Local Recurrence in Malignant Melanoma: Long-Term Results of the Multiinstitutional Randomized Surgical Trial

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Background: In the past, radical margins of excision were prescribed for cutaneous melanoma based on preconceived notions rather than on hard clinical evidence.

Methods: In a prospective study of 742 patients with intermediate-thickness melanoma (1-4 mm), 470 patients with trunk or proximal extremity lesions were randomized into a 2- or 4-cm margin. Patients with distal extremity or head and neck lesions (n = 272) received uniformly a 2-cm margin.

Results: The overall rate of local recurrence was 3.8%. This rate in the randomized portion (n = 470) was 2.1% for the 2-cm margin and 2.6% for the 4-cm margin (p = 0.72). A progressive increase in local recurrence rates was observed with thickness: 2.3% for lesions 1.0-2.0 mm, 4.2% for those 2.01-3.0 mm, and 11.7% for those 3.01-4.0 mm thick (p = 0.001). Local recurrence occurred in 1.5% of those without ulceration and in 10.6% of those with ulceration of the primary lesion (p = 0.001). The local recurrence rate was not significantly affected by the margin of resection even among the thicker or ulcerated lesions. It also was not affected significantly by the method of closure of the primary site or management of the regional nodes, or the age or gender of the patients.

Conclusions: A 2-cm margin is as effective as a 4-cm margin in local control and survival of intermediate-thickness melanomas. The local recurrence rate is significantly affected by the thickness of the primary lesion and the presence or not of ulceration.

Key Words: Melanoma—Local recurrence—Resection margins.
and analysis of the relevant prognostic parameters for the entire population of patients randomized and not randomized with respect to surgical margin. As in the original report (1), according to the protocol, local recurrence was considered as one occurring within 2 cm from the surgical scar of the first definitive operation for the primary lesion (a patient with multiple in-transit metastases and a lesion within 2-cm of the scar was not counted as a local recurrence). This is a well accepted, clinically useful, albeit biologically arbitrary definition. However, it is obvious that a recurrent lesion near the primary site may be variously classified as local recurrence or in-transit metastasis according to the definition of local recurrence. To avoid any effect the arbitrariness of the definition may have had in estimating the rates of local recurrence, in the following analysis, in addition to the local recurrence rates, the rates of in-transit metastases, combined rates of local and in-transit recurrences, and rates of distant metastases were compared between the two surgical margin groups.

MATERIALS AND METHODS

A total of 742 patients with intermediate-thickness (1.0-4.0 mm) localized melanoma were entered in the trial from 1983 to 1992. Patients with lentigo maligna melanoma or history of cancer (except skin cancer) were excluded. The study population was composed of 374 men and 368 women. Their mean age was 48.9 years (median 47.7; range 16.1-86.0). The patients were randomized to immediate (elective) node dissection or delayed dissection (upon appearance of palpable, suspicious nodes later).

Patients with trunk or proximal (above knee or elbow) extremity melanomas (n = 470) were randomized to a 2- or 4-cm margin. Patients with head and neck and distal extremity melanomas (n = 272) all received a 2-cm margin of excision because it was not technically feasible or clinically appropriate to perform a 4-cm excision in these anatomical areas.

The mean thickness of the lesions according to Breslow for the entire group was 1.97 mm (median 1.8). The frequency of the various subcategories of thickness (by 1-mm increments) is given in Table 1, and that of the various levels according to Clark is given in Table 2. Of the 725 patients for which information was available, ulceration of the primary lesion was present in 181 (25%).

Survival was calculated as the months from the first surgical treatment on protocol to the last follow-up or death. Disease-free survival was calculated to the date of first recurrence. Estimated survival distributions were calculated by the method of Kaplan and Meier (2). Tests of significance with respect to survival distributions were based on the log-rank test (3). Prognostic parameters considered were the thickness, Clark's level, presence or absence of ulceration and anatomic location of the primary lesion, margin of resection, type of repair (primary or split-thickness skin graft), and gender and age of the patient. Factors found to be significant on univariate analysis were entered into multivariate analysis.

RESULTS

At a mean follow-up of 92 months (median 91; range 1.0-126) the local recurrence rate observed for the entire series of patients was 3.8%.

In the randomized portion of the trial (n = 470), local recurrence was noted in five patients (2.1%) of those treated with a 2-cm margin (n = 238) and in

<table>
<thead>
<tr>
<th>Thickness (mm)</th>
<th>Total No.</th>
<th>Local recurrence</th>
<th>In-transit metastases</th>
<th>Regional nodal recurrence</th>
<th>Distant recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>1.0-2.0</td>
<td>445</td>
<td>60</td>
<td>2.3</td>
<td>16</td>
<td>3.6</td>
</tr>
<tr>
<td>2.01-3.0</td>
<td>215</td>
<td>29</td>
<td>9.4</td>
<td>18</td>
<td>8.4</td>
</tr>
<tr>
<td>3.01-4.0</td>
<td>77</td>
<td>10</td>
<td>11.7</td>
<td>13</td>
<td>16.9</td>
</tr>
<tr>
<td>Total</td>
<td>737</td>
<td>100</td>
<td>3.8</td>
<td>47</td>
<td>6.4</td>
</tr>
</tbody>
</table>

*p = 0.001.