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ORIGINAL ARTICLE

Predictors of Sentinel Lymph Node Status in Cutaneous Melanoma: A Classification and Regression Tree Analysis[☆]



A. Tejera-Vaquerizo,^{a,*} P. Martín-Cuevas,^a E. Gallego,^b E. Herrera-Acosta,^a
V. Traves,^c E. Herrera-Ceballos,^a E. Nagore^d

^a Servicio de Dermatología, Instituto de Biomedicina de Málaga (IBIMA), Hospital Universitario Virgen de la Victoria/Universidad de Málaga, Málaga, Spain

^b Servicio de Anatomía Patológica, Instituto de Biomedicina de Málaga (IBIMA), Hospital Universitario Virgen de la Victoria/Universidad de Málaga, Málaga, Spain

^c Departamento de Anatomía Patológica, Instituto Valenciano de Oncología, Valencia, Spain

^d Servicio de Dermatología, Instituto Valenciano de Oncología, Valencia, Spain

Received 10 July 2014; accepted 24 October 2014

Available online 26 February 2015

KEYWORDS

Melanoma;
Sentinel lymph node biopsy;
Prognosis;
Mitotic index;
Tumor infiltrating lymphocytes

Abstract

Objective: The main aim of this study was to identify predictors of sentinel lymph node (SN) metastasis in cutaneous melanoma.

Patients and methods: This was a retrospective cohort study of 818 patients in 2 tertiary-level hospitals. The primary outcome variable was SN involvement. Independent predictors were identified using multiple logistic regression and a classification and regression tree (CART) analysis.

Results: Ulceration, tumor thickness, and a high mitotic rate (≥ 6 mitoses/mm²) were independently associated with SN metastasis in the multiple regression analysis. The most important predictor in the CART analysis was Breslow thickness. Absence of an inflammatory infiltrate, patient age, and tumor location were predictive of SN metastasis in patients with tumors thicker than 2 mm. In the case of thinner melanomas, the predictors were mitotic rate (> 6 mitoses/mm²), presence of ulceration, and tumor thickness. Patient age, mitotic rate, and tumor thickness and location were predictive of survival.

[☆] Please cite this article as: Tejera-Vaquerizo A, Martín-Cuevas P, Gallego E, Herrera-Acosta E, Traves V, Herrera-Ceballos E, et al. Factores predictivos del estado del ganglio centinela en el melanoma cutáneo: análisis mediante un árbol de clasificación y regresión. Actas Dermosifiliogr. 2015;106:208–218.

* Corresponding author. Tel.: +0034653440826.

E-mail addresses: antonio.tejera@aedv.es, antonio.tejera@globalderm.es (A. Tejera-Vaquerizo).

PALABRAS CLAVE

Melanoma;
Biopsia de ganglio linfático centinela;
Pronóstico;
Índice mitótico;
Linfocitos que infiltran los tumores

Conclusions: A high mitotic rate predicts a higher risk of SN involvement and worse survival. CART analysis improves the prediction of regional metastasis, resulting in better clinical management of melanoma patients. It may also help select suitable candidates for inclusion in clinical trials.

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Factores predictivos del estado del ganglio centinela en el melanoma cutáneo: análisis mediante un árbol de clasificación y regresión**Resumen**

Objetivo: El objetivo principal de este estudio es identificar factores predictivos de la afectación metastásica del ganglio centinela (GC).

Pacientes y método: Se trata de un estudio de cohortes retrospectivo realizado en 2 centros hospitalarios de tercer nivel. Se incluyeron un total de 818 pacientes. La medida de resultado principal fue la afectación del GC. La valoración de predictores independientes de esta afectación se realizó mediante una regresión logística múltiple y un árbol de clasificación y regresión (CART).

Resultados: El análisis de regresión logística múltiple mostró que la ulceración, el grosor tumoral y un alto índice mitótico (IM) (≥ 6 mitosis/mm 2) se relacionaron con la afectación metastásica del GC de forma independiente. El CART mostró que el grosor de Breslow fue el factor más importante como predictor de la afectación linfática. Para los melanomas gruesos (>2 mm) las variables predictoras fueron la ausencia de infiltrado inflamatorio, la edad y la localización. Para los melanomas menores de 2 mm las variables predictoras fueron el IM (>6 mitosis/mm 2), la ulceración y el grosor. El grosor tumoral, la edad, la localización y el IM fueron predictores de la supervivencia de estos pacientes.

Conclusión: Un alto IM se asocia con una mayor afectación metastásica del GC y una peor supervivencia. Con la metodología CART es posible una mejor predicción de la afectación metastásica regional con vistas al mejor manejo clínico de estos pacientes o su inclusión en ensayos clínicos.

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Introduction

Sentinel lymph node (SN) metastasis is currently the most important predictor of survival in patients with melanoma.¹ Although early dissection of affected lymph nodes has not been proven to improve overall survival,² it is accepted that knowledge of regional involvement permits a more accurate prognosis and helps in the planning of treatment.³

Breslow thickness and presence of ulceration have been systematically linked to a higher likelihood of SN involvement in melanoma.⁴⁻⁷

In recent years, however, mitotic rate has gained increasing recognition as both a prognostic and predictive factor for SN metastasis, particularly since the best method for calculating this rate was established.⁸⁻¹¹ Nonetheless, in the latest version of the Cancer Staging Manual of the American Joint Committee on Cancer (AJCC), mitotic rate is recognized only as a prognostic factor in thin melanomas.¹

When taking decisions in medicine, it is important to consider evidence based on sound methods to resolve problems that arise when classifying or stratifying patients or assessing prognosis.¹² Decision trees are being increasingly used for this purpose, and one particularly useful tool is classification and regression tree (CART) analysis.¹³ CART offers several advantages over logistic regression. It is simpler to use and interpret, and furthermore, the fact that it is based

on a nonparametric method means that no prior assumptions need to be made regarding the distribution of predictors, the relationships between predictors and outcome, or interactions between predictors.

The main aim of this study was to identify predictors of SN metastasis in cutaneous melanoma using CART and logistic regression. A secondary goal was to evaluate the role of these factors in predicting disease-free survival and melanoma-specific survival.

Material and Methods

This was a retrospective, observational study.

Study Population

The study participants were selected from the melanoma databases at Hospital Virgen de la Victoria (HVV) in Málaga, Spain and Instituto Valenciano de Oncología (IVO) in Valencia, Spain. All ethical requirements regarding the use of databases were complied with. The 2 databases have been described in detail in previous studies.¹⁴⁻¹⁶

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