

Original Paper

The Impact of Ultrasound Scanning in the Staging and Follow-up of Patients with Clinical Stage I Cutaneous Melanoma

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In 85 patients with intermediate to high risk cutaneous melanoma, concomitant palpation and ultrasound scanning (US) of the axillary and inguinal sites were performed in order to detect any loco-regional lymph node metastases at pre-operative staging and postoperative monitoring. At 12 months follow-up, US identified 12 out of 13 (92%) histologically proven metastases, while palpation indicated metastatic disease in only 3 (23%) patients. Metastases were intranodal in 6 out of 12 cases detected with US, and extranodal in all the 3 cases identified by palpation, thus confirming that US is more effective than palpation in the early detection of lymph node metastases from melanoma. US was also more effective in discriminating all non-neoplastic lymph nodes: its overall specificity was 100% versus 85% for palpation. Thus, when carried out by well-trained radiologists, US is a very useful diagnostic tool for the surgical oncologist dealing with melanoma patients. © 1997 Elsevier Science Ltd. All rights reserved.

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INTRODUCTION

It is widely agreed that the palpation of axillary and inguinal lymph nodes alone has a high rate of error in locating metastases from melanoma [1, 2], and high-resolution ultrasound scanning (US) is reported to be more efficient in the early detection of locoregional lymph node metastatic deposits than palpation alone [3, 4].

Although, as yet, no randomised studies have demonstrated an advantage in the survival rate of patients with melanoma undergoing prophylactic lymph node dissection [5, 6], it has recently been suggested that patients treated early for lymph node metastases have significant benefit. Multivariate analysis findings have indicated that, unlike extracapsular metastases, intracapsular lymph node metastases are independent variables with a positive prognostic value [7, 8].

The results of a randomised study, using adjuvant interferon for high-risk melanoma patients indicate that this treatment modality significantly increases the survival rate in all node-positive patients, including the group with non-palpable regional lymph-node metastases [9]. Furthermore, following lymphadenectomy, the incidence of local relapse from micrometastases is much lower than that from palpable metastases [10]. An early diagnosis of metastases from cutaneous melanoma is, therefore, advocated.

The aim of our study was to ascertain the current role of US of lymph node sites in the detection of metastases from melanoma, both for staging and during follow-up.

PATIENTS AND METHODS

From 1991 until June 1994, 85 patients (30 males, 55 females, mean age 47.4 years, range 19–85 years) with cutaneous melanoma and Breslow thickness ≥ 1 mm and/or Clark's level ≥ 3 entered our study at Clinica Chirurgica II, Padova University, Padova, Italy. Table 1 shows the distribution of patients according to the primary tumour site,

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Table 1. Details of 85 patients with primary melanoma

	n (%)
Localisation	
Upper limb	12 (14)
Lower limb	43 (51)
Trunk	30 (35)
Histological type	
Superficial spreading	59 (69)
Nodular	18 (21)
Lentigo maligna	4 (5)
Acrall lentiginous	4 (5)
Breslow (mm)	
≤1	27 (32)
1.1–1.5	14 (16)
1.6–3	34 (40)
3.1–5	7 (8)
>5	3 (4)
Clark level	
III	42 (49)
IV	39 (46)
V	4 (5)

melanoma classification, Breslow thickness and Clark's level.

3 patients were lost to follow-up and 2 died before the end of the follow-up period (at least 24 months, with examinations every 6 months), and were, therefore, excluded from the study. Each of the 80 remaining patients underwent staging and subsequently 4 further examinations, all of which included physical and US examinations. Physical examination (palpation) was performed by surgeons: if lymph nodes were enlarged but not painful, had progressively increased in size and/or were hard at palpation, they were considered positive. All the ultrasound scans were performed by the same radiologist (A.T.) using a high-frequency mechanical Sector probe (7.5–10 MHz). The differential US diagnosis of negative or positive lymph nodes was made using modified versions of Vassallo's parameters [11, 12], as follows:

—lymph nodes with a longitudinal and transverse axis ratio of less than 2 and without hyperechogenic central striae;

—presence of focal intralymphnodal lesions with distortion of the border and/or hyperechogenic central striae;

—lymph nodes with irregular borders;

—lymph nodes with a maximum diameter of more than 3 cm.

US-guided fine-needle aspiration biopsies (FNAB) were obtained if the US picture was positive, and if cytology was also positive, a complete loco-regional lymph node dissection was performed. If US was positive, but the FNAB negative, the patient was followed up regularly.

After staging, 6 patients underwent intra-operative lymphatic mapping and selective lymph node biopsy as described by Morton and associates [14, 15]. Only patients with positive lymph nodes at frozen or paraffin sections had lymph node dissection.

Lymph nodes were considered metastatic ('true positives') only after histological confirmation in specimens from lymph node dissection. 'True negatives' were cases in which lymph node metastases had not developed within 2 years following treatment for the primary melanoma. Cases considered 'false positives at palpation' were negative at US scan, and did not develop metastases within 2 years. 'False positives at US' were cases with negative cytology in which lymph node metastases had not developed within 2 years, whereas false negatives were cases negative at palpation and/or US, but in which lymph node metastases developed within two years.

The diagnostic efficacy (sensitivity, specificity and accuracy) of palpation, US alone and US combined with FNAB was evaluated at patients' staging and at 6 monthly intervals, for at least 24 months of follow-up after treatment for primary melanoma.

RESULTS

13 of the 80 patients considered in our series developed lymph node metastases, 2 at staging and 11 during follow-up, whereas the remaining 67 were negative 24 months after treatment of the primary tumour.

According to the natural history of lymph node metastases with progressive enlargement, the efficacy of the 3 methods improves with time, as shown in Table 2. After the 12-month follow-up, whether it was combined with FNAB or not, US revealed 12 out of 13 positive cases (sensitivity = 92%), while palpation identified only 3

Table 2. Palpation compared to US alone and US combined with FNAB in the detection of lymph node metastases at staging and follow-up for 80 melanoma patients

Metastases	Palpation			US			US + FNAB		
	Positive No.	Negative No.	Sensitivity/Specificity/Accuracy (%)	Positive No.	Negative No.	Sensitivity/Specificity/Accuracy (%)	Positive No.	Negative No.	Sensitivity/Specificity/Accuracy (%)
At staging									
Present	0	13	0/93/77	1	12	8/96/81	1	12	8/100/85
Not present	5	62		3	64		0	67	
After 6 months									
Present	1	12	8/90/76	8	5	62/91/86	8	5	62/100/84
Not present	7	60		6	61		0	67	
After 12 months*									
Present	3	10	23/88/77	12	1	92/90/90	12	1	92/100/99
Not present	8	59		7	60		0	67	

*No change after 18 or 24 months.

Table 3. Palpation compared to US alone and US combined with FNAB in the detection of lymph node metastases of 80 melanoma patients by anatomical sites

Metastases*	Palpation			US			US + FNAB		
	Positive No.	Negative No.	Sensitivity/Specificity/Accuracy (%)	Positive No.	Negative No.	Sensitivity/Specificity/Accuracy (%)	Positive No.	Negative No.	Sensitivity/Specificity/Accuracy (%)
Axillary									
Present	2	2	50/85/80	4	0	100/92/93	4	0	100/100/100
Not present	4	22		2	24		0	26	
Inguinal									
Present	1	8	11/90/76	8	1	89/88/88	8	1	89/100/98
Not present	7	37		35	36		0	41	

*After a minimum follow-up of 24 months.

(sensitivity = 23%). However, palpation and US alone had 8 (specificity = 88%) and 7 (specificity = 90%) false positive cases, respectively, which were all negative at FNAB (specificity = 100%). Among 6 patients who underwent intra-operative lymph node mapping and selective lymph node biopsy, there was only one false negative, due to a micrometastasis. No further positive cases occurred after 18 and 24 months of follow-up.

After 24 months of follow-up, we observed that metastatic lymph nodes of the axillary region were detected more reliably than those of the groin (Table 3). Although palpation alone failed to reveal 2 out of 4 cases in the axilla (sensitivity = 50%), US with or without FNAB identified all positive lymph nodes in this site (sensitivity = 100%). In the groin, palpation identified only 1 out of 9 patients with lymph node metastases (sensitivity = 11%) while US, alone or combined with FNAB, identified 8 out of 9 positive nodes (sensitivity = 89%). No notable differences were observed between the specificity of the three procedures with respect to the two sites.

Of the 13 metastases, 6 were extranodal and 7 intranodal. There were 3 axillary and 3 inguinal extranodal metastases, and 1 axillary and 6 inguinal intranodal metastases.

Of the 80 evaluable patients, 69 are alive and disease-free and 3 are alive with disease. Six patients died after the 24-month follow-up period, 4 of tumour progression and distant metastases and 2 of causes unrelated to melanoma.

DISCUSSION

The early detection of lymph node metastases from cutaneous melanoma may be useful in achieving better locoregional control of the disease (lower incidence of recurrences) and increasing the survival rate, particularly in view of recent improvements made in adjuvant therapy. The high rate of errors with palpation alone in identifying early stage metastatic deposits indicates the need for new investigational techniques that can identify lymph nodes that are already involved, although negative at clinical examination. US is currently advocated as one of the best available diagnostic procedures as it is effective, has low costs, is not invasive and is tolerated well by the patient [13]. As yet, however, few reports have dealt with this topic.

We found that the efficacy of US, whether combined with FNAB or not, was much higher than that of the physical examination alone. In our series, its sensitivity at 12 and 24 months was 92%. This percentage is comparable to those reported by other authors [3, 4]. The presence of lymph

node disease was highlighted in 12 out of our 13 positive cases. Only 1 patient, who had a micrometastasis <2 mm (not detected with US) was false negative at US; this case was identified with intra-operative mapping [14, 15]. Specificity, that is the possibility of discriminating non-neoplastic lymph nodes, was 100% for US combined with FNAB versus 90% for US alone and 85% for palpation at 12 and 24 months.

Unlike Prayer and associates [3], who found that palpation gave false negatives in 6% of cases with a sensitivity rate of 52%, we found that palpation gave false negatives in 12% with a sensitivity of 23%. The apparent discrepancies between these results may be due to the fact that it is difficult to discover intranodal metastases with the clinical approach alone. In fact, in our study, inguinal and axillary palpation was positive only in the presence of extranodal disease: 2 out of 3 in the axillary and 1 out of 3 in the inguinal site. No histological findings of metastases were reported in the study by Prayer and associates.

With regard to the incidence of false positives in our series, the efficacy of US alone (around 8%) was similar to that of palpation (around 10%) and higher than that in the study by Prayer and associates [3]. In fact, the US parameters considered 'suspect' in our study were more extensive than those adopted by other authors. It should be stressed that with combined US and FNAB all false positive cases at palpation or US alone were discovered, with a considerable reduction in the number of patients undergoing unnecessary lymph node dissection.

Furthermore, at first glance our results appear different from those reported by other authors because we subdivided the patients according to the anatomical site (axillary, inguinal). We found that the three methods were more effective at locating lymph node metastases at the axillary site than at the inguinal site, although US was better than palpation for the detection of metastases in both sites. However, it should be borne in mind that there was one false negative case at US, a micrometastasis located in the groin. Moreover, if we consider the histological evaluation of the metastases found in both sites, in our experience the efficacy of US seems to be higher in the inguinal area: overall, 6 out of 9 patients presented intranodal inguinal metastases, whereas only 1 out of 4 had intranodal axillary metastases.

Of course, US cannot detect micrometastases to the lymph nodes. This may be achieved routinely in the future with the new, promising, intra-operative mapping tech-

niques. Nevertheless, our findings show that US can identify small intracapsular metastatic deposits either at staging or during the early follow-up of melanoma patients. In fact, all the metastases detected in our series developed within 1 year of surgery on the primary tumour.

These observations suggest that since US has a relatively low cost, is non-invasive and well tolerated, it should be routinely performed in all melanoma patients at risk of lymph node metastases (Breslow ≥ 1 mm, Clark \geq III), both at the first examination and later (every 2–3 months), particularly within the first year of follow-up.

In conclusion, if carried out by well-trained radiologists, US is useful to the surgical oncologist in the treatment of patients with melanoma. The surgical and radiological teams should work alongside each other so that their work becomes mutually complementary. This will be conducive to an early diagnosis of lymph node metastases, which cannot be achieved with clinical examination alone.

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