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Elective Regional Lymph Node Dissection in Malignant Melanoma

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In patients with malignant melanoma elective regional lymph node dissection (ELND) is controversial. This retrospective study evaluated differences in prognosis in patients who were treated with or without ELND. 168 patients were included who initially presented with stage I melanoma (without palpable regional lymph nodes), and who had a minimum observation period of at least 5 years, or had died of malignant melanoma within 5 years of diagnosis. In 66 patients a wide local excision (WLE) followed by ELND was done. In 102 cases only a WLE was done. Assignment of patients to the two groups was non-random but there was no significant difference in age, sex, type and location of primary tumour and depth of invasion. No significant difference was found in survival of the two groups. The 5 year survival of the WLE group was 85.7% and that of the WLE plus ELND group was 89.1%. The 10 year survival rate was 77.9% and 73.1%, respectively. Neither in the whole series nor after sub-division of the patients into three classes according to Breslow depth of invasion (up to 1.5, 1.51–2.5, and greater than 2.5 mm) was a significant influence of ELND on the survival of patients apparent. Cox's regression model did not show ELND as a prognostic factor. ELND cannot be recommended as a routine treatment in patients with stage I melanoma.
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INTRODUCTION

ELECTIVE REGIONAL lymph node dissection (ELND) in primary malignant melanoma (stage I) is controversial [1]. Prospective randomized studies have failed to demonstrate improved disease-free interval and/or survival in melanoma patients by ELND [2–4]. But these studies have been criticised [5] and several investigators have claimed that at least some groups of melanoma patients—i.e. intermediate risk patients presenting with a melanoma of 1.5–4.0 mm invasion according to Breslow—might benefit from ELND [6–9]. Our retrospective study was done to evaluate differences in prognosis in patients who were treated with or without ELND.

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PATIENTS AND METHODS

The pigmented lesion group at the Department of Dermatology I, University of Vienna maintains a registry of melanoma patients that includes over 1200 patients. 168 patients with primary stage I melanoma qualified for this retrospective study. All had presented with stage I melanoma between 1970 and 1983, and were available for a minimum observation period of 5 years or had died before this period had elapsed. All patients received only surgical treatment; adjuvant immunotherapy and/or chemotherapy were not given. Surgical procedures consisted of a wide local excision (WLE) alone or WLE followed by ELND either immediately or within 2 weeks after WLE, according to standards at the time. 66 patients were treated with WLE followed by ELND and 102 with WLE alone.

The retrospective nature of this study precluded a randomization of the therapeutic procedures. In the 1970s it had been our strategy to recommend ELND to high-risk patients as

Table 1. Patients' characteristics

Characteristic	WLE + ELND	WLE only
Number	66	102
M/F	19/47 (29/71%)	40/62 (39/61%)
Mean age (range)	50.7 (20/77)	53.5 (22/82)
Site		
Head and neck	6 (9%)	7 (7%)
Lower limbs	30 (46%)	37 (36%)
Upper limbs	12 (18%)	15 (15%)
Trunk	18 (27%)	43 (42%)
Growth pattern		
ALM	2 (3%)	5 (5%)
NMM	34 (52%)	41 (40%)
SSM	30 (46%)	53 (52%)
LMM*	0 (0%)	3 (3%)
Level of invasion (Clark)		
III	9 (14%)	37 (36%)
IV	54 (82%)	60 (59%)
V	3 (5%)	5 (5%)
Mean thickness (S.D., range) (mm)	2.22 (1.14, 0.40–4.50)	1.82 (1.06, 0.30–4.80)
0.0–0.75	3	13
0.76–1.50	22	36
1.51–2.50	17	31
2.50	24	22
Mean duration of follow-up (yr)	7.12	5.30

*Small number of LMM in this study was due to the fact that during 1970–1983 most LMM cases without clinical evidence of vertical growth phase were not excised but treated by liquid nitrogen or radiation. ALM = acral lentiginous, NMM = nodular malignant, SSM = superficial spreading and LMM = lentigo maligna melanoma.

defined by level of invasion. After the appearance of reports on the questionable value of ELND [3, 4], the policy of performing ELND was discontinued and only therapeutic regional lymph node dissection (TLND) of clinically palpable regional lymph nodes, verified by ultrasound, was done.

In all of the 168 patients the diagnosis of primary malignant melanoma had been confirmed by histopathology. Data recorded and available for evaluation in all patients included age, sex, localization of primary tumour, histopathogenic type of melanoma, tumour thickness [10], level of invasion [11], type of surgical procedure, clinical and ultrasound data pertaining to the state of regional lymph nodes at the time of diagnosis and histopathology of lymph nodes excised either by ELND or TLND. Metastases diagnosed at follow-up were recorded, with regional lymph node metastases, cutaneous/subcutaneous metastases and visceral disease being distinguished. Patients were examined for evidence of metastatic disease every 3 months for 5 years and subsequently every 6 months. In addition, chest X-ray, abdominal ultrasound and bone scan were done every 6 or 12 months, respectively.

Survival curves were drawn according to the method of Kaplan–Meier [12] and analysed with the logrank test for censored data [13]. In addition, the clinical and pathological indices, including surgical treatment, were simultaneously compared for their relative prognostic value in a multiple regression analysis [14].

RESULTS

Although assignment to the two treatment groups was non-random, both groups of patients were similar with regard to sex, age, location of the primary tumour, clinical type of melanoma and depth of invasion. t and χ^2 tests showed no significant differences in these univariate risk factors (Table 1).

No significant differences were found in the survival of the two treatment groups. The 5 year survival rate of the WLE group was 85.7% and that of the WLE plus ELND group 89.1% (not significant, $P = 0.72$). The survival curves showed no tendency to diverge even after 8 years of follow-up (Fig. 1). The 10 year survival rate was 77.9% in the WLE group and 73.1% in the WLE plus ELND group (not significant, $P = 0.70$). When the patients were sub-divided into three classes according to the depth of invasion (Breslow), again no significant differences were found for 5 or 10 year survival (Figs. 2–4).

To establish the value of clinical and pathological indices and the surgical treatment as prognostic factors these variables were analyzed with the Cox regression model. Our data showed that only Breslow thickness and Clark level of invasion had significant prognostic value in determining the final outcome of stage I melanoma patients (Table 2).

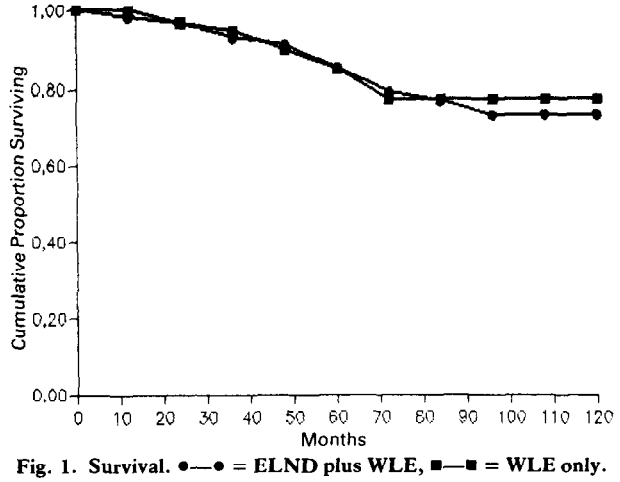

Fig. 1. Survival. ●—● = ELND plus WLE, ■—■ = WLE only.

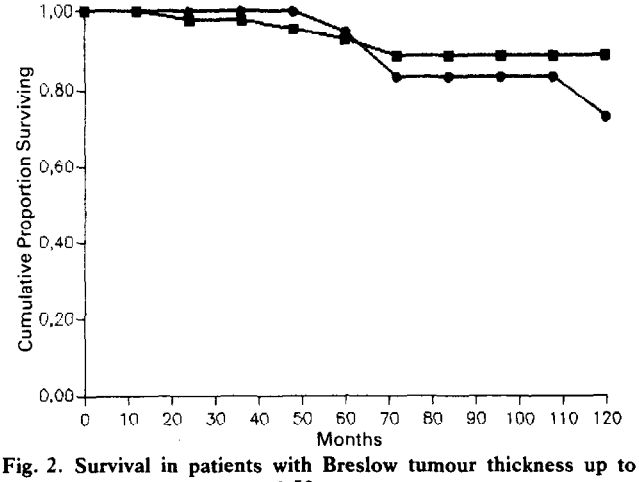

Fig. 2. Survival in patients with Breslow tumour thickness up to 1.50 mm.

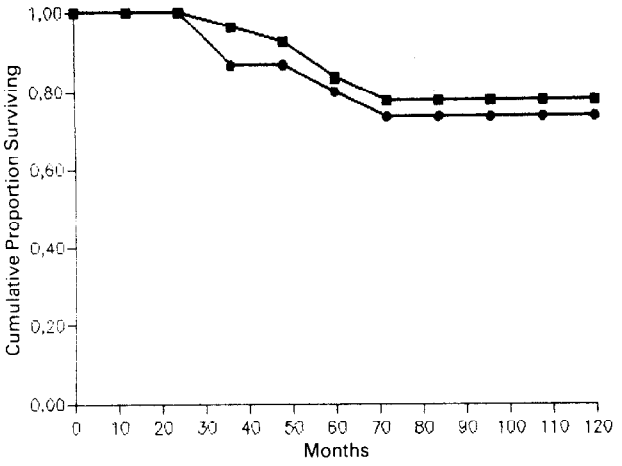

Fig. 3. Survival: tumour thickness 1.51–2.50 mm.

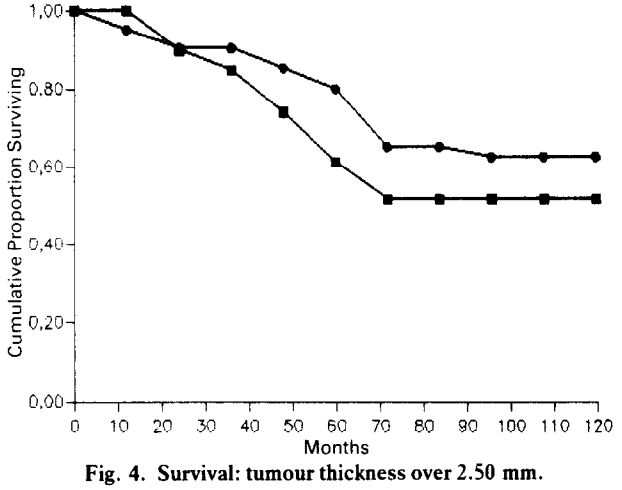

Fig. 4. Survival: tumour thickness over 2.50 mm.

DISCUSSION

We evaluated differences in prognosis in patients with malignant melanoma who were treated with or without ELND and failed to show a statistically significant difference in the two groups studied. Neither in the whole series nor after division of the patients into three classes according to depth of invasion was a difference observed in survival. The claim that some groups of patients might benefit from ELND [6–9] was thus not supported by our study.

To probe the possibility that our results might be a spurious consequence of an unknown bias in the initial case selection, the two treatment groups were assessed for the distribution of prognostically relevant factors. Tests of significance failed to show a non-random distribution of these univariate risk factors.

In addition we used a Cox model to investigate the possibility that several variables might be associated with survival but found that ELND was not a prognostic factor. However, a significant relation between both Breslow's thickness and Clark's level of invasion and survival was observed. A small association between age of the patient and survival ($P = 0.051$) was seen in our data. However, when the model was adjusted to Breslow's thickness, any influence of age on survival was not corroborated (data not shown).

We do not recommend ELND as a routine treatment in patients with stage I melanoma.

Table 2. Cox model

Variable	*P*
Breslow thickness	0.0008
Clark level (III/IV vs. V)	0.0018
Sex	0.9141
Location (trunk vs. axial)	0.5286
Growth pattern (NMM vs. other)	0.3817
ELND (WLE + ELND vs. WLE only)	0.4652
Age (<50 vs. >50 yr)	0.0510

P values < 0.05 were regarded as significant.

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