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Prognostic value of sentinel node biopsy in 327 prospective melanoma patients from a single institution

THESE

préparée sous la direction du Docteur Maurice Matter, maître d'enseignement et de recherche

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par

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Résumé

Etude de la valeur pronostique de la biopsie du ganglion sentinelle dans une étude prospective monocentrique de 327 patients atteints de mélanome malin

But
Il s'agit de confirmer la validité de la biopsie du ganglion sentinelle, d'en définir la morbidité, d'investiguer les facteurs prédictifs pour le statut du ganglion sentinelle ainsi que de déterminer les facteurs pronostiques pour la survie sans récidive et la survie spécifique liée à la maladie.

Matériel et méthode
D'octobre 1997 à décembre 2004, 327 patients consécutifs présentant un mélanome cutané primaire des membres, du tronc et de la tête, sans adénopathie clinique ni métastase à distance ont été inclus. La biopsie du ganglion sentinelle a été réalisée selon la triple technique (lymphoscintigraphie, colorant bleu vital et sonde de détection gamma). Les paramètres et la survie ont été évalués par différentes analyses de régression logistique multiple selon Cox et la survie évaluée selon Kaplan Meier.

Résultats
Vingt-trois pourcent des patients présentaient au moins un ganglion sentinelle métastatique, ce qui était associé de façon significative à l'épaisseur selon Breslow ($p<0.001$). Le taux de succès de la biopsie du ganglion sentinelle était de 99.1% et sa morbidité de 7.6%. Avec une durée médiane de suivi de 33 mois, la survie sans récidive à 5 ans était de 43% pour les patients avec un ganglion sentinelle positif et de 83.5% pour ceux avec un ganglion sentinelle négatif. La survie spécifique liée à la maladie à 5 ans était de 49% pour les patients avec un ganglion sentinelle positif et de 87.4% pour ceux avec un ganglion sentinelle négatif. Le taux de faux négatif de la biopsie du ganglion sentinelle était de 8.6%. L'analyse multivariée a démontré que la survie sans récidive était significativement péjorée par : l'épaisseur selon Breslow (RR=5.6, $p<0.001$), un ganglion sentinelle positif (RR=5.0, $p<0.001$), et le sexe masculin (RR=2.9, $p=0.001$). La survie spécifique liée à la maladie était significativement diminuée par : un ganglion sentinelle métastatique (RR=8.4, $p<0.001$), le sexe masculin (RR=6.1, $p<0.001$), l'épaisseur selon Breslow (RR=3.2, $p=0.013$), et la présence d'une ulcération (RR=2.6, $p=0.015$).

Conclusion
La biopsie du ganglion sentinelle est une procédure fiable avec une haute sensibilité (91.4%) et une faible morbidité (7.6%). L'épaisseur selon Breslow était le seul facteur prédictif significatif pour le statut du ganglion sentinelle. La survie sans récidive était péjorée selon un ordre décroissant par : l'épaisseur selon Breslow, un ganglion sentinelle métastatique, et le sexe masculin. De façon similaire la survie spécifique liée à la maladie était péjorée par : un ganglion sentinelle métastatique, le sexe masculin, l'épaisseur selon Breslow, et une ulcération. Ces données renforcent le statut du ganglion sentinelle en tant que puissant moyen pour évaluer le stade tumoral ainsi que le pronostic.

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Prognostic value of sentinel node biopsy in 327 prospective melanoma patients from a single institution

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Abstract

Aim: To confirm the accuracy of sentinel node biopsy (SNB) procedure and its morbidity, and to investigate predictive factors for SN status and prognostic factors for disease-free survival (DFS) and disease-specific survival (DSS).
Materials and methods: Between October 1997 and December 2004, 327 consecutive patients in one centre with clinically node-negative primary skin melanoma underwent an SNB by the triple technique, i.e. lymphoscintigraphy, blue-dye and gamma-probe. Multivariate logistic regression analyses as well as the Kaplan–Meier were performed.
Results: Twenty-three percent of the patients had at least one metastatic SN, which was significantly associated with Breslow thickness ($p < 0.001$). The success rate of SNB was 99.1% and its morbidity was 7.6%. With a median follow-up of 33 months, the 5-year DFS/DSS were 43%/49% for patients with positive SN and 83.5%/87.4% for patients with negative SN, respectively. The false-negative rate of SNB was 8.6% and sensitivity 91.4%. On multivariate analysis, DFS was significantly worsened by Breslow thickness (RR = 5.6, $p < 0.001$), positive SN (RR = 5.0, $p < 0.001$) and male sex (RR = 2.9, $p = 0.001$). The presence of a metastatic SN (RR = 8.4, $p < 0.001$), male sex (RR = 6.1, $p < 0.001$), Breslow thickness (RR = 3.2, $p = 0.013$) and ulceration (RR = 2.6, $p = 0.015$) were significantly associated with a poorer DSS.
Conclusion: SNB is a reliable procedure with high sensitivity (91.4%) and low morbidity. Breslow thickness was the only statistically significant parameter predictive of SN status. DFS was worsened in decreasing order by Breslow thickness, metastatic SN and male gender. Similarly DSS was significantly worsened by a metastatic SN, male gender, Breslow thickness and ulceration. These data reinforce the SN status as a powerful staging procedure.

Keywords: Melanoma; Sentinel lymph node; Prognostic factors; Survival

Introduction

Sentinel node biopsy (SNB) is an important staging procedure and may be a potential therapeutic approach in the management of melanoma. Metastatic spreading from a primary melanoma can be explained by two possible theories.[1] In the "marker" hypothesis, the primary melanoma metastasizes simultaneously via lymphatic and haematogenous routes, so that the presence of regional lymph nodes metastases becomes a marker of the likelihood of systemic disease. In the "incubator" hypothesis, the primary melanoma targets regional lymph nodes where metastatic cells may survive and slowly grow but remain latent before spreading to distant sites. According to this second theory, it was suggested that early removal of involved regional lymph nodes in early- and intermediate-stage melanoma could prevent the progression of the metastases and thus improve survival. Four

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prospective randomized studies[2–6] failed to support an overall survival benefit for patients undergoing elective lymph node dissection (ELND) instead of nodal observation, apart from subgroups of patients (tumor thickness between 1 and 2 mm, tumor without ulceration, patients ≤60 years of age and patients with limb melanomas) in the Intergroup Melanoma Surgical Trial.[5,6] The development of lymphatic mapping and the introduction of SNB in melanoma patients by Morton et al.[7] allowed to identify node-positive patients prior to complete node dissection and thus to select patients who might benefit from complementary selective lymph node dissection (SLND). The sentinel node (SN) is defined as the first node(s) directly draining lymph from the primary melanoma, and following this concept if early lymphatic metastases are present, they are to be found within this sentinel node. SNB is now a recognised approach, but not yet the standard of care for melanoma patients without clinically evident nodal metastases. The knowledge of the SN status, which is included in the revised American Joint Committee on Cancer classification,[8,9] permits an ultra staging of melanomas, provides an important survival prognostic parameter and prevents node-negative patients from undergoing an unnecessary SLND that is associated with higher morbidity than SNB.[10] Recently published interim results[11] from the ongoing Multicenter Selective Lymphadenectomy Trial (MSLT)[12] showed that SNB with SLND in case of positive SN instead of observation with delayed lymph node dissection in case of nodal relapse significantly prolonged disease-free survival (DFS) but not disease-specific survival (DSS) in intermediate thickness (1.5–3.5 mm) primary melanomas.[11]

The aim of this prospective study was to analyse the results of the SNBs performed in our tertiary reference centre for melanoma, to verify the accuracy of the procedure and its morbidity, and to investigate predictive factors for SN status and prognostic factors for DFS and DSS.

Materials and methods

Patients

Between October 1997 and December 2004 all consecutive patients were included in a prospective systemic SNB program, and underwent an SNB performed by a single surgical team at the Centre Hospitalier Universitaire Vaudois (CHUV) in Lausanne in Switzerland. The protocol of this study was accepted by the Institutional Ethical Committee. Inclusion criteria were primary skin melanoma >1.00 mm without palpable adenopathy and absence of distant metastases (confirmed by CT scan or PET scan). Further patients with melanoma thickness ≤1.00 mm in the presence of specific histopathologic factors, such as ulceration, regression or Clark level IV/V were also included. If metastases were detected in the SN(s), an SLND was proposed. Patients were followed according to the stage of the disease at the outpatient clinic of the Oncology Unit with clinical and radiological regular examinations.

Surgical technique and pathological analysis

All patients' SN identification was performed according to the triple technique (lymphoscintigraphy, blue-dye and gamma-probe). Lymphoscintigraphy was performed on the day before surgery. Injections of m99Tc-nanocolloid (Nanocoll, Amersham Health, UK) around the excision–biopsy scar followed by dynamic and static imaging were performed to identify the draining lymphatic vessels and SN(s). The surface location of the SN(s) was marked after localisation with a hand-held gamma-probe (Scintiprobe® Pol.Hi.Tech, then Neoprobe gamma neo2000®) and/or an external ^{57}Cobalt pen. The day of surgery 2 ml of patent blue V (bleu patenté violet, Laboratoire Guerbet, France) were injected intradermally in four points around the scar or the primary tumor. Surgery was directed by the same gamma-probe with the systematic exploration of all possible basins. The SN was defined as any blue node, the node with the highest radioactive count, any node with >10% count rate of the most radioactive node. Any enlarged (>1 cm) suspicious node and some adjacent nodes (mainly for anatomical reason) were also dissected. SNB was followed by scar wide-excision (WE) with usual safety margins[13,14] (1 cm and 2 cm for melanoma, <1 mm and ≥1 mm thick, respectively). SN(s) were sent fresh or in formaldehyde solution directly to the Department of Pathology. Lymph nodes were bivalved and paraffin embedded. Three slices were cut for H–E and immunohistochemistry staining (Melan A and protein S100) at a regular 50 microns interval for at least six times. No PCR analysis has been performed. The SLND's nodes were only processed with H–E staining.

Statistical analysis

Quantitative variables were compared using the Student or the Wilcoxon test. Categorical variables were compared using the χ^2 test. A multivariate logistic regression model was used for clinicopathological characteristics predictive of SN metastases. Survival analysis involved the Kaplan–Meier method combined with log-rang test and multivariate Cox's proportional hazard regression models. Statistical analyses were performed with R software (Ihaka and Gentleman, 1996). p-Values <0.05 were considered statistically significant.

Results

During the study period, 327 consecutive patients with primary skin melanoma underwent an SNB and were included in this study.

Clinicopathologic characteristics

The 327 patients' clinicopathologic characteristics are presented on Table 1. Male and female patients (54% vs. 46%) had similar mean ages (55 years vs. 52 years). The 51

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Table 1
Clinicopathologic characteristics of 327 patients

Characteristic	Patients number
Male/female	175/152
Age mean/median (range)	53.5/54 (13–85)
Melanoma subtype	
Superficial spreading (SSM)	147
Nodular (NM)	90
Acral lentiginous (ALM)	36
Others	54
Breslow thickness, mean/median (range)	2.24/1.70 (0.25–12.00)
≤1.00 mm	51
1.01–2.0 mm	146
2.01–4.0 mm	96
>4.0 mm	34
Ulceration	
Present	88
Absent	239
Primary melanoma location	
Head and neck	28
Trunk	131
Extremity	168
Lymph node basin	
1	258
>1	69

patients included in the T1 group (Breslow thickness ≤1.0 mm) presented with a Breslow thickness close to 1.01 mm ($n = 6$), ulceration ($n = 3$), Clark level IV ($n = 23$), Clark level IV and ulceration ($n = 3$), regression ($n = 10$), status after laser treatment ($n = 1$) and further patients between 20 and 30 years ($n = 5$) were also included due to their young age.

Sentinel node identification

Among those 327 patients a total of 401 nodal basins were mapped: 258, 64 and five patients had one, two and three synchronous nodal basin, respectively. Inguinal and iliac basins were considered as two distinct basins. A total of 645 SNs were identified (1.97 SN/patient and 1.61 SN/nodal basin).

Sentinel node biopsy morbidity

The success rate of SNB was 99.1%. The three patients with SNB's failure had two synchronous basins each, with a failed SNB in only one of the two. The overall SNB + WE morbidity was 7.6% (Table 2). The only case of blue-dye anaphylaxis quickly responded to steroids and antihistamines, and the three cases of blue-dye skin reactions quickly responded to antihistamines. No surgery-related death occurred.

Sentinel node's characteristics

Metastases to SNs were detected in 74 out of 327 patients and in 94 out of 645 dissected SNs. Fifty-nine patients had one positive SN, 11 had two positive SNs, three had three positive SNs and one had four positive SNs. There were only two cases in which positive SNs were found in two different lymphatic basins. Micrometastases to SNs were distributed according to Starz classification[15] defined on Table 3. There were 253 S0 patients, 26 S1, 18 S2 and 30 S3.

Table 2
Complications associated with sentinel node biopsy

Complication	Patient number
Lymphocoele	10
Lymphedema	6
Blue-dye allergy: urticaria/anaphylaxis	3/1
Wound infection	1
Lymphocoele infection	2
Wound dehiscence	1
Pulmonary embolism	1
Total	25

Predictive factors of sentinel node metastases

Positive(s) SN(s) were found in 23% of patients. Mean Breslow thickness of primary melanoma was 1.95 mm for SN-negative cases and 3.22 mm for SN-positive cases. Three T1 patients had one or two metastatic SN. One with a 0.78 mm Clark IV melanoma had two metastatic SN and two with 0.95 mm Clark IV and 1.0 mm Clark III melanomas had each one positive SN. No T1 patients included due to regression ($n = 16$) presented with a metastatic SN.

Univariate analysis of risk factors of metastatic SN is presented on Table 4. Multivariate logistic regression analysis for predictive factors of SN metastases showed that only Breslow thickness was statistically significant (T3: $p = 0.009$, T4: $p < 0.001$).

Tumor recurrence and disease-free survival

With a median follow-up of 33 months (range: 12–95 months), 19% of patients (34 positive SN and 28 negative SN patients) presented tumor recurrences at a median time of 30 months (mean: 34 months). Overall 46% positive SN and 11% negative SN patients recurred.

Table 3
Definition of Starz classification[a]

	n[b]	d[c]
S0	$n = 0$	0
S1	$1 \leq n \leq 2$	≤1
S2	$n > 2$	≤1
S3	$n > 2$	>1

[a] According to S-staging concept.[15]
[b] n, Number of 1-mm-thin sentinel lymph node slices with detectable tumor cells.
[c] d, Maximum distance of tumor cells to the interior margin of the lymph node capsule.

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Table 4
Sentinel node (SN) status according to clinicopathological characteristics

Number of patients: 327	SN-positive, 74	SN-negative, 253	*p*-Value
Gender			NS
Male	43	132	
Female	31	121	
Age			NS
≥65 years	21	70	
<65 years	53	183	
Melanoma subtype			0.016
Superficial spreading (SSM)	27	120	
Nodular (NM)	31	59	
Acral lentiginous (ALM)	8	28	
Others	8	46	
Breslow thickness, mm			<0.001
≤1.00	3	48	
1.01–2.0	23	123	
2.01–4.0	32	64	
>4.0	16	18	
Ulceration			0.003
Present	30	58	
Absent	44	195	
Primary melanoma location			NS
Head and neck	4	24	
Trunk	35	96	
Extremities	35	133	
Lymph node basin			NS
1	55	203	
>1	19	50	

NS, not significant statistically.

A false-negative result of SNB was defined as a nodal recurrence in the previously dissected regional basin without previous local or in-transit metastases.[16] Our SNB's false-negative rate was 8.6% (7/81) and its sensitivity was 91.4%. We combined the reporting of local and regional metastases (satellite, in-transit (ITM) and nodal metastases), distinguishing them from distant metastases. Overall 62 patients recurred, 46 with loco-regional recurrence first (20 ITM, 18 nodal and eight local). SN-positive and SN-negative patients presented no significant difference concerning the first site of recurrence (loco-regional vs. distant). The incidence of ITM as site of first recurrence was 6.1% and was significantly higher ($p < 0.01$) among metastatic SN patients (10 out of 74) compared to negative SN patients (10 out of 253). None of the 51 T1 patients with a metastatic SN presented a tumor recurrence. The 5-year DFS was 43% (95%CI 0.306–0.604) for patients with positive SN and 83.5% (95%CI 0.776–0.989) for patients with negative SN. On univariate analysis (Fig. 1) metastatic SN ($p < 0.001$), Breslow index ($p < 0.001$), male sex ($p < 0.001$), ulceration ($p < 0.001$), age ≥65 years ($p = 0.035$) and melanoma type (ALM, $p = 0.03$) were significantly associated with tumor recurrence. Starz (S0 vs. S1 vs. S2 vs. S3), tumor location (trunk vs. extremities vs. head and neck) and number of lymph node basin (1 vs. >1) were not significant. On multivariate analysis (Table 5) DFS was significantly worsened by Breslow index ($p < 0.001$), positive SN ($p < 0.001$) and male sex ($p = 0.001$).

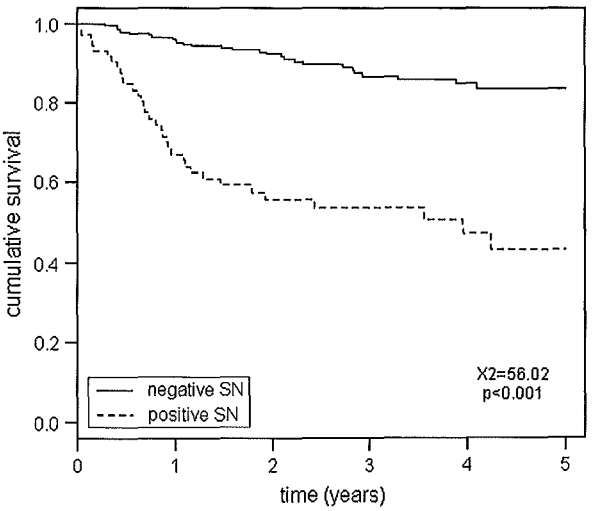

Figure 1. Disease-free survival according to sentinel node (SN) status (calculated from date of SN biopsy).

Disease-specific survival

Thirty-five patients died of melanoma's progression and five died of another cause. The 5 years DSS was 49.1% (95%CI 0.809–0.948) for SN-positive patients and 87.4% (95%CI 0.340–0.709) for SN-negative patients. On univariate analysis (Fig. 2) positive SN ($p < 0.001$), Breslow thickness ($p < 0.001$), male sex ($p = 0.003$) and ulceration ($p = 0.006$) were significantly associated with melanoma-related death. Starz, age, tumor type, tumor location and number of lymph node basin were not significant. On multivariate analysis (Table 6) the presence of a metastatic SN ($p < 0.001$), male sex ($p < 0.001$), Breslow thickness in T3 ($p = 0.013$) and ulceration ($p = 0.015$) were significantly associated with a poorer DSS.

Positive sentinel node subgroup analysis

Among the 74 positive SN patients, 64 underwent an SLND (59 and five patients underwent an SLND of one and two nodal basins, respectively), six refused this second operation and four were not proposed this operation. In 17% of cases (11/64 patients and 12/69 nodal basins) positive non-SNs were found. Risk factors of non-sentinel nodes[17,18] could not be evaluated in this study due to the small number of patients. On univariate analysis tumor recurrence was significantly associated with Breslow index ($p < 0.001$) and

Table 5
Multivariate Cox's analysis of disease-free survival

	RR	95%CI	*p*-Value
Breslow thickness	5.61	2.27–13.90	<0.001
Positive SN	5.00	2.84–8.82	<0.001
Male	2.91	1.57–5.38	0.001

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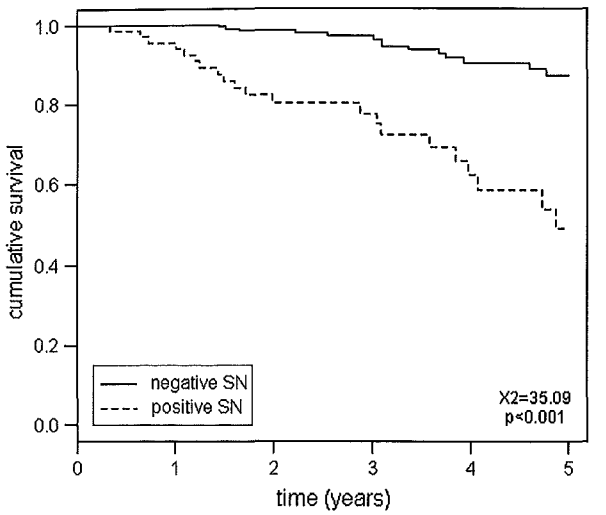

Figure 2. Disease-specific survival according to sentinel node (SN) status.

male gender ($p = 0.032$). On univariate analysis DSS was significantly associated with male gender ($p = 0.019$) and Breslow index ($p = 0.025$).

Discussion

Our present study is single institution based and surgical procedures were performed by a single surgical team. In a review of literature we only found two other reports with more than 200 patients[11,14] that also included prognostic factors' multivariate analysis for both DFS and DSS. In the current study we established that DFS was worsened in order of significance by Breslow index, metastatic SN and male gender. We also showed that in decreasing order a metastatic SN, male gender, Breslow thickness and ulceration were significantly associated with a poorer DSS. Morton et al.[11] and Gershenwald et al.[19] both showed that metastatic SN followed by increasing Breslow thickness and the presence of ulceration were significant predictors for DFS. Concerning DSS they both established that metastatic SN followed by Breslow thickness were significant prognostic factors. Morton et al.[11] found that additional independent prognostic factors were age ≥60 years for DFD, and ulceration as well as truncal location for DSS. Thus the SN status and the Breslow thickness are the most significant independent factors for both DFD and DSS. If we consider only SNB literature, the poorer prognosis associated with male gender for both DFS and DSS in this study has only been reported by Scoggins et al.[20] Since men having undergone SNB had a worse prognosis than women and that metastatic SN was the most powerful predictor of survival, one could suspect that men would be at higher risk of having a metastatic SN. But we established that gender was not predictive of the SN status. Our analysis of the metastatic SN subgroup showed that once the SN was positive only the Breslow thickness and male gender were significant predictive factors for both DFS and DSS. Unlike Starz et al.,[15] who reported that S classification was an independent factor influencing distant metastasis and survival, we found that S classification was not significant for prediction of both DFS and DSS. Other classifications of tumor burden in SN have been developed in order to evaluate the risk of positive non-SN,[21,22] and they will be subject to further analysis.

Table 6
Multivariate Cox's analysis of disease-specific survival

	RR	95%CI	*p*-Value
Positive SN	8.38	3.65–19.26	<0.001
Male	6.14	2.42–15.56	<0.001
Breslow index (T3)	3.18	1.28–7.91	0.013
Ulceration	2.60	1.21–5.61	0.015

Sentinel node biopsy and its complications

SNB has been designed as a staging procedure permitting to avoid the morbidity of unnecessary ELND in negative SN patients and might be useful in the future to study novel adjuvant therapies. The SN status is reported in various multivariate studies as the strongest independent prognostic factor for DFS,[11,19,23–26] DSS[11,19] and overall survival (OS).[27–29] With the use of the triple technique, we obtained an SNB success rate of 99.1% comparable to important series that also included head and neck melanomas.[12,23] The false-negative rate of this procedure was 8.6% which is situated within the range (4.7–11%) reported in the literature.[10,16,24,27–32] The SNB-associated complications rate in our study was 7.6%. This is between the values reported in the Sunbelt Melanoma Trial (4.6%)[31] and in the Multicenter Selective Lymphadenectomy Trial I (10.1%) where the complication rate increased to 37.2% with the addition of SLND after SNB.[10] Our main complications were lymphocoele and lymphedema. The 1.8% lymphedema incidence was similar to the 1.7% lymphedema incidence found by Wrone et al.[32] Allergic blue-dye anaphylaxis occurred in 0.3% which is slightly lower than the 0.7% in Leong et al. experience.[33] However, the comparison is not completely valid as we used patent blue V while these authors used isosulfan (lymphazurine). We observed that the incidence of ITM as site of first recurrence was 6.1%, and that it was significantly higher among metastatic SN patients (13.5%) compared to negative SN patients (4%) as reported in other studies.[34,35] The latter can be explained by the fact that metastatic SNs are found among patients whose tumor has already developed a metastatic potential. SNB is thus a safe procedure associated with a low morbidity and no mortality.

Predictive factors of sentinel node status

There are only few published studies that have evaluated predictive factors of SN metastases by multivariate analysis. McMasters et al.[36] found that Breslow thickness, Clark

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level, ulceration and age ≤60 years were significant predictors of SN metastases. Wagner et al.[37] found that a Breslow thickness cut point ≥1.25 mm, ulceration and high mitotic index were significant predictive factors of SN positivity. Rousseau et al.[38] found that Breslow thickness, ulceration, age ≤50 years and truncal location were significant predictors of SN metastases. Other histopathological factors published by others such as mitotic index,[37] tumor infiltrating lymphocytes,[39] or angiolymphatic invasion[40] were also predictive of SN positivity. Our multivariate logistic regression analysis for predictive factors of SN metastases showed that only Breslow thickness was statistically significant (T3: $p = 0.009$, T4: $p < 0.001$). Ulceration ($p = 0.071$) and truncal location ($p = 0.066$) were close to reach statistical significance.

Breslow thickness and ulceration are constantly reported as predictive factors of metastatic SN in various univariate analyses.[25,27,36–38] In our study we also found that Breslow thickness stratified according to the AJCC classification and ulceration were significantly correlated with SN positivity. Nodular melanoma was also a predictive factor of SN positivity which is consistent with Nowecki et al. experience.[27]

Indications of sentinel node biopsy

The indication of SNB in thin (≤1 mm) cutaneous melanoma is still controversial. In the new AJCC staging system,[8] tumors ≤1 mm thick are classified as T1a if they are non-ulcerated and T1b if they are ulcerated or Clark IV or V. This is based on the reported 10 years survival rates of 87.9% for the T1a group and of 83.1% for the T1b group.[41] The rate of tumor-positive SN in melanoma ≤1 mm thick is reported to be 3% in two published reports.[42,43] In the current study we showed that 6% of melanoma ≤1 mm thick had metastatic SN, but all SLND were tumor-free. During a mean follow-up of 33 months of these T1 patients there was no relapse and no patient died of the disease. The presence of regression as inclusion criteria for SNB is also questionable; it has been described either as an unfavourable[44,45] or as a protective[46] prognostic factor. Moreover, Topping et al.[47] reported in their study that all patients having histological features of regression had a negative SN. In our study all the patients presenting with regression associated with a Breslow thickness ≤1 mm ($n = 16$) had a negative SN and did not relapse. This observation, despite the small number of patients, could suggest that regression associated to a Breslow thickness <1 mm should not be considered as an inclusion criterion anymore.

Conclusion

This present single institution study confirms that SNB is a reliable and reproducible procedure with high sensitivity (91.4%) as well as a low morbidity (7.6%). Our multivariate logistic regression analysis for predictive factors of SN metastases showed that only Breslow thickness was statistically significant. We concluded that DFS was worsened in order of significance by Breslow index, metastatic SN and male gender. And finally we found that in decreasing order a metastatic SN, male gender, Breslow thickness and ulceration were significantly associated with a poorer DSS. These data reinforce the SN status as a powerful staging procedure.

Conflicts of interest

The authors have no conflicts of interest.

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