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Management of Melanoma: A European Perspective

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Conservative surgical approach

In Europe, because of the outcomes of randomized, controlled trials during the last 3 decades, the adjuvant surgical procedures of wide excision margins (>2 cm), elective lymph node dissection (ELND), and prophylactic isolated limb perfusion (ILP) have disappeared from practice. Only sentinel node biopsy (SNB) is widely practiced, although it is increasingly being supplanted by the use of ultrasound, as discussed in detail below.

Excision margins

Breslow's demonstration in 1970 that prognosis is related to the thickness of the primary lesion challenged the then-prevailing view that a 5-cm-wide excision margin was necessary to treat primary cutaneous melanoma adequately [1]. Since then a number of randomized trials have investigated the relevance of width of excision. Four trials involved patients who had thin/intermediate melanomas (< 2 mm). They compared margins of 1 cm versus 3 cm (World Health Organization [WHO]-10 Trial [2]) (N. Cascinelli, personal communication, 1995) and 2 cm versus 5 cm (French [3] and Swedish [4] Melanoma Study Group trials). A United States Intergroup Trial [5,6] randomly assigned patients who had 1- to 4-mm melanomas to undergo an excision of 2 cm or 4 cm. The results from all these trials were consistent: local recurrence rates, disease-free survival (DFS), and overall survival (OS) were virtually identical, irrespective of the width of excision.

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The lack of impact of width of excision on efficacy also applies to thick melanomas. A large, nonrandomized study suggested a 2-cm excision margin was safe in patients who had primaries thicker than 4 mm [7], and this finding has been confirmed by the results of a large, randomized trial from Scandinavia that was reported at the Sixth Melanoma World Conference in Vancouver in 2005 [8]. The study involved 936 patients who had melanomas thicker than 2 mm and compared 2-cm versus 4-cm margins of excision. There were no significant differences between the treatment arms in locoregional recurrences, DFS, or OS.

One large, randomized trial has given slightly discordant results. The United Kingdom Melanoma Study Group [9] compared excision margins of 1 cm versus 3 cm in 900 patients who had melanomas more than 2 mm thick. Outcome was inferior in the 1-cm arm, with significantly more locoregional metastases (local, in transit, regional lymph nodes; hazard ratio [HR], 1.26; $P = .05$) and a trend for worse DFS (HR, 1.21; $P = .06$). No differences in OS were observed, however (HR, 1.07; $P = .6$). The Scandinavian trial results avoid the argument about extending margins to 3 cm, because it found that 2-cm margins are as effective as 4-cm margins. All in all, it can be concluded that a 1-cm margin is adequate for melanomas less than 2 mm thick, and a 2-cm margin is safe for patients who have primary melanomas thicker than 2 mm.

Elective lymph node dissection

It is acknowledged that lymphatic spread usually occurs concurrently with hematogenous metastasis in most solid tumors, including melanoma, and that lymph node metastases are ''indicators rather than governors of survival'' [10]. Four randomized trials have evaluated the role of immediate ELND in relation to survival [11–14]. None of these four trials demonstrated a survival benefit for ELND, and as a result, ELND was largely abandoned. In one of these trials (WHO-14), however, a subset analysis suggested that in patients who have thick truncal melanomas and micrometastases in the dissected ELND specimen, ELND had a survival advantage compared with delayed dissection following clinically diagnosed relapse in the regional lymph nodes [14]. These data could be interpreted as supportive evidence for the concept of SNB as an ideal staging procedure with the hypothesis of a potential, albeit small, impact on survival because of complete lymph node dissection in patients who are sentinel node positive [15].

Sentinel node biopsy

Any sentinel node staging system is based on the hypothesis that melanoma lymphatic metastases follow an orderly progression through afferent lymphatic channels to sentinel lymph nodes before spreading into other regional, nonsentinel nodes [16]. Simultaneously, especially in the thicker melanomas, hematogenous spread occurs, and thus the axiom that lymph node