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Original Research

Effects of time interval between primary melanoma excision and sentinel node biopsy on positivity rate and survival

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Abstract ***Background:*** Sentinel node biopsy (SNB) is essential for adequate melanoma staging. Most melanoma guidelines advocate to perform wide local excision and SNB as soon as possible, causing time pressure.
Objective: To investigate the role of time interval between melanoma diagnosis and SNB on sentinel node (SN) positivity and survival.
Methods: This is a retrospective observational study concerning a cohort of melanoma patients from four European Organization for Research and Treatment of Cancer Melanoma Group tertiary referral centres from 1997 to 2013. A total of 4124 melanoma patients underwent SNB. Patients were selected if date of diagnosis and follow-up (FU) information were

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available, and SNB was performed in <180 d. A total of 3546 patients were included. Multivariable logistic regression and Cox regression analyses were performed to investigate how baseline characteristics and time interval until SNB are related to positivity rate, disease-free survival (DFS) and melanoma-specific survival (MSS).

Findings: Median time interval was 43 d (interquartile range [IQR] 29–60 d), and 705 (19.9%) of 3546 patients had a positive SN. Sentinel node positivity was equal for early surgery (≤43 d) versus late surgery (>43 d): 19.7% versus 20.1% ($p = 0.771$). Median FU was 50 months (IQR 24–84 months). Sentinel node metastasis (hazard ratio [HR] 3.17, 95% confidence interval [95% CI] 2.53–3.97), ulceration (HR 1.99, 95% CI 1.58–2.51), Breslow thickness (HR 1.06, 95% CI 1.04–1.08), and male gender (HR 1.58, 95% CI 1.26–1.98) (all $p < 0.00001$) were independently associated with worse MSS and DFS; time interval was not.

Interpretation: No effect of time interval between melanoma diagnosis and SNB on 5-year survival or SN positivity rate was found for a time interval of up to 3 months. This information can be used to counsel patients and remove strict time limits from melanoma guidelines.

1. Introduction

Worldwide, sentinel node biopsy (SNB) has become essential for adequate staging of melanoma patients. It is the current gold standard to detect early lymph node involvement, as recommended by the American Joint Committee on Cancer (AJCC), the American Society of Clinical Oncology, the Society of Surgical Oncology as well as the European Society of Medical Oncology [1–3].

Currently, no uniform recommendation exists on the maximum allowable time interval between melanoma diagnosis (i.e. date of excisional biopsy) and wide local excision (WLE) combined with SNB. Most melanoma guidelines advise to perform WLE and SNB as soon as possible, within an acceptable time frame. The Dutch national melanoma guideline for instance advocates a strict maximum time interval of 6 weeks after primary melanoma diagnosis [4]. Promoting a relatively short time frame for performing WLE and SNB suggests a detrimental effect if not adhered to [5].

Advising a short time frame for WLE and SNB negatively affects the referral system, as it forms an incentive for general practitioners and dermatologists to perform high urgency referrals. High urgent referral implies influence of time interval (i.e. a longer interval may be detrimental), and therefore, wait time to surgery can increase patient anxiety.

However, most melanoma specialists will not be expecting a link between SNB time interval and prognosis for two main reasons: first of all, to date, SNB has been a strong predictor of prognosis, but whether the procedure has a prognostic effect itself remains subject to debate [5], let alone, the interval to the procedure. Second, the time interval between diagnosis and SNB is likely to be very short as compared to the duration of melanoma development prediagnosis. Variation in SNB timing of a few weeks (30–60 d) will probably represent only a fraction in the whole melanoma development story and thus is unlikely to be of any effect on melanoma course.

The aim of this study is to investigate if time interval until WLE and SNB is associated with sentinel node (SN) positivity rate, disease-free survival (DFS) and melanoma-specific survival (MSS) in a large European melanoma population.

2. Methods

2.1. Patients

For purposes of the current study, a retrospective cohort was collected of melanoma patients undergoing SNB in one of four European Organization for Research and Treatment of Cancer (EORTC) Melanoma Group centres. The study was approved and performed in accordance with local ethics committee guidelines and national legislation.

Between 1997 and 2013, 4124 patients underwent SNB in one of four EORTC Melanoma Group centres. In total, 3546 patients were selected with known date of primary melanoma diagnosis (i.e. diagnostic excisional biopsy) and SNB within 180 d, and available follow-up (FU) information. Collected data included the following: gender, age, diagnosis date, date of SNB, primary tumour characteristics; i.e. location, Breslow thickness, ulceration, histological subtype, outcome of SNB, details on completion lymph node dissection, and FU.

2.2. Diagnosis

Diagnosis of the primary melanoma was based on histopathologic examination of an excisional biopsy in all