

Margin of Resection in the Management of Primary Melanoma

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In the last 20 years, it has become evident that the continued use of 4 to 5 cm margins of resection around a primary melanoma is not justified. A prospective randomized trial by the World Health Organization (WHO) Melanoma Group showed that for melanomas up to 2 mm thick, a 1 cm margin provides local control similar to that observed after a 3 cm margin. Another prospective randomized trial by the Melanoma Intergroup Committee in the United States concluded that for melanomas 1 to 4 mm in thickness, a 2 cm margin of resection provides local control that is as good as a 4 cm margin. For melanomas thicker than 4 mm, the current evidence suggests that a 2 cm margin is adequate, the chief manifestation of recurrence for these thick lesions being hematogenous and lymphogenous spread. The adoption of the narrower surgical margins suggested above should reduce the morbidity caused by the radical margins of the past without compromising local control of the disease. *Semin. Surg. Oncol.* 14:272-275, 1998. © 1998 Wiley-Liss, Inc.

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INTRODUCTION

While there is agreement that the excision of cutaneous melanoma should reach muscular fascia in depth, the width of the margins of resection is still a controversial issue. Whether or not muscular fascia should be included was a matter of strong debate in the early 1970s following Olsen's reports indicating higher frequencies of metastases in patients who had the excision of muscular fascia [1]. These data were not confirmed by later reports [2]. Most surgeons believe that muscular fascia should be left essentially intact because the outcome of surgery is better. However, if the primary melanoma is deeply invasive, the excision of the muscular fascia ensures a deep margin that is histologically negative for melanoma [3].

Wide excision of primary melanoma with 3 to 5 cm margins of normal skin was considered a must until the late 1970s. This strong opinion probably was not based on reports by Handley [4] or Pringle [5], but more likely on reports by eminent investigators on the biological course and behavior of malignant melanomas [6,7]. Reports of 5-year survival rates of around 40 to 50% in a large number of patients submitted to "radical surgery" with wide and deep margins of resection had to be very impressive at a time when malignant melanoma was considered to be inevitably fatal. In 1958, Wilson [8] strongly recommended wide excision. He reported 5-year survival of 24% in five of 21 patients initially treated with narrow margins of ex-

cision, but a 5-year survival of 41% when the initial surgery was wide excision or amputation. In 1970, Olsen [1] found a higher rate of metastases from malignant melanomas in patients treated with narrow margins of excision. At the end of the 1970s, Elias et al. [9] purported to show the superiority of wide excision, that local excision permitting primary closure of the surgical wound gave a frequency of local recurrence four times higher than that in patients who were treated by excision so wide as to require skin grafting.

These observations were also supported by histopathological findings; morphologically bizarre melanocytes were occasionally observed in normal skin to a distance of 5 cm from the borders of primary melanoma [10]. In skin adjacent to melanoma, a higher number of melanocytes [11] were observed that could become involved in a field effect caused by substances given off by primary tumor (the so-called Olsen's contamination theory)[12].

The use of microstaging led to the identification of groups of patients with different risks of death from lesions in clinical Stage I, and microstaging (Clark's levels

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and Breslow's thickness) became a guide for optimal widths and depths of resection. In 1977, Everall and Dowd [13] supported narrow excision (1 cm or somewhat more) in patients with lentigo maligna of level I and level II and with superficial spreading malignant melanoma of level I. They recommended borders of 3 cm of normal skin around superficial spreading melanoma that were level II and "radical excision" (margins of 5 cm or more whenever possible) for lentigo maligna, superficial spreading and nodular malignant melanomas of levels III to V. Their rationale for these recommendations was based on survival rates they found reported in the literature, not their personal experience. In the same year, the first review based on statistical evaluation of a personally observed series was published by Breslow and Macht [14]. They reported that none of 62 patients with primary malignant melanomas thinner than 0.76 mm had recurrence of the disease 5 years or more after surgery in which the margins of resection varied from 0.1 cm to 5.5 cm. One-third of these patients had margins of excision no more than 1 cm. A few months later, at the 31st Annual Meeting of the Society of Surgical Oncology, Balch et al. [15] reported no recurrences in 36 patients with thin malignant melanomas (Breslow's thickness less than 0.76 mm). Three of these 36 patients had excisions with margins less than 1 cm and five of the 36 patients had excisions with margins between 1 cm and 2 cm. From their own experience and that of other authors [16,17], Balch et al. suggested excision with margins of 2 cm for such cases.

Other authors also criticized the concept of wide excision. Bagley et al. [18] suggested excisions of normal skin in diameters double those of the neoplasms. With margins of resection of 1 cm, these authors found a 13% frequency of local recurrences. Day et al. [19] recommended different margins according to thickness and site or origin of primary malignant melanomas, i.e., 1.5 cm for primary malignant melanomas less than 0.85 mm thick at any site and for the so-called non-back/arms/neck/scalp (BANS) malignant melanomas measuring between 0.85 mm and 1.69 mm in thickness.

In 1983, Ackerman and Scheiner concluded a paper entitled "How wide and deep is wide and deep enough? A critique of surgical practice in excisions of primary cutaneous malignant melanoma" as follows; ". . . surgery for primary cutaneous melanoma should be no different from surgery for any other malignant neoplasm that is primary in the skin. . . . We believe that wider excisions for thicker malignant melanomas are unnecessary and unjustified." [20].

In our opinion, there were not enough data to justify such a conclusion. Studies published at that date, including our own analysis of the data of the World Health Organization (WHO) Melanoma Group [21], were very weak because surgeons still routinely performed wide excisions and, thus, the number of patients submitted to narrow ex-

cisions was very small. Only 36 of the 593 patients with Stage I malignant melanomas treated at the WHO Collaborating Centers and meeting the requirements of the study have had excisions with margins of 1 cm or less. Similarly meager figures have been reported by others [9,14,19]. Moreover, narrower margins were taken in excisions of malignant melanomas on the head, neck, and extremities.

The critical point in evaluation of the feasibility of reducing the size of resection margins lay in the analysis of local recurrences. The point was extremely difficult to evaluate for one main reason; the low incidence of local recurrences in general. In the experience of the WHO Melanoma Programme, 25 of 593 patients with Stage I and II melanoma (4.2%) had local recurrences. The rate of failure per year seemed to fall after the second year, but even if low, is still the same 11 years after the treatment of primary [22].

MATERIALS AND METHODS

Taking into consideration the different opinions expressed by different authors, the weakness of data available for evaluation, the excellent prognosis of patients with clinical Stage I malignant melanomas thinner than 2 mm, and the low incidence of local failure in this group of patients (which does not seem related to margins of resection), the WHO Melanoma Group decided to carry out a randomized prospective clinical trial to determine whether or not narrow excisions may be considered the treatment of choice for thin cutaneous malignant melanomas [23,24]. The trial started on 1 January 1980.

Six-hundred twelve patients entered into the study; 305 were randomized to receive narrow excision (1 cm margin) and 307 to receive wide excision (at least 3 cm). The overall survival of patients is given in Figure 1. The 12-year survival rates were 87.2% and 85.1% for patients submitted to narrow and wide excisions, respectively.

The two groups of patients were comparable according to the main prognostic criteria. It must be stressed that the different mean thicknesses of the primary melanomas in the two groups do not bias the evaluation of long-term results; the observed difference of 0.03 mm was minimal and statistical evaluation of this difference did not reach a significant value. No significant differences related to the width of excision were observed when disease-free and overall survival was evaluated in the subgroups of patients with primary melanomas not thicker than 1 mm and between 1.1 and 2.0 mm. The frequency of adverse events during follow-up was similar in the two groups when regional lymph node metastases, in-transit metastases, and metastatic spread to distant sites were taken into consideration.

Local recurrences need some discussion. It must be stressed that local recurrences were defined as cutaneous

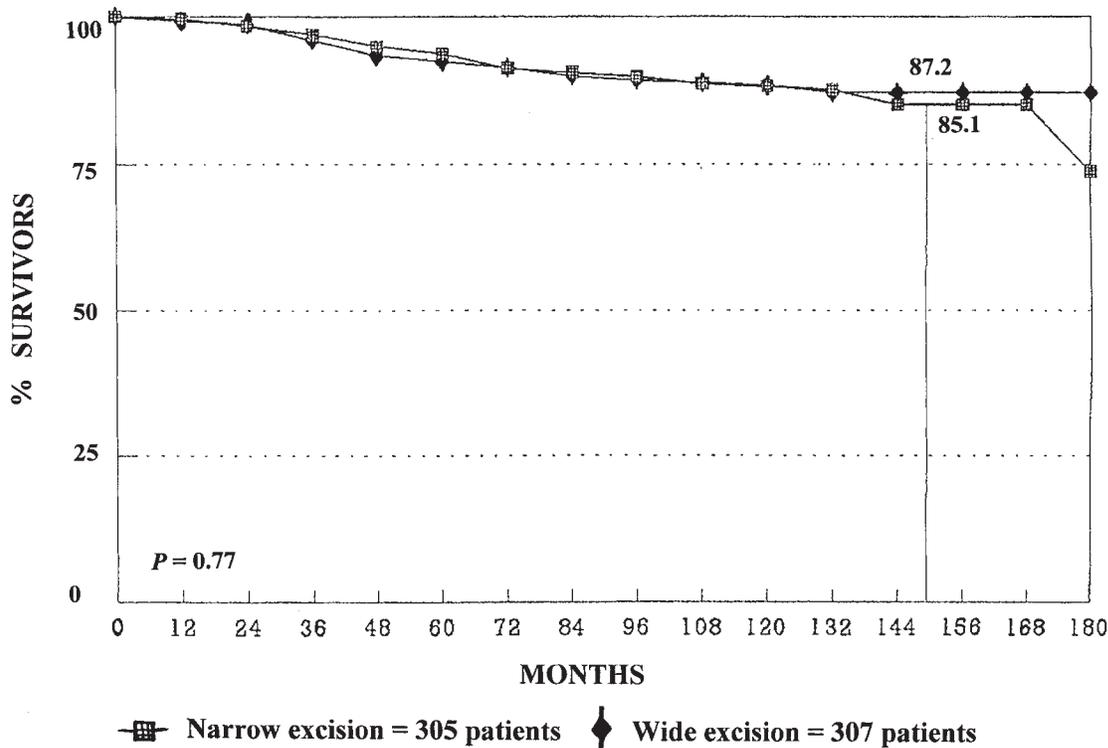


Fig. 1. World Health Organization Melanoma Group Trial 10. Overall survival of 612 evaluable patients according to type of treatment (head and neck sites are excluded). Updated April 1996.

or subcutaneous nodules that appeared along the scar or in an area of 1 cm or less in radius from the surgical scar; they were infrequent (1.8% of the 612 patients). The distribution of local recurrences by thickness and type of treatment is given in Table I; 1.1% of the 359 with a primary melanoma not thicker than 1 mm and 2.8% of the 253 patients with a melanoma thickness between 1.1 mm and 2.0 mm had a local recurrence as first relapse of the disease. The frequency of recurrences in patients submitted to narrow and wide excision (2.6% and 0.1%, respectively) was not different at a statistically significant level. **The frequency of local recurrences in the patients submitted to 1 cm margin excision is within the range of reported values following wide excision.**

Obviously, it is impossible to answer the question of whether wide excision of the primary melanoma could have reduced the appearance of local recurrences in these pa-

tients. The following considerations seem to support the hypothesis that local recurrences are unrelated to the width of excision of primary melanoma; 1) the time elapsed from primary treatment and diagnosis of local recurrence varied considerably in these patients, 2) the elapsed time was not related to the thickness of the primary melanoma, and 3) the evolution of the disease was different after surgical wide excision of the local recurrence.

A second randomized multicentric clinical trial has been carried out in the United States by the Melanoma Inter-group Committee [25]. Patients with a primary melanoma of 1 to 4 mm in thickness were eligible to enter the study. Four hundred eighty-six patients were evaluable for survival; of these, 244 were randomized to receive a 2 cm excision and 242 to receive 4 cm excision. The overall 5-year survival rates were 79.5% and 83.7% in patients submitted to a narrow excision and wide excision, respectively.

TABLE I. Number of Local Recurrences (LR) as First Sign of Recurrent Melanoma by Tumor Thickness and Resection Margins (World Health Organization Melanoma Group Trial 10) [23,24]

Thickness of primary	Narrow excision		Wide excision		Total	
	No. of patients	LR	No. of patients	LR	No. of patients	LR
≤ mm	186	3	173	1	359	4
1.01–2.0 mm	119	5	134	2	253	7
Total	305	8	307	3	612	11

The difference was not statistically significant. The local recurrence rate was 0.8% in patients who received a 2 cm excision and 1.7% in patients who had a 4 cm excision.

CONCLUSIONS

It seems reasonable to conclude that there is enough evidence to state that an excision with 1 cm margin is a safe procedure for primary melanoma not thicker than 2 mm, and that a 2 cm margin excision is adequate for primary melanoma between 2.1 mm and 4.0 mm.

As for melanomas thicker than 4 mm, it is difficult to make a definitive statement because results from randomized trials are not available. However, it seems reasonable to suggest that the resection margins should not exceed 2 cm, because authoritative authors have suggested that there seems to be no logical reason to treat melanoma differently from any other tumor [20]. In addition, the review of the WHO Melanoma Programme Register gave evidence that the prognosis of patients with Stage I and II melanoma depends on thickness of the primary tumor, not on the margins of excision [21].

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