

Original Paper

Lymph Node Sonography Versus Palpation for Detecting Recurrent Disease in Patients with Malignant Melanoma

M. Binder,¹ H. Kittler,¹ A. Steiner,¹ R. Dorffner,² K. Wolff¹ and H. Pehamberger¹

¹Department of Dermatology; and ²Department of Radiology, University of Vienna Medical School, Währingerguertel 18–20, A-1090 Vienna, Austria

The aim of this study was to examine the efficacy of lymph node palpation versus high resolution lymph node sonography for the detection of lymph node metastases in patients with malignant melanoma. We retrospectively evaluated 2256 pairwise lymph node examinations of the cervical, axillary and inguinal region by palpation and sonography in 264 patients with resected melanomas greater than 0.75 mm of invasion thickness. Lymph node metastases occurred in 50 patients (19%) which were detected in 38 (76%) by both methods in agreement. In 7 cases (14%) palpation failed, in 3 cases (6%) sonography failed and in 2 cases both methods failed to identify metastases. The overall sensitivity of detecting metastatic disease was 82% for palpation and 90% for sonography which was statistically not different. The overall specificity by sonography (99%) was significantly better than for lymph node palpation (88%). Taking into account the results of this analysis, we conclude that patients with a negative result by lymph node palpation do not need further sonography for verification. However, any suspect result by palpation should be additionally evaluated by lymph node sonography in order to rule in or out metastatic disease. © 1997 Elsevier Science Ltd.

Key words: melanoma secondary, neoplasms epidemiology, follow-up-studies incidence, lymph nodes ultrasonography lymphatic metastasis, neoplasm staging, retrospective studies, sensitivity and specificity, time factors

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INTRODUCTION

ALTHOUGH THE incidence of malignant melanoma is increasing worldwide [1, 2], prognosis and survival rates are improving primarily because the tumour is being recognised in earlier phases [3–5]. Metastases to the regional lymph nodes represent the most common site of progressive disease in melanoma patients and early detection of lymph node metastases needs to be addressed [6–8].

A cheap and simple approach is the manual palpation of the regional lymph nodes. However, palpation has a reported negative rate of up to 39% [9] in malignant melanoma. In contrast, there have been many reports on the excellent test performance of lymph node sonography for the detection of metastatic disease [10–15], although lymph node sonography represents an additional test for the

patient associated with additional stress [16] and financial cost.

Our aim was to evaluate the use of simple lymph node palpation and high resolution sonography for the detection of regional lymph node metastases, and to determine whether palpation or sonography are routinely indicated in the postoperative care of melanoma patients.

PATIENTS AND METHODS

Patients

From June 1991 to September 1994, patients with surgically resected malignant melanoma greater than 0.75 mm of invasion depth according to Breslow [17] were enrolled in this study. Patients were routinely scheduled to be followed up every 3 months. At each follow-up examination, the regional lymph nodes were palpated by an experienced dermatologist. In each case lymph node sonography was performed within two weeks after palpation.

Correspondence to M. Binder.

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Definition of results by palpation

Lymph node palpation of the cervical, axillary and inguinal region was performed by specifically trained dermatologists during the follow-up of patients. A lymph node suspected of harbouring metastatic disease was defined as at least one enlarged lymph node with the presence of a firm resistance or rubbery appearance. For the differentiation of benign causes of adenopathy, history or evidence of injury or infection was necessary. Generally, common clinical experience was used for the distinction of lymph nodes with inflammatory reaction [7, 8].

Definition of results by sonography

Sonography was performed by experienced radiologists using a UM9 unit (ATL, Bothell, WA, U.S.A.) with a 10–15 MHz linear focus transducer. The visible lymph nodes were documented in longitudinal and cross-sections. Circular and oval masses with poor echo were regarded as indicative of metastatic changes; longitudinal configured lymph nodes, the hilum of which appeared as an echogenic eccentric area, were regarded as reactive [10, 12, 13].

Definition of truth

A positive result from palpation or sonography was considered as *true-positive* when the histopathology from an immediate lymph node dissection (LND) revealed the diagnosis of lymph node metastasis.

A positive result from palpation or sonography was considered as *false-positive* when the histopathology from an immediate lymph node dissection (LND) did not reveal lymph node metastasis; or, if an immediate LND was not performed, the results from palpation and sonography remained negative for the next two follow-up visits. A negative result from palpation or sonography was considered as *true-negative* when the histopathology from an immediate LND was negative or at least the next two follow-up visits did not give further evidence for lymph node metastases by palpation and sonography. A negative result from palpation or sonography was considered as *false-negative* when the histopathology from an immediate lymph node dissection revealed lymph node metastases or when lymph node metastases were histologically detected within the next follow-up cycle. In addition, results were only considered false-negative when the preceding examination was without evidence of enlarged lymph nodes by palpation and sonography.

The rules listed above were used as *a priori* definitions in order to classify all possible results as true-positive, false-positive, true-negative or false-negative, respectively.

Statistical methods

A retrospective follow-up design was used for this study. Data were recorded and extracted using Statistics for Windows (StatSoft, Inc., Tulsa, Oklahoma, U.S.A.). Descriptive data are presented as mean or median as appropriate. Sensitivity and specificity were calculated with standard formulae [18], and 95% confidence intervals were calculated using the formula $1.96 \cdot \sqrt{(p \cdot q)/n}$, where p = sensitivity or specificity expressed as a fraction of 1, $q = 1 - p$ and n = number of observations. Differences of $p < 0.05$ were regarded as statistically significant.

RESULTS

Demographics and clinical information

A total of 264 patients with resected malignant melanoma were enrolled in this study. Mean age was 54 years ranging from 17 to 82 years. 137 (52%) of the patients were male. In 91 patients (34%), invasion depth was between 0.76 and 1.5 mm, in 85 patients (32%) between 1.51 and 3.0 mm and in 88 patients (33%) greater than 3.0 mm. Median Breslow's thickness was 1.80 mm (interquartile range 1.1–3.0 mm).

2256 paired examination for palpation and sonography of the locoregional lymph nodes were obtained. The median number of examinations per patient was 8 with an interquartile range of 4–12. Lymph node sonography was performed within a maximum of two weeks after palpation.

Overall data analysis

In 50 of 264 patients (19%) who developed locoregional lymph node metastases, 38 (76%) were correctly diagnosed both by palpation and sonography in agreement. In 7 cases (14%), locoregional lymph node metastases were not detected by palpation but by sonography. In 3 cases (6%) sonography failed to identify metastases detected by palpation. In 2 cases, both methods (4%) failed to identify metastases. True negative results by both methods were found in 1925 examinations (85%). In 258 examinations (11%), a false-positive result was found by palpation but not by sonography, and in 10 examinations (0.44%) the result was false-positive by sonography but not by palpation. In 13 negative cases (0.58%) both methods exhibited a false-positive result.

Overall sensitivity of detection of metastatic disease in the locoregional lymph nodes by palpation was 82% (41/50; 95% confidence interval 71–93%), not significantly different from the 90% sensitivity for lymph node sonography (45/50, 95% confidence interval 82–98%).

Overall specificity in the locoregional lymph nodes by palpation was 88% (1935/2206, 95% confidence interval 87–

Table 1. Results of palpation of lymph nodes in order to detect locoregional lymph node metastases in patients with malignant melanoma

Anatomical site	True-positive	False-negative	False-positive	True-negative	Sensitivity (%) (95% confidence interval)	Specificity (%) (95% confidence interval)
Inguinal	12	3	125	821	80 (60–100)	87 (85–89)
Axillary	25	6	114	818	81 (67–95)	88 (86–90)
Cervical	4	0	32	296	100*	92 (89–95)
All groups	41	9	271	1935	82 (71–93)	88 (86–89)

*Confidence limit exceeds 100%.

Table 2. Results of sonography in order to detect locoregional lymph node metastases in patients with malignant melanoma

Anatomical site	True-positive	False-negative	False-positive	True-negative	Sensitivity (%) (95% confidence interval)	Specificity (%) (95% confidence interval)
Inguinal	14	1	13	933	93 (80-∞)*	99 (98-100)
Axillary	27	4	6	926	87 (75-99)	99 (98-100)
Cervical	4	0	4	324	100*	99 (98-100)
All groups	45	5	23	2183	90 (82-98)	99 (98.6-99.4)

*Confidence limit exceeds 100%.

Table 3. Results of palpation of lymph nodes in order to detect locoregional lymph node metastases in patients with malignant melanoma by invasion depth of the primary melanoma

Invasion depth (mm)	True-positive	False-negative	False-positive	True-negative	Sensitivity (%) (95% confidence interval)	Specificity (%) (95% confidence interval)
0.76-1.50	3	2	75	708	60 (17-∞)*	90 (88-92)
1.51-3.0	13	1	81	680	93 (79-∞)*	89 (87-92)
>3.0	25	6	115	547	81 (67-95)	83 (80-86)
All groups	41	9	271	1935	82 (71-93)	88 (86-89)

*Confidence limit exceeds 100%.

Table 4. Results of sonography in order to detect locoregional lymph node metastases in patients with malignant melanoma by invasion depth of the primary melanoma

Invasion depth (mm)	True-positive	False-negative	False-positive	True-negative	Sensitivity (%) (95% confidence interval)	Specificity (%) (95% confidence interval)
0.76-1.50	5	0	3	780	100*	100 (99-100)
1.51-3.0	14	0	9	752	100*	99 (98-100)
>3.0	26	5	11	651	84 (71-97)	98 (97-99)
All groups	45	5	23	2183	90 (82-98)	99 (98.6-99.4)

*Confidence limit exceeds 100%.

89%), significantly different than for lymph node sonography (2183/2206, 99% (95% confidence interval 98.6-99.4%)).

Analysis according to site of examination and depth of invasion

Data analysed according to anatomical site of examination are presented in Tables 1 and 2. Both palpation and sonography had the highest sensitivity and specificity for the cervical region. Generally, sensitivity and specificity were higher for sonography than for palpation.

Data analysed according to the depth of invasion are shown in Tables 3 and 4. Palpation showed low sensitivity (60%, 95% confidence interval 17-∞) for thin melanomas (0.76-1.5 mm), with decreasing specificity as the depth of the melanoma increased. Sonography was highly sensitive and specific for all depths, the lowest sensitivity of 84% occurring for a depth of >3 mm.

DISCUSSION

In patients with malignant melanoma, the locoregional lymph nodes are the most common site of metastatic disease [7, 8]. During follow-up, vigilance is mandatory for the detection of metastatic locoregional lymph nodes because some patients can be cured when appropriate treatment is initiated [7].

Two different non-invasive diagnostic methods are routinely used for the identification of lymph nodes suspected of

harbouring metastatic disease. The basic method of examination is the simple palpation of the locoregional lymph nodes. Lymph nodes containing metastatic melanoma are generally firmer, more rubbery and non-tender compared with inflammatory nodes [7]. However, nodes invaded by melanoma do not always continue to grow inexorably after they have been diagnosed, and may actually shrink, leading to a false sense of security [7].

Sonography permits a clear presentation of the regions examined and exact ascertainment of location, size and relation of the lymph nodes is possible. Because of distinct morphology, differentiation between reactive lymph nodes and lymph node metastases can be made by sonography [10, 12]. However, this method needs a trained radiologist and technical equipment. In addition, the patient is confronted with an additional examination and its concomitant psychological stress [16] and there is also the extra financial burden of the examination.

Three useful conclusions can be drawn from this study. First, both methods, palpation and sonography, exhibited a high overall sensitivity for detecting metastatic disease. The sensitivity by sonography (90%) was higher compared with that of palpation (82%), but this difference was statistically not significant. Both methods exhibited good but not excellent agreement for detecting metastatic disease. In 76%, both methods detected metastases in agreement. However, in 7 cases (14%), palpation failed and in 3 cases (6%) sono-

graphy failed to identify correctly metastatic disease which was identified by the alternate test.

Second, specificity by sonography (99%) was significantly better than specificity by palpation (88%), indicating that palpation was responsible for approximately 11% of false-positive results, whereas only 0.44% of the cases were false-positive by sonography.

Third, when the data were analysed with regard to the anatomical site, the cervical region exhibited the highest sensitivity and specificity by both methods. When the data were analysed according to the invasion depth of the melanoma, palpation exhibited a relatively low sensitivity (60%) in thinner melanomas. In contrast, lymph node sonography did not demonstrate a discernible trend of test performance according to the invasion depth. This observation may be due to the fact that clinicians are more influenced by additional clinical information than sonologists.

The results of this study are in agreement with those of several other groups that have reported sonography with the superior test performance [10–12, 15, 19]. Our data indicate that simple palpation and sonography exhibit sufficient, comparable sensitivity for the detection of metastatic lymph nodes in patients with malignant melanoma. However, a 99% specificity by sonography allows those cases which have been classified as false positive by palpation to be eliminated. Thus, suspect findings by lymph node palpation necessitate lymph node sonography for including or excluding metastatic disease. Cases with a negative result by palpation do not need a further test for further verification. Besides the obvious concerns for duration of life and quality of life, the financial burden of additional lymph node sonography should also be considered. In summary, for the follow-up patients with malignant melanoma, we do not recommend routine screening of lymph nodes by sonography without a preceding suspect result by palpation.

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