

## Age as predictor in patients with cutaneous melanoma submitted to sentinel lymph node biopsy

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### Abstract

**Aims:** To analyse the age as prognostic factor exploring the melanoma database at the National Cancer Institute in Naples.

**Methods:** Three hundred and ninety-nine patients with cutaneous melanoma were treated with sentinel lymph node biopsy from 1996 to 2003 at the National Cancer Institute of Naples. The results were analysed with particular attention to the overall survival among patients younger or older than 50 years of age.

**Results:** No differences were recorded between the younger and older group in terms of the identification rate and incidence of metastases. The analyses of disease-free survival and overall survival showed a significantly more favourable outcome in younger patients. The 5-year overall survival and the 5-year disease free survival were 81.8% vs. 68.0% and 76.3% vs. 59.1% for the younger and older group, respectively.

**Conclusions:** The results suggest that in the management of cutaneous melanoma, age might be considered as prognostic factor both for disease free survival and overall survival.

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**Keywords:** Cutaneous melanoma; Sentinel biopsy; Lymph node metastasis; Prognostic factors

### Introduction

Sentinel lymph node biopsy (SN) is widely applied at diagnosis as the staging procedure in patients with cutaneous melanoma, but its role might be clarified by results from a multicentre randomised trial. The role of age as a prognostic factor has not been widely considered nor reported in the literature, though it influences the clinical outcome of patients with cutaneous melanoma. In the Intergroup Melanoma Trial, Balch et al. reported a better survival in patients younger than 60 years old.<sup>1</sup> The goal of the present paper was to evaluate the significance of patient age in determining prognosis in cases with cutaneous melanoma who underwent sentinel lymph node biopsy.

### Materials and methods

At the National Cancer Institute of Naples (NCI), 399 sentinel lymph node biopsies were performed in patients with cutaneous melanoma from 1996 to 2003. Patients with a primary tumour thicker than 1 mm or Clark level IV–V, according the last version of the AJCC Classification, without clinical evidence of nodal metastases, underwent the sentinel lymph node biopsy (SLB) procedure. Data were retrospectively analysed to evaluate sentinel node identification rate, incidence of micrometastases and mortality rate between patients younger and older than 50 years of age. The cut-off age of 50 was chosen because it matches with the median age of the population studied.

Prior to SLB, all patients underwent clinical evaluation with liver ultrasound, chest X-ray and LDH (lactate dehydrogenase) to rule out the presence of distant metastases. Patients who had received a wide excision of the primary (more than 3 cm) or had undergone reconstruction with a cutaneous rotation flap were excluded, because the probable disruption of lymphatic drainage.

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Technetium-99m radiolabelled nanocolloid was injected intradermally around the tumour. Coronal, sagittal and oblique images were obtained, and the sentinel node “hot spot” was marked on the skin. Lymphoscintigraphy was performed 2–4 h before surgery and about 20 min before the surgical procedure, 1 ml of Patent Blue V was injected intradermally around the primary scar. A hand-held gamma probe guided the identification of sentinel nodes with correlation of radioactivity in vivo, ex vivo and in the operative field after the removal of all possible sentinel nodes. Serial sections of SN were analysed by standard stain with hematoxylin and eosin (H&E) and immunohistochemical (IHC) staining with S-100 and HMB-45 antibodies.<sup>2</sup> Patients with tumour-positive SN underwent complete lymph node dissection of the involved basin. Stage I–II patients were followed every 3 months for the first 2 years and every 6 months thereafter, with clinical evaluation, liver ultrasound, serum biochemistry and chest X-ray every 6 months. CT scans, FDG-PET and bone scans were performed only in cases of disease spread. They were followed every 3 months for the first 5 years and every 6 months thereafter. The work-up was similar to that of Stage I–II patients; however, a total body CT scan or an FDG-PET scan were performed every year.

### Statistical methods

Descriptive statistical procedures have been used to evaluate frequency distributions and relationships of patients' characteristics. Survival has been evaluated analysing Kaplan–Meier curves in patients distinguished for age groups, gender, Breslow stage, ulceration (present or absent) and SN status. Log rank tests have been calculated to compare survival between different groups of patients. Cox regression analyses have been used to identify in a multivariate model the relationship between the characteristics observed and patient survival.

### Results

Clinical and pathological characteristics of these patients are listed in Table 1. Overall, there were 196 females and 203 males with a median age of 50.1 years, ranging from 17 to 80 years.

The analysis of the most important prognostic factors between the younger and older group showed some interesting features. In the older group there were more males than females and patients older than 50-year-old had a thicker tumour and a higher rate of ulceration compared to the younger group (43.0% and 57%, respectively). Tumour-positive sentinel node rate was similar in the two groups and was 49.4% and 50.6% in the younger and older group, respectively; all cases (83) with tumour-positive SN underwent complete lymph node dissection.

The median follow-up was 37.1 months, ranging from 4 to 98 months. The false negative rate, calculated as the rate

Table 1  
Clinical and pathological factors of 399 patients who underwent SLB

| Characteristics      | <i>n</i> | Age < 50 | Age > 50 |
|----------------------|----------|----------|----------|
| Sex                  |          |          |          |
| Female               | 196      | 109      | 87       |
| Male                 | 203      | 89       | 114      |
| Primary site         |          |          |          |
| Extremity            |          |          |          |
| Lower                | 128      | 65       | 63       |
| Upper                | 49       | 29       | 20       |
| Trunk                | 204      | 97       | 107      |
| Head and neck        | 18       | 8        | 10       |
| Breslow (mm)         |          |          |          |
| T1                   | 63       | 42       | 21       |
| T2                   | 131      | 68       | 63       |
| T3                   | 133      | 51       | 82       |
| T4                   | 72       | 37       | 35       |
| Clark level          |          |          |          |
| III                  | 180      | 96       | 84       |
| IV                   | 203      | 92       | 111      |
| V                    | 16       | 8        | 8        |
| Ulceration           |          |          |          |
| Yes                  | 142      | 61       | 81       |
| No                   | 257      | 137      | 120      |
| Sentinel node status |          |          |          |
| Negative             | 316      | 157      | 159      |
| Positive             | 83       | 41       | 42       |

of lymph node recurrence in the tumour-negative SLB basin previously treated, was 5.7% (23 cases). Twenty cases recurred in the same basin, while three showed lymph node metastases in a basin not identified at lymphoscintigraphy and anatomically distant from the site of the primary. The 5-year overall disease-specific survival and the 5-year disease-free specific survival were 81.8% and 68.0% ( $p < 0.03$ ) and 76.3% and 59.1% ( $p < 0.024$ ) for the younger and older group, respectively (Figs. 1 and 2).

The multivariate analyses with Cox regression test showed that all prognostic factors analysed are independent

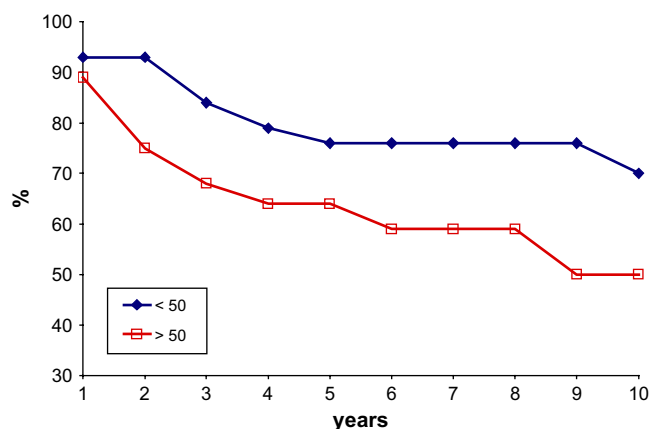


Figure 1. Kaplan–Meier curves for disease-free survival for patients undergoing successful lymphatic mapping and SLB stratified by age. The 5-year disease free survival for patients for patients younger and older than 50-year-old was 76.3% and 59.1%, respectively ( $p < 0.03$  by log rank test).

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