3	14 (9.7)	8 (5.6)	22 (15.3)	
4	31 (21.4)	8 (5.6)	39 (27.0)	
Breslow thickness, mm ± SD	2.5 ± 1.8	3.4 ± 2.1	2.7 ± 1.9	0.012
Clark level				0.325
II	11 (7.7)	2 (1.3)	13 (9.0)	
III	35 (24.3)	8 (5.6)	43 (29.9)	
IV	51 (35.4)	24 (16.7)	75 (52.1)	
V	10 (6.9)	3 (2.1)	13 (9.0)	
Ulceration				0.052
No	69 (47.9)	17 (11.8)	86 (59.7)	
Yes	38 (26.4)	20 (13.9)	58 (40.3)	
Blood vessel infiltration				0.010
No	100 (69.5)	29 (20.1)	129 (89.6)	
Yes	7 (4.8)	8 (5.6)	15 (10.4)	
Lymph vessel infiltration				<0.001
0	29 (20.1)	3 (2.1)	32 (22.2)	
1	25 (17.4)	10 (6.9)	35 (24.3)	
2	47 (32.6)	14 (9.7)	61 (42.3)	
3	6 (4.3)	10 (6.9)	16 (11.2)	
Mitoses				0.019
1	39 (27.0)	6 (4.3)	45 (31.3)	
2	50 (34.7)	18 (12.5)	68 (47.2)	
3	18 (12.5)	13 (9.0)	31 (21.5)	

For abbreviations see footnote of Table 1

biopsy alone (6.73%) was significantly lower compared with radical lymph node dissection (20.00%). In patients undergoing SLN biopsy alone (N=104), lymphorrhoea occurred in 4, haematoma formation in 2 and hypertrophic scar in 1. In patients undergoing SLN biopsy followed by radical lymph node dissection (N=40), lymphorrhoea occurred in 7 and haematoma formation in 1 (x^2, $p < 0.025$).

Factors predictive of SLN positivity

The comparison between SLN positive and negative groups is summarized in Table 4.

The percentage of positive SLN biopsies was higher in men (16.1%) than in women (9.8%; p=0.095) and was also higher in patients with melanoma ulceration (14.0%) than without ulceration (11.9%; p=0.052). The percentage of positive SLN biopsies increased with increased mitotic

Table 5. Multivariate analysis of recurrence and mortality rates

Characteristics	*Recurrence rate %*	*DFS (months, average) (95% CI)*	*p-value*
Overall recurrence	6.25	70 (68, 73)	-
Overall mortality	1.4	74 (73, 75)	-
Sex			0.7619
Male	6.94	64 (60, 67)	
Female	5.56	71 (67, 75)	
Melanoma type			0.6891
ALM	0	-	
LMM	0	-	
NM	7.77	69 (66, 73)	
SSM	2.86	66 (63, 70)	
Clark level			0.3758
II	0.00	-	
III	4.65	66 (61, 70)	
IV	9.33	69 (64, 73)	
V	0.00	-	
Location			0.9537
1	8.00	63 (56, 70)	
2	6.90	65 (60, 69)	
3	4.55	72 (66, 78)	
4	5.13	67 (62, 71)	
Ulceration			0.0711
No	3.49	68 (65, 70)	
Yes	10.34	67 (61, 73)	
Blood vessel infiltration			0.2054
No	5.43	71 (68, 74)	
Yes	13.33	60 (47, 73)	
Lymph vessel infiltration			<0.0001
0	0	-	
1	0	-	
2	4.92	67 (63, 70)	
3	37.50	32 (22, 41)	
Mitoses			0.1060
1	2.22	68 (65, 70)	
2	5.82	71 (67, 75)	
3	12.90	60 (50, 69)	
SLN			0.0039
Negative	3.80	73 (71, 75)	
Positive	16.22	60 (52, 67)	

DFS: disease free survival. For other abbreviations see footnote of Table 1

Table 6. Recurrence rate: comparison for patients with lymph node dissection

Characteristics	*Recurrence rate %*	*DFS (months) (95% CI)*	*p-value*
Overall recurrence	23.08	55 (47, 64)	-
Lymph nodes			<0.0001
Negative	4.00	68 (63, 72)	
Positive	58.14	33 (19, 47)	
Location			0.6921
1	30.00	39 (19, 59)	
2	20.00	53 (44, 62)	
3	22.22	55 (38, 73)	

1: Neck area, 2: Axilla, 3: Inguinal area, DFS: disease free survival

rate, the extent of lymph vessel infiltration and the Breslow thickness. The percentage of positive SLN biopsies was higher in patients with Clark level IV, in patients with blood vessel infiltration, and in patients with trunk and nodular melanomas than the other corresponding subgroups.

The results of univariate analysis, when the previously described factors were considered alone, showed that nodular melanomas (p=0.047), blood (p=0.010) and lymph (p<0.001) vessel infiltration, mitotic rate (p=0.019) and Breslow thickness (p=0.012) had a significant correlation with the incidence of one or more positive SLNs.

Multivariate logistic regression analysis revealed that only lymph vessel infiltration and Breslow thickness were significantly associated with the occurrence of a positive SLN biopsy. The addition of melanoma type, blood vessel infiltration or the mitotic rate to the multivariate model gave almost identical results. There was no interaction between lymph vessel infiltration and Breslow thickness with the probability of a positive SLN.

According to the results of multivariate analysis, patients with lymph vessel infiltration had higher chance of getting a positive SLN biopsy than those without (adjusted odds ratio was 6.39 with 95% CI 1.63, 25.00). Also, in patients with lymph vessel infiltration, the likelihood of a positive SLN increased with increasing Breslow thickness (adjusted odds ratio was 1.36 with 95% CI 1.11, 1.67).

Recurrence and survival rates

Sex, type of melanoma, Clark level, location of melanoma, ulceration and mitotic rate, blood and lymph vessel infiltration were analysed with re-

gard to disease recurrence (Table 5). Nine (6.25%) out of 144 patients experienced recurrence. Of the 107 patients with a negative SLN biopsy, 3 (2.81%) experienced recurrence and of the 37 patients with a positive SLN biopsy 6 (16.22%) recurred (p=0.01).

In this series, the overall recurrence rate was 6.25%, the overall mortality rate 1.4% and the overall DFS rate 93.75%. According to statistical analysis, the existence of lymph vessel infiltration (p<0.0001) and a positive SLN biopsy (p=0.0039) were stronger predictors of recurrence. All the above are summarized in Table 5.

The overall recurrence rate for patients with positive SLN biopsy was 23.08%. Existence of positive lymph node (p<0.0001) after radical lymph node dissection was a strong predictor for disease recurrence. Comparison of the recurrence rate for patients with lymph node dissection is summarized in Table 6.

Discussion

SLN status has long been introduced into the clinical practice of surgical management of malignant melanoma [16]. SLN biopsy offers accurate nodal staging with low morbidity [17, 18], demonstrates usefulness in selecting patients who will most likely benefit from elective lymph node dissection and provides substantial prognostic information.

Literature review of the examined factors

In our series, nodular melanomas, blood and lymph vessel infiltration at the site of the primary tumor, Breslow thickness, high mitotic rate were predictive of a positive SLN biopsy in univariate analysis, while Breslow thickness and the presence of lymph vessel infiltration, were independent predictors of positive SLN biopsy.

Age and sex of our patients were not proved to bear predictive value of a positive SLN biopsy (p=0.283 and p=0.095, respectively). According to Sondak et al. [19] younger age has a significant relationship with a positive SLN biopsy. On the other hand, Balch et al. [20] suggested that increasing age is a negative prognostic factor for survival of patients with melanoma. Moreover, Gershenwald et al. [21] suggested that age is not a predictive factor of a positive SLN biopsy in patients with thick melanomas (Breslow ≥ 4.00 mm). Our results stand in contrast to other studies that have reported an association between age and a positive SLN. This difference may be attributed to the high melanoma thickness in our cohort (the overall mean Breslow thickness was 2.773 mm). Gender is well known to be an important prognostic factor for melanoma; it is well established that men have a worse outcome than women [20,22]. However, several studies have shown that gender does not predict SLN status [23,24], a fact confirmed also in our study.

Melanoma type was proved to be of predictive value of a positive SLN biopsy (p=0.047). In our series, the main histological type was the nodular melanomas (N=103). According to Topar et al. [25], SLN positivity, in their series, was significantly associated with the type of the primary tumor. Our findings confirm Topar's observation [25], despite the general belief in the literature [26]. Anatomic location of the primary tumor was not proved to be of predictive value of a positive SLN biopsy in our series (p=0.15). According to Balch et al. [20] the anatomic site of the primary melanoma is correlated with survival and patients with head and neck and trunk melanomas have poorer prognosis than those with extremity melanomas. On the contrary, Chao et al. [27] reported that patients with head and neck melanomas had a significantly lower incidence of SLN metastasis compared with melanomas of the trunk and the extremities. In our series, the site of primary melanoma was not correlated with SLN status.

Breslow thickness has been claimed by several authors to adversely affect the occurrence of positive SLN [20, 28-32]. Our data confirm the observed correlation of Breslow thickness with SLN positivity (p=0.012). According to Topar et al. [25], the mean Breslow thickness in SLN-positive patients, in their series, did not exceed significantly the mean Breslow thickness of the SLN-negative patients; it merely showed a statistical trend. It is noteworthy, however, that the expected correlation between tumor thickness and disease progression was statistically significant, which may indicate that SLN positivity is overestimated as a prognostic tool. In our series, the mean Breslow thickness for SLN-positive patients was 3.48 ± 2.102 mm and for SLN-negative patients it was 2.54 mm ± 1.866 mm . Our data did not confirm Topar's observation.

On the contrary, we did not find any correlation between Clark level of the primary melanoma and the SLN status (p=0.325), a fact that is consistent with previous reports [33,34]. In contrast, other authors [35] reported that Clark level was a significant predictor in their multivariate analysis. This discrepancy may be attributed to differences in the inclusion criteria for each study.

Many studies have reported an association between the presence of ulceration of the primary melanoma and a positive SLN status [33,34,36]. Our data fully support the reported observations ($p < 0.05$). On the contrary, Sondak et al. [19] reported no correlation between ulceration and positive SLN status and attributed this difference to possible differences in the diagnostic criteria used to define ulceration or to differences in the end point measured or to the number of the histological features studied.

Angiolymphatic vessel invasion from the primary melanoma is widely accepted as an independent prognostic factor of the SLN status [37,38]. In our series, a strong correlation existed between angiolymphatic vessel invasion and positive SLN biopsy ($p=0.010$ for blood vessel infiltration and $p<0.001$ for lymph vessel infiltration). Moreover, the effect of the lymph vessel infiltration on the likelihood of a positive SLN was significant when the grade of lymph vessel infiltration was increased.

In the present study mitotic rate (number of mitoses) was identified as a predictor of a positive SLN ($p=0.019$). Sondak et al. [19] suggested that younger age and the number of mitoses in combination with Breslow thickness are strong predictors of a positive SLN. On the contrary, there are studies which do not confirm this correlation [39]. According to our results, the effect of mitotic index on the likelihood of a positive SLN was significant when the mitotic range was increased. Moreover, our results did not reveal any correlation between ulceration of the melanoma and the likelihood of a positive SLN biopsy, which is in contrast with other studies [33,34,36].

The multivariate model revealed Breslow thickness and the presence of lymph vessel infiltration to be closely correlated with the likelihood of a positive SLN biopsy. Although Breslow thickness is consistently reported to be correlated with SLN status, conflicting results have been reported for the impact of lymph vessel infiltration on the SLN biopsy status. Due to the fact that many of the histological factors of melanoma are correlated with each other, it is not surprising that different studies find slightly different sets of predictive factors of a positive SLN biopsy. Again, referring to our controversial data, we believe that some of the observed differences may reflect the relatively low number of patients in our study as compared with other published series [20, 32].

Factors related to recurrence

In the present study the overall recurrence rate was 6.25% and the overall DFS rate was 93.75%. Recurrence rate in SLN positive patients was 16.22% and 3.80% in SLN negative patients ($p=0.012$).

Our analysis showed that recurrence occurred in patients with the presence of lymph vessel infiltration and a positive SLN biopsy. According to Gershenwald [34] the presence of a positive SLN biopsy has been characterized as the best predictor of recurrence in patients with clinically node-negative cutaneous melanoma. Although in the current study Breslow thickness, mitotic rate and ulceration were closely related, statistical interaction in the multivariate model could explain the unexpected lack of significance of ulceration and mitotic rate as predictors of recurrence. Moreover, the presence of lymph nodes positive for metastasis after radical lymph node dissection was another factor which was strongly correlated with recurrence.

A review of the literature reveals that melanoma recurrence has been correlated with Breslow thickness, ulceration of the primary tumor, Clark level > II, younger age and tumor location; these factors have been claimed to adversely affect DFS rate [40]. Node positive patients are a heterogeneous group recognized to have a wide range of clinical outcomes depending on the number of positive lymph nodes and other factors, like ulceration. In our series, lymph vessel infiltration was a predictor of recurrence. This factor is not widely recognized to be strongly correlated with disease relapse.

We also had 3 patients with negative SLN biopsy who experienced relapse of melanoma. Two out of these 3 patients developed local disease relapse and the third recurred in the SLN basin. Wagner et al. [41] suggested that patients with negative SLN biopsy are at much lower risk for early recurrence, though the first recurrences are more likely to be locoregional. Moreover, this group seems to have a more favorable prognosis than patients who recur with distant metastases. In the patient with relapse in the SLN basin there were no other manifestations of lymphatic metastases.

Various recurrence rates of melanoma after SLN biopsy have been reported by several authors.

Gershenwald et al. in 1998 [42], and Gadd et al. in 1999 [43] reported recurrence rate of 11% in SLN negative patients. Leong in 2000 [44] reported 23% recurrence rate in SLN positive and 9% in SLN negative patients. Clary et al. in 2001 [23] reported 40% recurrence rate in SLN positive and 14% in SLN negative patients with primary extremity melanomas. Caraco et al in 2002 [45] re-

ported 18.5% recurrence rate in SLN positive and 4% in SLN negative patients. In 2003 Fincher et al. [46] reported 26% recurrence rate in SLN positive and 10% in SLN negative patients.

Conclusions

This report confirms that SLN biopsy yields clinical information that is useful for predicting early treatment failure. In our series, nodular melanomas, blood and lymph vessel infiltration at the site of the primary tumor, Breslow thickness, and high mitotic rate were predictive of a positive SLN biopsy. With all the examined factors considered together, the likelihood of a positive SLN biopsy was relatively dependent on Breslow thickness and the presence of lymph vessel infiltration. Recurrence was correlated with a positive SLN, the existence of lymph vessel infiltration and the number of positive lymph nodes after radical lymph node dissection. Although literature on melanoma substantiates our findings, the role of lymph vessel infiltration as an independent predictor of melanoma recurrence is not sufficiently evaluated.

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