Does acral melanoma need a distinctive prognostic staging system?

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Acral melanoma remains a challenge in terms of reducing melanoma mortality worldwide. In addition to delayed detection and the fact that this disease affects older patients, there seem to be other distinctive prognostic factors involved that relate to poor outcome. The role and interaction of Breslow thickness, mitotic index and ulceration of primary tumours, together with other traits such as pigmentation, histopathological subtype and molecular pathways involved specifically in acral melanoma progression, remain unclear.

In this issue of the *BJD*, Wei *et al.*[1] show that ulceration could play an important role in prognosis for patients with thin acral melanoma (≤ 1 mm); however, this would be a nonrelevant prognostic factor for patients with intermediate/thick or stage III acral melanomas. In this retrospective multicentric study that included more than 1000 Chinese patients diagnosed with melanoma with a median follow-up of 5 years, ulceration was markedly prevalent (more than 60% of cases) and, as expected, was more frequent as thickness increased. Ulceration impacted the melanoma-specific survival (MSS) with a hazard ratio of 1·41 (95% confidence interval 1·09–1·82). The MSS rates at 5 years and 10 years were lower for those with ulceration (54·7% and 34·4%, respectively) than for those without (72·9% and 57·7%, respectively).

Importantly, the impact was much greater among patients affected by thin melanoma (≤ 1 mm), showing a 10-year MSS of 49·1% among patients with ulceration compared with 89·7% for the nonulcerated group. However, no prognostic effect of ulceration was found among patients with thicker or stage III melanomas.

In view of the role of ulceration in the present American Joint Committee on Cancer (AJCC) staging system, where both stages I and II (Ta–Tb) and stage III (with lymph nodal involvement) depend on ulceration of the primary tumour, the authors suggest simplifying the present subcategory of T1b solely based on ulceration regardless of thickness (< 0·8 mm or ≥ 0·8 mm), where stage IA would only include nonulcerated tumours of < 1 mm, but would not include tumours categorized as T1b (< 1 mm, ulcerated). If these results are validated, clinicians should consider ulceration in thin melanoma as being much more important than lymph node status and accordingly, for stages II and III, ulceration should be removed from the staging system as it does not have measurable survival impact for these stages.

The study by Wei *et al.* also highlights the weakness of the AJCC system in different clinical settings of cutaneous melanoma. A recent study comparing the 7th edition of the AJCC staging system with the 8th edition observed a loss of linearity and group overlap among the different stages, meaning that a worse AJCC classification is not necessarily related to a worse prognosis.[2] Other concerns related to acral melanoma that require further investigation include whether the histopathological subtype of melanoma and location alone could have an impact on prognosis.[2,3] There have been several studies demonstrating that the acral lentiginous melanoma subtype could be inherently more aggressive than other types of cutaneous melanoma at acral sites, suggesting that molecular biology may impact the aggressiveness of the disease more than the location or delayed diagnosis. Therefore, we have to understand that the AJCC classification has its limitations and that it does not consider important prognostic factors such as tumour location or the biology of the tumour.

Interestingly, there are distinctive molecular pathways involved in acral melanoma, such as point mutations in KIT and recurrent genomic copy number alteration gains in *cyclin D1*, *aurora kinase A* and *telomerase reverse transcriptase* genes, and these melanomas could also be influenced by ultraviolet radiation at different sites of acral skin.[4,5] Indeed, volar location also seems to be associated with a worse prognosis than melanoma occurring in the nailbed, and the prognosis for melanoma occurring on soles is worse than for melanoma located on the palms.[6] Pigmentation could be another trait associated with outcome, where amelanotic or hypomelanotic acral melanomas could more likely be associated with visceral (lung) metastasis and poor outcome.[7–9]

In conclusion, the recent study by Wei *et al.* poses another important question – 'could acral melanoma need a more accurate staging system in view of the fact that ulceration may play an important role in thin melanoma, but not in more advanced cases?' Acral melanoma could involve different biological behaviour and consequently, management, surveillance regimen and adjuvant therapy can vary widely according to this categorization.

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