Melanoma in the Elderly Patient

C. K. Chang, MD; Ira A. Jacobs, MD; Vida M. Vizgirda, RN, PhD; George I. Salti, MD

Background: The incidence of cutaneous melanoma is rising steadily, and the rate of increase is among the highest for any form of cancer. Although the reliability of age as a prognostic factor is debatable, several studies suggest that age has an important prognostic use.

Hypothesis: Age alone does not predict a poor prognosis in the older patient with melanoma.

Setting: University teaching hospital.

Methods: A retrospective review was undertaken to identify patients aged 65 years or older with intermediate-thickness melanoma (1-4 mm). Two hundred thirteen such patients were identified. Data are given as mean±SD.

Results: The mean age was 72.2±6.1 years. The mean follow-up was 49 months. By univariate analysis, the mean disease-free survival (DFS) and overall survival (OS) for lymph node–positive patients was 36.0±9.6 and 56.0±10.6 months, respectively. The mean DFS for node-negative patients was 155.0±9.8 months, and the mean OS was 166.0±9.2 months (P<.001 for both). The mean DFS and OS for women were 151.0±11.2 and 163.0±10.9 months, respectively. In contrast, men had 116.0±9.5 months’ DFS and 127.0±9.0 months’ OS (P=.01 for both). By multivariate analysis, lymph node status was the most predictive variable for DFS and OS (P<.001 for both). Sex tended to affect OS (P=.02) but did not achieve prognostic significance on DFS (P=.09). Other factors such as location, ulceration, histological type, and mitoses per square millimeter failed to show any prognostic significance. Stratification into 3 age groups (65-70, 71-80, and >80 years) had no significant effect on DFS (P=.95) or OS (P=.92).

Conclusions: Lymph node status is the most important prognostic factor in older patients with intermediate-thickness melanoma. Identification of high-risk factors may help stratify these patients for recommendation of more aggressive treatment or adjuvant therapies. Among these patients, age alone was not a significant prognostic factor in the clinical management of melanoma.

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RESULTS

PATIENT CHARACTERISTICS

Two hundred thirteen patients (129 men [60.6%]; 80 women [39.4%]) underwent surgical treatment for intermediate-thickness melanoma (1-4 mm) during the study. Their ages ranged from 65 to 95 years (mean age, 72.2±6.1 years). Of these 213 patients, 128 underwent LND.

TUMOR CHARACTERISTICS

Primary tumor location was in the lower extremity in 67 (31.5%), trunk in 57 (26.8%), head and neck in 49 (23.0%), and upper extremity in 40 (18.8%) (Table 1). The most common histological finding was superficial spreading melanoma in 100 patients (46.9%). Seventy-seven patients (36.2%) had nodular melanoma, 23 (10.8%) had acral lentiginous melanoma, and 11 (5.2%) had lentigo maligna melanoma. Melanoma was ulcerated in 65 patients (30.5%). We identified 88 patients (41.3%) with 5 or more mitoses per square millimeter.

Of the 128 patients who underwent elective LND, 36 (28.1%) had node-positive disease. Table 1 summarizes the patient and tumor characteristics.

SURVIVAL

Mean follow-up was 49 months. Mean DFS and OS for the entire population were 142 and 146 months, respectively (Figure 1). Results of univariate analyses of several prognostic factors with respect to DFS and OS are given in Table 2. Univariate analysis predicted worse DFS and OS when patients had positive results of pathological examination after LND (P<.001 for both) and when the patient was male (P=.01 for both). Mean DFS and OS for node-positive patients were 36.0±9.6 and 56.0±10.6 months, respectively. Mean DFS and OS for node-negative patients were 155.0±9.8 and 166.0±9.2 months, respectively (P<.001 for both). Mean DFS and OS for women were 151.0±11.2 and 163.0±10.9 months, respectively. In contrast, men had 116.0±9.5 months and 127.0±9.0 months of DFS and OS, respectively (P<.001 for both). Other factors such as location, ulceration, histological type, and mitoses per square millimeter failed to show any prognostic significance. Stratification into 3 age groups (65-70, 71-80, and >80 years) demonstrated no significant effect on DFS (P=.95) or OS (P=.92) (Figure 2).

By multivariate analysis (Table 3 and Figure 3), lymph node status was the most predictive variable for DFS and OS (P<.001 for both). Sex significantly affected OS (P=.02) but did not achieve prognostic significance on DFS (P=.09). After multivariate analysis, other prognostic factors did not demonstrate significance relative to the outcomes.

COMMENT

Older patients comprise an important group among those with melanoma. The incidence in the geriatric popula-

Table 1. Clinical and Pathological Patient Characteristics*

<table>
<thead>
<tr>
<th>Sex</th>
<th>Male 129 (60.6)</th>
<th>Female 84 (39.4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>Mean ± SD 72.2 ± 6.1</td>
<td>Range 65-95</td>
</tr>
<tr>
<td>Location of primary tumor</td>
<td>Lower extremity 67 (31.5)</td>
<td>Trunk 57 (26.8)</td>
</tr>
<tr>
<td>Histological features of primary tumor</td>
<td>Superficial spreading 100 (46.9)</td>
<td>Nodular 77 (36.2)</td>
</tr>
<tr>
<td>Ulceration</td>
<td>Present 65 (30.5)</td>
<td>Absent 148 (69.5)</td>
</tr>
<tr>
<td>Mitoses per square millimeter</td>
<td>&lt;5 125 (58.7)</td>
<td>≥5 88 (41.3)</td>
</tr>
<tr>
<td>Nodal status†</td>
<td>Positive 36 (28.1)</td>
<td>Negative 92 (71.9)</td>
</tr>
</tbody>
</table>

*Data are given as number (percentage) unless otherwise indicated.
†One hundred twenty-eight patients underwent lymph node dissection.

Figure 1. Disease-free (A) and overall (B) survival in the entire population. The mean follow-up was 49 months.
tion continues to rise, although the incidence in the younger populations appears to be leveling off or decreasing. Nearly 50% of all melanoma deaths in the United States are in white men older than 50 years. Similarly, 50% of deaths from melanoma in New South Wales, Australia, occur in males older than 50, although this age group only accounts for 12% to 14% of the population.

The mean DFS and OS for all patients in our series were 142 and 146 months, respectively. Univariate analysis of the prognostic variables in our cohort of patients demonstrated significantly worse survival in patients with node-positive disease. Multivariate analysis showed lymph node status to be most predictive of survival. Our data suggest that older patients with intermediate-thickness melanoma may have favorable survival with aggressive surgery alone when disease has not spread to the regional lymph nodes.

In our study, women had an increase in OS that did not achieve prognostic significance on DFS. Whether this increase in OS is due to a hormonal factor or an increased life expectancy for women in the United States is hard to substantiate. In addition, we did not evaluate the effect of use of exogenous estrogen on DFS or OS. In comparison, O’Doherty et al reported that older men had a poorer prognosis than older women, but this difference could relate to a lower cutoff age used in their study. The potential sex difference in prognostic outcome may likely be due to differences in physiological levels of sex hormones. However, there is no clear evidence that hormonal factors have a protective role in melanoma.

Stratification of the sample into 3 age groups (65-70, 71-80, and >80 years) relative to disease-free (A) and overall (B) survival demonstrated no significant effect on survival. The mean DFS and OS for all patients in our series were 142 and 146 months, respectively. Univariate analysis of the prognostic variables in our cohort of patients demonstrated significantly worse survival in patients with node-positive disease. Multivariate analysis showed lymph node status to be most predictive of survival. Our data suggest that older patients with intermediate-thickness melanoma may have favorable survival with aggressive surgery alone when disease has not spread to the regional lymph nodes.

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necrose or skin thickness plays any important role in the OS of older patients with melanoma is uncertain.

Sentinel lymph node (SLN) biopsy has become widely accepted as a method of staging the regional lymph nodes in patients with melanoma. Outpatient biopsy can be performed at the same time as wide local excision of the primary melanoma. It is less morbid than an elective LND and is cost-effective. The advantage of SLN biopsy in melanoma is that it spares 75% to 80% of patients the need for complete regional lymphadenectomy, while identifying those patients at highest risk. The presence of a positive SLN has been shown to be the single most important prognostic factor for recurrence and survival. We perform SLN biopsies on all patients with intermediate-thickness melanoma (1-4 mm). We also perform SLN biopsies on those with melanomas less than 1 mm if they demonstrate ulceration or Clark invasion level IV or V. The usefulness of SLN biopsies on lesions thicker than 4 mm is not clearly defined. In a recent study by Essner et al., the SLN status in thick melanoma was predictive of DFS but not reflective of OS. We routinely perform completion LND if the SLN is found to be positive. The use of this minimally invasive procedure in older populations may help select those who may benefit from completion LND or adjuvant therapy.

Public health initiatives should inform older populations that melanoma is a significant and potentially curable health problem. Marks et al. demonstrated the mismatch between the age at which pigmented lesions are excised and older age at which melanoma is likely to occur. Among patients aged 21 to 40 years, the ratio of benign nevus to melanoma among excised lesions was 27.2, compared with 1.4 in those older than 60. Consequently, health care practitioners who work with older persons should increase melanoma screening.

In conclusion, lymph node status is the most important prognostic factor in older patients with intermediate-thickness melanoma. Identification of high-risk factors may help stratify these patients for recommendation of more aggressive treatment or adjuvant therapies. Among these patients, age alone was not a significant prognostic factor in the clinical management of melanoma. Therefore, treatment of patients with melanoma who are 65 years or older should be based on prognostic factors, not advanced age.

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REFERENCES