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Effect of time to sentinel-node biopsy on the prognosis of cutaneous melanoma

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Abstract ***Introduction:*** In patients with primary cutaneous melanoma, there is generally a delay between excisional biopsy of the primary tumour and sentinel-node biopsy. The objective of this study is to analyse the prognostic implications of this delay.
Patients and method: This was an observational, retrospective, cohort study in four tertiary referral hospitals. A total of 1963 patients were included. The factor of interest was the interval between the date of the excisional biopsy of the primary melanoma and the date of the sentinel-node biopsy (delay time) in the prognosis. The primary outcome was melanoma-specific survival and disease-free survival.
Results: A delay time of 40 days or less (hazard ratio (HR), 1.7; confidence interval (CI), 1.2–2.5) increased Breslow thickness (Breslow $\geqslant$2 mm, HR, >3.7; CI, 1.4–10.7), ulceration (HR, 1.6; CI, 1.1–2.3), sentinel-node metastasis (HR, 2.9; CI, 1.9–4.2), and primary melanoma localised in the head or neck were independently associated with worse melanoma-specific survival (all $P < 0.03$). The stratified analysis showed that the effect of delay time was at the expense of the patients with a negative sentinel-node biopsy and without regression.
Conclusion: Early sentinel-node biopsy is associated with worse survival in patients with cutaneous melanoma.

1. Introduction

Sentinel lymph node is a standard staging procedure in melanoma management. Although its relevance in overall survival has not been clearly demonstrated so far, its value to stratify melanoma patients into prognostic groups is unquestionable [1].

There is, usually a delay between excision of the primary tumour and performance of sentinel-node biopsy, attributable to multiple factors, including surgical scheduling, preoperative assessment and planning, and sometimes, limited health care resources. The influence of this delay in prognosis remains unclear to date. Three decades ago, Sim et al. [2] evaluated the therapeutic value of elective lymph node dissection and compared immediate lymphadenectomy versus delayed lymphadenectomy between 2 and 4 months bearing in mind the possible role of the regional lymph defensive system of the host against melanoma. They found no significant differences in survival but the arm of patients treated by immediate lymphadenectomy ($n = 54$) showed a slight tendency to metastasise before with a worse prognosis ($n = 55$). More recently, Parrett et al. evaluated the effect of time to sentinel-node biopsy on sentinel-node involvement, recurrence, and mortality, and found no significant differences in survival on comparing a delay time of less than 40 days with one of 40 days or more [3]. They did, however, detect a trend towards higher melanoma-specific mortality in patients who underwent early sentinel-node biopsy (less than 40 days) and attributed this to a higher frequency of ulceration and thicker tumours in this group. They also admitted that their results were underpowered due to the relatively small number of patients evaluated ($n = 492$).

This delay time has not been sufficiently studied regarding the prognosis of these patients.

The objective of this study was to further evaluate in a large series of patients the effect on survival of the delay between excision of a primary melanoma and performance of sentinel-node biopsy.

2. Patients and methods

We performed a multi-institutional retrospective observational study in which we selected all cases of primary cutaneous melanoma registered in databases at four hospitals: Hospital Universitario 'Virgen de la Victoria' (HUVV) in Malaga, Spain; Instituto Valenciano de Oncología (IVO) in Valencia, Spain; Hospital Clínic Universitari de Barcelona (HCUB) in Barcelona, Spain; and Gustave-Roussy (GR) in Villejuif-Paris, France. It is noteworthy that all databases included patients' data in a prospective way. Relevant ethical standards regarding the use of databases were applied in all cases.

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