Frequency of and risk factors for tumor upstaging after wide local excision of primary cutaneous melanoma

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Background: Detecting a more advanced stage of the primary melanoma after wide local excision and reconstruction can complicate patient counseling about prognosis, management of surgical margins, and indications for sentinel lymph node biopsy.

Objective: To identify the frequency of and risk factors associated with upstaging after wide local excision of primary melanoma.

Methods: Retrospective, single center, cross-sectional study of 1332 consecutive in situ to stage T4a melanomas treated with wide local excision.

Results: The overall rate of upstaging of melanoma was 3.9% (52/1332). After multivariate analysis, the greatest risk factor for upstaging was anatomic location on the head, neck, hands, feet, genitals, or pretibial leg (odds ratio [OR] 7.06, $P < .001$) followed by extension of the melanoma to the base of the biopsy specimen (OR 3.42, $P < .001$); the need for multiple preoperative scouting biopsies (OR 1.89, $P = .004$); older age (OR 1.03 per year, $P = .002$); and nonlentigo maligna histologic subtype (OR 3.6, $P = .002$).

Limitations: This was a single-site, retrospective observational study.

Conclusions: Clinicopathologic characteristics, particularly anatomic location on the head, neck, hands, feet, genitals, or pretibial leg and subtotal diagnostic biopsies, identify melanomas with an increased risk for upstaging. (J Am Acad Dermatol 2017;77:341-8.)

Key words: conventional excision; guidelines; melanoma; Mohs surgery; prognosis; reconstruction; sentinel lymph node biopsy; upstaging; wide local excision.

When residual melanoma remains after the diagnostic biopsy, upstaging (defined as an increase in the T stage designated by the American Joint Committee on Cancer [AJCC] classification system for melanoma)[1] might be detected after wide local excision in 5%-22% of cases.[2-11] Upstaging might complicate patient counseling about prognosis and surgical management of melanoma.

AJCC tumor stage is a powerful predictor of prognosis, with 10-year survival ranging from 93% for T1a melanoma to 39% for T4b melanoma.[1] Patients who are counseled about an excellent

Abbreviations used:

AJCC:	American Joint Committee on Cancer
AUC:	appropriate use criteria
CI:	confidence interval
LM:	lentigo maligna
OR:	odds ratio
SLNB:	sentinel lymph node biopsy

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prognosis before surgery might be surprised and confused to learn of a worse prognosis if the tumor upstages after a wide local excision.

Surgical management might also be complicated by upstaging because the Breslow depth, ulceration status, and mitotic rate from the diagnostic biopsy of a primary cutaneous melanoma dictate the surgical excision margins and the indications for sentinel lymph node biopsy (SLNB).[12] First, if an inaccurate diagnostic biopsy leads to undertreatment with narrower surgical margins than those recommended by consensus guidelines, patients might need additional surgery either to clear the tumor or to comply with wider margins recommended for the upstaged tumor. Neither the randomized trials that inform guidelines for surgical management of primary cutaneous melanoma nor consensus guidelines address surgical margins after upstaging.[12-18] Second, 1.3%-10% of upstaged tumors will meet criteria for SLNB.[2,5,6,11] While some case series have demonstrated that SLNB can be performed after reconstruction, especially after linear repairs, with good sensitivity and rare false negatives,[19-21] the accuracy of SLNB after flap and graft reconstruction remains uncertain.[12,22,23]

Clarifying risk factors for upstaging is important to help clinicians improve preoperative counseling about prognosis and surgical management, particularly when deciding whether or not to delay reconstruction for final staging of the wide local excision specimen.[6] Current data about upstaging must often be gleaned from reports that focus primarily on surgical technique[2-4,6-9] or biopsy method.[11,24-27]

Factors other than surgical technique and biopsy method might independently increase the risk for upstaging. One previous study correlated microstaging accuracy with biopsy method as well as several other clinicopathologic factors.[27] Compared with excisional biopsy, punch and shave biopsy had a significantly increased risk for inaccurate microstaging.[27] Among partially biopsied lesions, tumor thickness (increased risk for thicker tumors) was the only clinicopathologic factor that significantly affected microstaging accuracy after multivariate analysis. However, these results might not be generalizable because excision was the method of biopsy in a high percentage (78.6%) of the cohort. Nonexcisional biopsy methods (shave, punch, or incisional) to diagnose melanoma are more common than excisional biopsy in many patient populations[24,26,28] and have been noted to increase the risk for inaccurate microstaging.[11,27]

This study adds to the work of previous authors by examining the impact on upstaging of the widest reported array of clinicopathologic risk factors in a large cohort of melanomas diagnosed with a blend of excisional and nonexcisional preoperative biopsies, which might be more generalizable to many patient populations.[24,26] The principal aims of this study were to describe the rate of upstaging after wide local excision of cutaneous melanoma and to evaluate clinical and pathologic risk factors associated with upstaging. Secondarily, we aimed to describe how frequently consensus recommendations for surgical management differ for discrepant tumor stages before and after wide local excision.

CAPSULE SUMMARY

- Tumor upstaging after wide local excision complicates surgical management of melanoma.
- Risk factors for upstaging include tumor location in cosmetically or functionally sensitive areas, partial preoperative biopsies, older patient age, and nonlentigo maligna histologic subtype.
- The possibility of upstaging should be considered during patient counseling and surgical planning.

METHODS

Experimental design

This retrospective cross-sectional study was approved by the institutional review board at the Hospital of the University of Pennsylvania. Inclusion criteria for this study were age ≥18 years, pathologic T stage on diagnostic biopsy of in situ to T4a (T4b were excluded because they have no risk for upstaging), biopsy-proven melanoma whose diagnostic biopsy and excision specimens were interpreted by a board-certified dermatopathologist at the University of Pennsylvania from January 1, 2008, through December 31, 2013, and initial treatment with conventional wide local excision by a University of Pennsylvania Health System provider. Wide local excision was defined as excision of a biopsy-proven melanoma with a margin of clinically normal skin and immediate reconstruction, followed by microscopic margin assessment via formalin-fixed, paraffin-embedded bread loaf tissue sections. Eligible cases were identified via a search of the Dermatopathology database for "melanoma" and "lentigo maligna" (LM), which resulted in the identification of 7657 pathology reports containing either term in the line diagnosis. Review of the medical record identified 1332 melanomas that met inclusion criteria for this study. Each melanoma