Ultrasoundography Using Simple Diagnostic Criteria vs Palpation for the Detection of Regional Lymph Node Metastases of Melanoma

Philippe Saiag, MD, PhD; Marion Bernard, MD; Alain Beauchet, MD; Marie-Lise Bafounta, MD; Isabelle Bourgault-Villada, MD, PhD; Sophie Chagnon, MD

Objectives: Our aims were (1) to compare the respective ability of ultrasonography and palpation to detect nodal metastasis during initial staging and follow-up in patients having melanomas and (2) to assess, we believe for the first time, which ultrasound criteria should be used to define metastasis in cases of cutaneous or mucosal melanoma.

Design: Prospective single-center study. Nodal metastasis was confirmed by histopathologic evaluation.

Setting: Dermatology and radiology departments of a university hospital.

Patients: A total of 160 new consecutive patients with stage I to stage III melanoma.

Intervention: Experienced operators independently performed 391 paired palpation and ultrasonographic examinations.

Main Outcome Measures: Firm enlarged nodes found on palpation were considered metastatic. On ultrasonographic examination, circular or oval hypoechoic lymph nodes lacking hyperechoic hila were considered metastatic (stringent criteria). Nodes with 2 or fewer of these patterns and other published signs of metastasis (ie, intranodal nodular hypoechoic focus and irregularity of the node margin) were considered suspicious.

Results: Over the 6-year study period 33 patients developed nodal metastasis. For palpation and ultrasonography using the stringent criteria, respectively, sensitivity was 41.5% (95% confidence interval [95% CI], 29.6-53.5) and 76.9% (95% CI, 66.7%-87.2%) (P<.001) and specificity was 95.7% (95% CI, 93.5%-97.9%) and 98.4% (95% CI, 97.1%-99.8%) (P<.05). Including ultrasonographically suspicious lymph nodes significantly lowered specificity (86.2% [95% CI, 82.5-89.9]) (P<.05) without improving sensitivity. Previous lymphadenectomy had little impact on ultrasonographic findings.

Conclusion: Ultrasonography using stringent criteria of nodal metastasis, which are easy to identify and reliable, is superior to palpation for early detection of regional lymph node metastases of melanoma.

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MELANOMA INCIDENCE has increased dramatically over the last decades, and the regional lymph nodes are the most common first sites of melanoma progression. According to the largest analysis of prognostic factors conducted to date, the prognosis for patients having melanoma with lymph node involvement has depended on the number of metastatic nodes, whether nodal metastases were palpable, and the presence or absence of primary tumor ulceration. Because treatment of distant melanoma metastases is poorly effective, attempts to diagnose early nodal spread are warranted to initiate earlier therapeutic lymphadenectomy (LD) even though the efficacy of this strategy on patient survival has not been verified in randomized controlled clinical trials. Early detection can be achieved by intraoperative lymphatic mapping and sentinel lymphadenectomy (LM/SL) during initial cancer staging and/or by careful surveillance after excision of the primary tumor. Although recent retrospective and prospective studies have demonstrated the effectiveness of this approach, recommended follow-up protocols vary from country to country, with significant differences in expert opinions and practices.

Previous studies have suggested that ultrasonographic scans, which are inexpensive to perform, are better able to detect

See also pages 217 and 269

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Author Affiliations: Service de Dermatologie (Drs Saiag, Bafounta, and Bourgault-Villada), Service de Radiologie (Drs Bernard and Chagnon), and Antenne d’Informatique Médicale (Dr Beauchet), Hôpital Ambroise-Paré, Assistance Publique–Hôpitaux de Paris, Université Versailles–Saint-Quentin-en-Yvelines, Boulogne, France.

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lymph node metastases of melanoma than palpation, but Binder et al did not find ultrasonography to be significantly more sensitive than palpation. However, most of those studies were biased, mainly because the definition of true-negative was absent, incomplete, or questionable, and because an uneventful follow-up of 6 or more months after ultrasonographic evaluation was required in only 2 studies. Also, the independence between physical examination and ultrasonographic evaluation (ie, the assurance that ultrasonography results did not influence palpation) was stated in only 2 studies. Finally, ultrasonographic criteria of lymph node metastasis varied from study to study, and the impact of these variations on the diagnostic accuracy of ultrasonography has not yet been assessed. The most frequently used ultrasonographic criteria were nodal shape (circular/oval) or low Solbiati index (ie, a low longitudinal-transverse diameter ratio) and low echogenicity. Most authors added other criteria, but the relative importance of each to detect metastasis was not clearly specified. In contrast, other imaging techniques were of little value in the routine follow-up of asymptomatic patients with localized melanoma.

To better assess the contribution of lymph node ultrasonography to initial cancer staging and follow-up in patients with melanoma, our aims were (1) to compare, in a prospective study, the ability of high-resolution lymph node ultrasonography with that of palpation to detect nodal metastasis in patients with melanoma; (2) to evaluate, we believe for the first time, which ultrasonographic criteria should be used to define metastasis in cases of cutaneous or mucosal melanoma; and (3), because scar tissue can modify ultrasonographic images, to evaluate whether ultrasonography remains useful once patients have undergone radical LD.

**METHODS**

**SELECTION CRITERIA AND STUDY VARIABLES**

All patients with cutaneous or mucosal melanoma seen in our dermatology department from May 1993 to May 2003 were prospectively followed up and their outcomes were entered into a computerized database. If primary excision had been performed elsewhere, the original slides were reexamined by an experienced pathologist. All patients had confirmed diagnoses of melanoma, and the lesions were staged using the classification of the American Joint Committee on Cancer. Beginning in September 1995, follow-up visits of patients with melanoma were conducted according to the 1995 guidelines of the French consensus conference. Patients with a melanoma 1.5 mm or less in thickness were to be examined every 6 months during the first 10 years after primary tumor resection, and patients with a melanoma greater than 1.5 mm in thickness or with histopathologic signs of melanoma regression were to be examined every 3 months during the first 5 years, then every 6 months through the 10th year. Patients with stage III melanoma were monitored every 3 months. Particular emphasis was placed on teaching patients self-examination as well as how to recognize symptoms of recurrence and the appearance of a second melanoma. Each consultation consisted of complete history taking, and the inspection of the entire skin surface as well as the primary resection scar, the lymphatic drainage area(s), and all lymphatic regions. No routine chest radiograph, abdominal ultrasonographic scan, or blood test was performed after the initial evaluation in patients with nonsymptomatic stage I or stage II melanoma, but these tests were performed every 3 months in patients with stage III melanoma. Follow-up examinations took place alternatively in our department and at private dermatology practices, with all imaging techniques performed in our hospital.

After September 1995, and as optionally proposed by the French Consensus Conference, we added ultrasonographic evaluation of the resected tumor scar, lymphatic drainage area(s), and regional node region(s) to the routine initial and follow-up examinations performed in our department for all new patients with stage I to III melanoma. The study followed the principles outlined in the Declaration of Helsinki. All patients gave informed oral consent. Ultrasonographic procedures were precisely defined. Moreover, the operators were asked to describe prospectively longitudinal and cross sections of all abnormal lymph nodes as well as the shape, echogenicity, size, and appearance of the margins of abnormal nodes.

For the interim analysis we identified from our database all new patients with stage I to III disease seen between September 1, 1995, and August 31, 2001, excluding patients with in situ melanoma. All paired palpation and ultrasonographic examinations performed during this period were selected for analysis. Original radiologic reports and images were collected by a radiologist (M.B.) with great experience in ultrasonography who was blinded to the patients’ outcomes.

**PALPATION AND ULTRASONOGRAPHY**

Lymph nodes were palpated by specifically trained dermatologists. Enlarged lymph nodes with firm resistance were clinically considered metastatic. Soft, tender, enlarged lymph nodes with a history or evidence of injury or infection were considered inflammatory.

On the same day as clinical examination for nearly all patients, ultrasonography was performed by radiologists experienced in ultrasonography who were blinded to the result of palpation and had little information concerning the patients’ melanoma characteristics (ie, Breslow index, location, American Joint Committee on Cancer staging, and presence or absence of previous elective or sentinel LD). A Power Vision 6000 (Toshiba Medical France SA, Puteaux, France) was used, with a 6- to 12-MHz linear transducer set between 7.5 and 12 MHz according to the depth of nodes being explored. When the interpretation of images was doubtful, a consensus was reached with the main investigator from the Department of Radiology (S.C.). The ultrasound examination started at the site of the excised primary melanoma scar and followed the paths of the lymphatic vessels to the lymph node area(s), as previously described. A longitudinally configured lymph node with an echogenic hilum was considered reactive. Various features were used to define ultrasonographic lymph node involvement. A circular/oval hypoechoic lymph node with a Solbiati index less than 1.5 and no hyperechoic hilum constituted the major criteria for metastatic involvement. Minor criteria for nodal metastasis were a nodular hypoechoic focus within a lymph node with an irregular lymph node margin, and stringent criteria were the presence of all 3 major criteria (Figure 1). Nonstringent criteria of nodal metastasis were the presence of 1 or 2 major criteria and/or 1 or 2 minor criteria (Figure 2). Patients with ambiguous images were reexamined clinically and by ultrasonography within 6 weeks; only the final conclusion was retained for analysis. Because our aim was to assess the diagnostic efficacy of palpation vs ultrasonography, ultrasonographic examinations performed to monitor treatment of a previously known lymph node metastasis were also excluded from

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DEFINITIONS OF NODAL STATUS

The mode of nodal status assessment was left to individual dermatologists. Nodal status was defined histologically or based on evolution. All nodes with histologically proven tumoral deposits, no matter their size, were considered metastatic. The definitions given below were used as a priori criteria to classify all possible results of palpation and ultrasonography.

A positive palpation or ultrasonographic finding was considered true-positive when histopathologic studies of LD, FNAB, or LM/SL performed during initial imaging revealed lymph node metastasis. A positive palpation or ultrasonographic finding was considered a false-positive when immediate histopathologic studies of a LD or LM/SL did not reveal lymph node metastasis, or when FNAB result was negative and no further surgery was performed and the results of palpation and ultrasonography remained negative at least 6 months.

A negative palpation or ultrasonographic finding was considered a true-negative when the result of the initial LM/SL was negative or follow-up visits over 6 months did not provide any evidence of nodal metastasis. A negative palpation or ultrasonographic finding was considered a false-negative when histopathologic studies of LD, FNAB, or LM/SL revealed lymph node metastasis, or when nodal metastasis was histologically detected within the next 6 months. In addition, patients with negative findings at the last paired examinations had to remain lymph node negative for at least 12 months after the last paired examinations included in the analysis for these findings to be considered true-negatives or false-positives. Diagnoses of postsurgical lymphocele, hematoma, or fibrosis were given following laboratory results for the aspiration sample or a compatible outcome.

STATISTICAL ANALYSIS

Based on the findings of the study conducted in the early 1990s by Binder et al, we calculated that 230 patients had to be included to demonstrate, with α and β set at .05 and .2, respectively, a statistically significant difference in the sensitivity of ultrasonography to detect lymph node metastasis compared with palpation. An interim analysis was scheduled to be performed after the inclusion of two thirds of the scheduled number of patients. Sensitivity, specificity, and positive and negative likelihood ratios and their 95% confidence intervals were calculated for palpation and ultrasonography, with stringent and non-stringent criteria for nodal metastasis, using standard formulas. Comparisons were done using the McNemar test for paired samples or the χ² test for independent variables. P values less than .05 were considered significant. The Standards for Reporting of Diagnostic Accuracy checklist was used.

RESULTS

During a 6-year period, 197 consecutive new patients having melanoma were considered for this study. However, 8 patients presenting with stage IV melanoma and 19 with melanoma in situ were excluded, as were the 10 patients with thin melanomas (Breslow thickness ± SD, 0.58±0.41 mm) who opted to be followed up only by their private practice dermatologists. None of the latter experienced melanoma progression.

OVERALL DATA ANALYSIS

Table 1 lists the clinical characteristics of the 160 patients included in this study. Long-term follow-up was available for all patients. For patients with multiple melanomas (there were 10 patients with 2 melanomas, 1 patient with 3, and 1 patient with 4), ultrasonographic studies covered all draining lymphatic vessels. During the study period, melanoma spread in 42 patients (26%). Recurrence occurred as regional lymph nodes with or without other metastases in
33 patients (21%); distant metastases in 7 patients; and isolated in-transit metastasis in 2 patients. Among the 33 patients with nodal recurrences, 2 had stage I, 28 had stage II, and 3 had stage III melanoma. Six ultrasonographic procedures initially yielded ambiguous results; their repetition within 6 weeks, however, enabled the operator to reach a definitive conclusion. In all, 391 paired palpation and ultrasonographic examinations were available, for a mean ± SD of 2.44 ± 2.23 paired examinations per patient (range, 1-12). There were 101 paired examinations in patients with stage I, 183 in patients with stage II, and 107 in patients with stage III melanomas. Ninety-three paired examinations were performed in patients with lymph node areas previously treated with radical LD and 14 in patients with in-transit metastases without previous radical LD. Nodal status was defined histologically in 113 patients and on the basis of evolution in 278 patients. Among the patients who had paired examinations and histologically defined nodal status, 34 had undergone LM/SL, and the procedure had allowed detection of lymph node metastases in 7. Fine-needle aspiration biopsy was performed in 21 patients who had undergone paired examinations and results were positive in 7. Surgical interventions were found necessary for 58 patients following paired examinations. No adverse effects of ultrasonography were recorded.

There were 65 paired palpation and ultrasonographic examinations performed in patients whose nodal status was metastatic. Metastatic status was detected by both methods of examination in 26 patients (40%); by ultrasonography only in 24 patients (37%); by palpation only in 1 patient; and by neither method in 14 patients (22%). In the latter group of patients, 8 paired examinations with negative results were followed by ultrasonography and/or palpation with positive results a mean ± SD of 86 ± 39 days later, and 6 paired examinations were performed immediately before LM/SL.

The overall sensitivity of the palpation method for the detection of nodal metastasis differed significantly from that of stringent ultrasonography (P < .001) (Table 2). The overall specificity of the palpation method also differed significantly from that of ultrasonography with stringent criteria (P < .05). The markedly higher positive likelihood ratio and the lower negative likelihood ratio of detection of lymph node metastasis using ultrasonography with stringent criteria further support the superiority of ultrasonography over palpation in the detection of lymph node metastasis.

## ULTRASONOGRAPHIC CRITERIA

The respective contribution of the ultrasonographic criteria to accurately diagnose nodal invasion is reported in Table 2. Compared with the stringent criteria, the non-stringent criteria provided only 3 more true-positive results without significantly improving sensitivity; moreover, they generated 40 additional false-positive results. Compared with the specificity of the stringent criteria, the specificity of the nonstringent criteria was significantly lower (P < .05); moreover, their positive likelihood ratio was much lower while their negative likelihood ratio remained essentially unchanged.

## IMPACT OF PREVIOUS RADICAL LD

The impact of prior LD on the findings of palpation and ultrasonography with stringent criteria in lymph node area(s) for the detection of melanoma recurrence is reported in Table 3. In patients who did or did not undergo prior radical LD, no significant differences were observed regarding sensitivity, specificity, and negative likelihood ratios between palpation and ultrasonography with stringent criteria. Positive likelihood ratios were higher for both methods in the absence of prior radical LD. However, ultrasonography correctly diagnosed clinically unsuspected lymphoceles in 6 patients, hematoma in 1 patient, and fibrosis in 1 patient.

## MELANOMA STAGE AND LOCATION

The respective sensitivity and specificity of palpation and ultrasonography with stringent criteria to detect lymph node recurrence of melanoma were not significantly different regarding melanoma stage (I, II, or III) or the location of the thickest melanoma (data not shown).

### Table 1. Relevant Characteristics of 160 Patients With Melanoma

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD (range), y</td>
<td>55.6 ± 17.1 (19-92)</td>
</tr>
<tr>
<td>Male-female ratio</td>
<td>86.74</td>
</tr>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>Head and neck</td>
<td>22 (12.6)</td>
</tr>
<tr>
<td>Trunk</td>
<td>71 (40.6)</td>
</tr>
<tr>
<td>Extremities</td>
<td>80 (45.7)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Breslow thickness, mm†</td>
<td>2.1 ± 2.2 (0.18-15)</td>
</tr>
<tr>
<td>Histopathologic subtypes</td>
<td></td>
</tr>
<tr>
<td>Superficial spreading melanoma</td>
<td>108 (61.7)</td>
</tr>
<tr>
<td>Nodular melanoma</td>
<td>42 (24.0)</td>
</tr>
<tr>
<td>Acro lentiginous</td>
<td>5 (2.9)</td>
</tr>
<tr>
<td>Lentigo maligna melanoma</td>
<td>3 (1.7)</td>
</tr>
<tr>
<td>Other</td>
<td>17 (9.7)</td>
</tr>
<tr>
<td>Melanoma thickness, mm†</td>
<td></td>
</tr>
<tr>
<td>&lt;0.76</td>
<td>39 (24.3)</td>
</tr>
<tr>
<td>0.76-1.50</td>
<td>45 (28.1)</td>
</tr>
<tr>
<td>1.51-3.00</td>
<td>37 (23.1)</td>
</tr>
<tr>
<td>&gt;3.01</td>
<td>30 (18.8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>9 (5.6)</td>
</tr>
</tbody>
</table>

*Values are given as number (percentage) unless otherwise indicated. †For the 12 patients with more than 1 melanoma, the thicker melanoma was used for analysis.

Our results showed that, for experienced dermatologists and radiologists, ultrasonography was much more sensitive than palpation for the detection of nodal extension of melanoma. Although both techniques had good specificity, ultrasonography was slightly but significantly more specific. These findings were maintained even for lymph node areas that had previously undergone radical LD and were not influenced by melanoma stage or location.
Minor criteria for nodal metastasis were nodular hypoechoic focus within a lymph node and irregularity of lymph node margin.20 Stringent criteria for metastatic nodes were the presence of all 3 major criteria. Nonstringent criteria of nodal metastasis were the presence of 1 or 2 major criteria and/or 1 or 2 minor criteria.

To be only 39%.17 Second, our definition of true-negative patients for whom nodal status was defined by LM/SL, in this study than in previous reports. First, we included patients for whom nodal status was defined by LM/SL, in whom the sensitivity of ultrasonography has been shown to be only 39%.17 Second, our definition of true-negative results required an uneventful follow-up period of at least 6 months, whereas in most published studies the definition of true-negative results was absent, incomplete, or questionable. Third, we applied stringent ultrasonographic criteria of lymph node invasion, and thus probably increased the number of false-negative results. Notably, when the uneventful follow-up period defined a true-negative result after an ultrasonographic examination was set at 3 months, sensitivity increased to 80.4% while specificity remained unchanged (data not shown).

Although we used very strict criteria to accurately define nodal status, we were able to statistically demonstrate that ultrasonography with stringent criteria had higher sensitivity and specificity than palpation for the detection of nodal metastases of melanoma. Only 1 other study reported similar findings.14 The authors of 2 previous studies reported higher sensitivity for ultrasonography than for palpation but no significant difference in specificity.13,15 A higher specificity for ultrasonography was also found in another study, but not a higher sensitivity.16 Other investigations failed to provide adequate statistical comparisons of palpation and ultrasonography. Like others, we were unable to demonstrate statistically significant differences in diagnostic accuracy between the 2 methods regarding melanoma location or staging.

We used a 6- to 12-MHz linear transducer, whereas the upper transducer frequencies used by other authors ranged predominantly from 5 to 10 MHz, with only one 15-MHz transducer used (Table 4).16 A high-frequency scanhead can better visualize lymph node structure.13 We did not use color Doppler sonography and the only study to assess its use in patients with melanoma evaluated only patients with palpable nodes.23 Although most metastatic nodes lacked hilum vessels and showed complete or partial perfusion in this study, their resistance and pulsatility indices were lower than those reported for malignancies other than melanoma, and, because of the overlap between metastatic and nonmetastatic groups, these indices had no diagnostic value. We also did not use the newly developed sonography-enhancing agents that may improve vessel identification.24

### Table 2. Results of 391 Paired Palpation and Ultrasonographic Examinations of Lymph Node Area(s) to Diagnose Lymph Node Metastasis in Patients With Stage I to Stage III Melanoma

<table>
<thead>
<tr>
<th>Diagnostic Method</th>
<th>False Negative</th>
<th>False Positive</th>
<th>True Negative</th>
<th>True Positive</th>
<th>Sensitivity*</th>
<th>Specificity*</th>
<th>Positive LR*</th>
<th>Negative LR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpation</td>
<td>38</td>
<td>14</td>
<td>312</td>
<td>27</td>
<td>41.5 (29.6-53.5)</td>
<td>95.7 (93.5-97.9)</td>
<td>9.7 (6.3-14.8)</td>
<td>0.61 (0.49-0.75)</td>
</tr>
<tr>
<td>Ultrasonography†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Criteria</td>
<td>Nonstringent</td>
<td>12</td>
<td>45</td>
<td>281</td>
<td>53</td>
<td>81.5 (72.1-91.0)</td>
<td>86.2 (82.5-88.9)</td>
<td>5.9 (4.4-7.9)</td>
</tr>
<tr>
<td>Stringent</td>
<td>15</td>
<td>5</td>
<td>321</td>
<td>50</td>
<td>76.9 (66.7-87.2)</td>
<td>98.4 (97.1-98.6)</td>
<td>50.1 (20.8-120.8)</td>
<td>0.23 (0.15-0.36)</td>
</tr>
</tbody>
</table>

Abbreviation: LR, likelihood ratio.
*These values are given as percentage (95% confidence interval).
†A circular/oval hypoechoic lymph node with a Solbiati index less than 1.5 and no hyperechoic hilum constituted the major criteria for metastatic involvement.

### Table 3. Impact of Prior Radical Lymphadenectomy (LD) on the Results of Paired Palpation and Ultrasonographic Examination Using Only Stringent Criteria of Lymph Node Area(s) to Diagnose Melanoma Recurrence in Patients With Stage I to Stage III Melanoma

<table>
<thead>
<tr>
<th>LD Status and Method of Examination</th>
<th>False Negative</th>
<th>False Positive</th>
<th>True Negative</th>
<th>True Positive</th>
<th>Sensitivity*</th>
<th>Specificity*</th>
<th>Positive LR*</th>
<th>Negative LR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No prior LD (n = 298)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palpation</td>
<td>27</td>
<td>9</td>
<td>244</td>
<td>18</td>
<td>40.2 (25.6-54.3)</td>
<td>96.4 (94.1-98.7)</td>
<td>11.2 (5.4-23.3)</td>
<td>0.62 (0.49-0.79)</td>
</tr>
<tr>
<td>Ultrasonography</td>
<td>12</td>
<td>1</td>
<td>252</td>
<td>33</td>
<td>73.3 (60.4-86.2)</td>
<td>99.6 (98.8-100)</td>
<td>185.5 (26.0-1322.2)</td>
<td>0.27 (0.16-0.43)</td>
</tr>
<tr>
<td>Prior radical LD (n = 93)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palpation</td>
<td>11</td>
<td>5</td>
<td>68</td>
<td>9</td>
<td>45.2 (23.2-66.8)</td>
<td>93.2 (87.3-98.9)</td>
<td>6.6 (2.5-17.4)</td>
<td>0.59 (0.39-0.88)</td>
</tr>
<tr>
<td>Ultrasonography</td>
<td>3</td>
<td>4</td>
<td>69</td>
<td>17</td>
<td>81.0 (69.3-100)</td>
<td>94.5 (89.2-99.7)</td>
<td>15.5 (5.9-40.9)</td>
<td>0.16 (0.05-0.45)</td>
</tr>
</tbody>
</table>

Abbreviation: LR, likelihood ratio.
*These values are given as percentage (95% confidence interval).
We compared, we believe for the first time, the diagnostic values of stringent and nonstringent sets of ultrasonographic criteria of nodal involvement and could clearly conclude that the use of the latter criteria was associated with significantly lower specificity and unimproved sensitivity. This finding has obvious practical implications, as our stringent criteria are easy to recognize (and thus to teach), thereby shortening the diagnostic process. We were unable to find any other study evaluating during follow-up the diagnostic value of the criteria proposed by Vassallo et al.25 for patients with stage I and stage II melanomas. Voit et al.13 and Prayer et al.8 detected ultrasonographically “uncertain” lymph nodes in addition to melanoma metastases, but their findings only led to a control graphically “uncertain” lymph nodes in addition to melanoma metastases. In previous cases clearly included patients with stage III along with patients with stage I and II melanoma.8,12-14 but the impact of prior LD on the diagnostic accuracy of ultrasonography was not assessed. In these advanced cases, it was sometimes impossible to prove nodal localization histologically because of total architectural destruction of the metastatic node(s), and some patients may have had in-transit metastases. However, this limitation has no practical impact on patient management. Moreover, differential diagnoses of lymphocele, hematoma, or fibrosis were frequently made on ultrasonographic examination.

There are some other methodological advantages to our approach, namely its prospective design, the precisely defined criteria used for assigning nodal status, the strictly defined follow-up protocol after melanoma excision, and the availability of follow-up information to all patients. Ultrasonography was performed independently from palpation, which was done by dermatologists—a feature stated in only 2 other studies.7,8 However, our study has some disadvantages. Although patients’ follow-up and ultrasonographic procedures had both been prospectively established, ultrasonography did not have to be performed at every follow-up visit conducted in our department, and more ultrasonographic examinations were prescribed by dermatologists for patients with poor prognoses. Nodal status was not assessed histologically in all patients. The impact of this verification bias (when disease status is not determined in all examined subjects and when the probability of verification depends on the diagnostic test result, other variables, or both), which may markedly increase the apparent sensitivity of the test and lower its apparent sensitivity,26 must be considered. As a long-term recurrence-free follow-up was required to define nonmetastatic nodes, however, this bias did not seem to distort our conclusions. Finally, and as in all published studies (except one in which nodal status was defined by initial LM/SL,13 and another in which only 1 set of paired clini-
ical and ultrasonographic examinations was performed per patient4) paired palpation and ultrasonographic examinations were not independent events for a single individual, as a given patient with stage I or stage II melanoma has only 1 probability of progressing to nodal involvement during follow-up. This fact may have artificially enhanced the diagnostic accuracy of both palpation and ultrasonography, although this is difficult to establish.

In our study, ultrasonography was superior to palpation to diagnose lymph node metastasis in patients with stage I, stage II, or even stage III melanoma. Stringent ultrasonographic criteria, which are easy to recognize, should be used. Ultrasonography should be a part of the patients’ surveillance program.5 However, this strategy is based on an unproven postulate, ie, that the earlier melanoma nodal metastasis is diagnosed and treated, the better the prognosis will be. However, Garbe et al9 in their prospective evaluation of follow-up of patients with melanoma classified metastases as an early or late discovery according to status at the time of detection. Organ or lymph node metastases no greater than 2 cm in diameter and with an indication for surgery with a curative intent were graded as early discoveries. More advanced metastases were considered to be late discoveries. The rate of detection of metastasis at an early stage of development varied according to the examination method used, with 71% of lymph nodes found with ultrasonography and 56% with palpation being classified as early discoveries. Among the other imaging techniques used, 30% of the recurrences detected by computed tomographic scans were discovered at an early stage of development, and chest radiographs and abdominal ultrasonographic examinations only detected 25% of early recurrences. On the other hand, our finding that lymph nodes discovered with only nonstringent criteria (as opposed to our stringent criteria) should be regarded as having a low probability of being invaded should be confirmed by other studies. For the moment, such nodes should undergo repeated ultrasonographic examinations at short intervals, FNAB, or even surgical excision.

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Correspondence: Philippe Saiag, MD, PhD, Service de Dermatologie, Hôpital Ambroise-Paré, 9, Ave Charles-de-Gaulle, 92104 Boulogne CEDEX, France (philippe.saiag@apr.ap-hop-paris.fr).

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