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Association of Excision Margin Size With Local Recurrence and Survival in Patients With T1a Melanoma at Critical Structures

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IMPORTANCE Melanoma guidelines recommend surgical excision with 10-mm margins for T1 melanoma. However, this procedure may be problematic at sites close to critical structures such as the scalp, face, external genitalia, acral, periumbilical, and perineal areas.

OBJECTIVE To compare outcomes of wide (10-mm margins) vs narrow (5-mm margins) excision in patients with T1a melanoma near critical structures.

DESIGN, SETTING, AND PARTICIPANTS This cohort study was a retrospective comparison of 1341 consecutive patients aged 18 years or older from the National Cancer Institute of Milan, Italy, diagnosed between 2001 and 2020 with T1a cutaneous melanoma close to critical structures who accepted wide excision vs narrow excision.

EXPOSURES Local recurrence and melanoma-specific mortality (MSM) rates with 5-mm vs 10-mm excision margins.

MAIN OUTCOMES AND MEASURES The primary aim of the study was to ascertain whether a narrower (5-mm) vs wider (10-mm) excision margin was associated with local recurrence and MSM. The secondary aim was to compare the need for reconstructive surgery in the groups defined by excision margin width. Between April 28 and August 7, 2022, associations were assessed by weighted Cox and Fine-Gray univariable and multivariable models.

RESULTS A total of 1179 patients met the inclusion criteria (median [IQR] age, 50.0 [39.5-63.0] years; female, 610 [51.7%]; male, 569 [49.3%]). Six hundred twenty-six patients (53.1%) received a wide excision (434 [69.3%)] with linear repair and 192 [30.7%] with flap or graft reconstruction) and 553 (46.9%) received a narrow excision (491 [88.8%] with linear repair and 62 [11.2%] with flap or graft reconstruction) . The weighted 10-year MSM was 1.8% (95% CI, 0.8%-4.2%) in the wide group and 4.2% (95% CI, 2.2%-7.9%) in the narrow group; the weighted 10-year local recurrence rate was 5.7% (95% CI, 3.9%-8.3%) in the wide group and 6.7% (95% CI, 4.7%-9.5%) in the narrow group. Breslow thickness greater than 0.4 mm (subdistribution hazard ratio [sHR] for 0.6 vs 0.4 mm, 2.42; 95% CI, 1.59-3.68; $P < .001$) and mitotic rate greater than 1/mm^2 (sHR for a single increment, 3.35; 95% CI, 2.59-4.32; $P < .001$) were associated with worse MSM. Multivariable analysis showed that acral lentiginous melanoma, lentigo maligna melanoma, and increasing Breslow thickness were associated with a higher incidence of local recurrence.

CONCLUSIONS AND RELEVANCE The study's findings suggest that local excision with 5-mm margins for T1a melanoma may not be associated with an increased risk of local recurrence. Breslow thickness greater than 0.4 mm, mitotic rate greater than 1/mm^2, and acral lentiginous melanoma and lentigo maligna melanoma subtypes were associated with a higher risk of recurrence. These findings may be useful for future melanoma treatment guidelines.

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Supplemental content

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Thin melanomas (T1, Breslow thickness ≤1 mm) constitute nearly 70% of newly diagnosed cutaneous melanomas. Standard treatment is wide local excision (WLE) with 10-mm margins,[1-3] and prognosis is generally excellent.[4] According to the latest *American Joint Committee on Cancer Staging Manual*, the 5- and 10-year melanoma-specific survival for patients with T1a melanomas is 99% and 98%, respectively.[5] T1a is, therefore, an early disease stage, with less ability to metastasize and a better outcome than stage T1b, which may have consequences for treatment planning.[5] With regard to the width of surgical margins for thin melanomas, a clinical trial that evaluated 612 patients with invasive melanoma less than 2 mm thick randomly assigned to WLE with 1-cm vs 3-cm margins[6,7] found no differences in outcomes between groups.

Current melanoma guidelines reaffirm WLE with 10-mm margins for T1 melanomas.[1-3] However, no studies have evaluated T1 melanomas as 2 distinct subgroups (T1a and T1b) in association with surgical margins,[6,7] and the guidelines do not indicate whether T1a or T1b stage affects the adequacy of margins.[1-3]

Wide local excision with 10-mm margins cannot always be performed at sites close to critical structures, such as the scalp or face. Furthermore, patients with melanoma at such sites who are candidates for WLE with 10-mm margins may decline the procedure after being informed about potential adverse effects (eg, scarring, other cosmetic issues) and functional compromise. The melanoma guidelines[1-3] acknowledge these difficulties by noting that final surgical margins may vary depending on lesion location and functional or cosmetic considerations.

The primary aim of this study was to investigate whether outcomes of a narrower (5-mm) WLE are associated with local recurrence and melanoma-specific mortality (MSM) in patients with T1a melanomas close to critical structures. We retrospectively assessed patients who declined WLE with a 10-mm margin in favor of a 5-mm margin and compared outcomes in these 2 groups. We confined our attention to T1a melanomas because the clinical behavior of these lesions may be similar to that of in situ melanomas for which WLE with a 5-mm margin is acceptable.[1] Our secondary aim was to compare the complexity of reconstructive surgery (need for flaps or grafts) in both groups.

Key Points

Question In patients with T1a melanoma near critical structures, is a narrow (5-mm) excision margin associated with local recurrence and melanoma-specific mortality?

Findings In this cohort study of 1179 patients with T1a melanoma on scalp, face, external genitalia, acral, periumbilical, or perineal areas, the weighted 10-year melanoma-specific mortality was 1.8% and 4.2% in those undergoing wide (10-mm) and narrow (5-mm) excision, respectively. The weighted 10-year local recurrence rate was 5.7% and 6.7% in the wide and narrow groups, respectively.

Meaning The study's finding indicated that 5-mm margins may be adequate for T1a melanoma excision near critical structures.

Methods

Clinicopathological Characteristics

In this cohort study, 1341 patients aged 18 years or older consecutively treated between 2001 and 2020 at the National Cancer Institute, Milan, Italy, for localized T1a primary cutaneous melanoma of head and face areas with functional or cosmetic considerations, acral areas (sole of foot, palm of hand, digital and interdigital areas), external genitalia, or periumbilical and perineal areas, were considered for study inclusion. Excluded patients included 85 (6.3%) with missing data, 38 (2.8%) with a history of other invasive cancer (other than basal cell carcinoma), and 8 (0.6%) with primary mucosal melanomas. A further 31 patients (2.3%) were excluded because they had incomplete excision margins after WLE. These patients had lentigo maligna melanoma (LMM) with in situ residual disease or melanocytic atypia at the resection margins (17 in the narrow and 14 in the wide group), but refused further WLEs. They underwent topical treatment with imiquimod[8] at other centers. Thus, 1179 patients were included in the study.

The following data were retrieved from a prospectively maintained database: age, sex, tumor site, melanoma subtype (LMM, Spitz melanoma [SM], superficial spreading melanoma [SSM], and acral lentiginous melanoma [ALM]), vertical growth phase (VGP), Breslow thickness, mitotic rate per square millimeter, Clark level, tumor-infiltrating lymphocytes, lymphovascular invasion, and tumor regression. All slides were reviewed by dermatopathologists (M.C., A.B., and B.V.) according to a common protocol.[9] Diagnoses and staging of all patients were revised according to the *American Joint Committee on Cancer Staging Manual, 8th edition*.[5]

The data from our study concerned clinical margins measured at the time of surgery. Patients received an initial diagnostic excision with a median clinical margin of 2 mm of normal skin. After histologic confirmation of pT1a melanoma, patients who accepted the recommendations of the then-current guidelines[1,2,10-12] underwent WLE with median clinical margins of 8 mm (range, 7-9 mm) to achieve the recommended minimum margin of 10 mm. Patients who declined the standard procedure[1,2,10-12] underwent WLE with median clinical margins of 3 mm (range, 2-4 mm) to achieve a total margin of 5 mm. In all cases, clear lateral (with 5- and 10-mm clearance in the narrow and wide groups, respectively) and deep (with preservation of the muscular fascia) margins were obtained as verified by dermatopathologists (M.C., A.B., and B.V.). No shave or incisional biopsies were performed to diagnose melanoma or as definitive surgical treatment.

Surgery was performed after discussing the benefits and risks with each patient and obtaining their written informed consent. Final WLE margins of 5 mm and 10 mm defined the narrow and wide groups, respectively. After WLE, patients were followed by physicians of our melanoma unit according to a predefined protocol (every 6 months for the first 5 years and once annually for the following 5 years). The study was conducted in accordance with applicable laws, regulations, and

guidelines for the protection of human participants. The Fondazione IRCCS Istituto Nazionale dei Tumori di Milano institutional review board exempted the study from review because data were deidentified. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Statistical Analysis

The primary aims of the study were to compare the crude cumulative incidence (CCI) of MSM, CCI of local recurrence, overall survival, and disease-free survival between the wide and narrow groups, as assessed from the date of diagnosis. The CCIs of regional relapse and distant metastasis were also described. To take into account the nonrandomized treatment, the inverse probability treatment weighting method was used to adjust for imbalances between the surgical groups.[13] The logistic model used to estimate individual weights for each patient included all retrieved data. Overall survival was defined as the time to death from any cause; disease-free survival was defined as the time to recurrence or death, whichever occurred first. The MSM and CCIs of local recurrence, regional relapse, and distant metastasis were estimated in a competing risk setting, with death due to other causes and different relapse and death considered as competing events, respectively. Times were censored at the latest follow-up for patients still alive and free from any relevant event. Weighted overall survival and disease-free survival curves were estimated using the Kaplan-Meier method and compared using the weighted log-rank test. Weighted MSM and CCI curves were compared using the weighted Gray test.

General and clinicopathological differences between groups were assessed by the standardized mean difference (SMD).[13,14] As a measure of the magnitude of mean differences, SMD takes continuous values from 0 to infinity; the higher the SMD, the greater the difference. An SMD of approximately 0.3 is considered to indicate a possible between-group imbalance, although the clinical relevance of SMDs also needs to be assessed.

With regard to the secondary aim of comparing the complexity of reconstructive surgery (need for flaps or grafts) in both groups, associations between the requirement for reconstruction and each group were assessed by logistic models. Associations among margin group, a priori–selected clinicopathological characteristics (including melanoma subtype, VGP, Breslow thickness, mitotic rate, and tumor regression), and outcome were assessed by the weighted Cox (overall survival, disease-free survival) and Fine-Gray (MSM and CCI of local recurrence) univariable and multivariable models. Model results are reported as hazard ratios (HRs) for the Cox models and subdistribution HRs (sHRs) for the Fine-Gray models, with 95% CIs and 2-sided *P* values. Breslow thickness was modeled using 3-knot restricted cubic splines to obtain a flexible fit.[15]

Median follow-up was estimated from weighted overall survival data with the reverse Kaplan-Meier method.[16] Analyses were conducted between April 28 and August 7, 2022, using SAS, version 9.2 (SAS Institute Inc) and R, version 4.1.2 (R Foundation for Statistical Computing)[17] statistical software.

Results

Excision Margins and Tumor Characteristics

All patients (median [IQR] age, 50.0 [39.5-63.0] years; female, 610 [51.7%]; male, 569 [49.3%]) underwent an initial excisional biopsy followed by 1 or more WLEs: 626 (53.1%) with 10-mm margins and 553 (46.9%) with 5-mm margins. The most common lesion site was the head and face (997 [84.6%]); the most common subtype was SSM (855 [72.5%]). Median Breslow thickness was 0.5 mm (range, 0.1-0.7 mm), and median mitotic rate per mm^2 was 0 (range, 0-4). Patients in the wide group were slightly older (52 vs 49 years; SMD, 0.148 years) and had a higher Breslow thickness (0.5 vs 0.4 mm; SMD, 0.711 mm). The characteristics of the narrow and wide groups, as observed and after weighting, are summarized in **Table 1**.

Survival and Recurrences

The median follow-up was 115 months (IQR, 63-183 months) in the wide group and 111 months (IQR, 62-184 months) in narrow group, for an overall weighted median follow-up of 112 months (IQR, 63-184 months). At the end of follow up, the weighted 10-year MSM rate in the wide vs narrow group was 1.8% (95% CI, 0.8%-4.2%) vs 4.2% (95% CI, 2.2%-7.9%); weighted 10-year CCI of local recurrence, 5.7% (95% CI, 3.9%-8.3%) vs 6.7% (95% CI, 4.7%-9.5%); weighted overall survival rate, 95.9% (95% CI, 93.9%-98.0%) vs 94.5% (95% CI, 91.7%-97.5%); and weighted 10-year disease-free survival, 88.5% (95% CI, 85.6%-91.6%) vs 86.3% (95% CI, 82.8%-90.0%). No significant differences were observed in CCI of regional relapse and distant metastasis (**Figure 1**; eFigure in Supplement 1).

Analysis of MSM and local recurrence differences between groups according to melanoma subtype (**Figure 2**) showed that in LMM, the MSM and CCI of local recurrence did not differ, while in ALM they appeared lower in the wide group vs the narrow group, with MSM diverging in the far part of the curves, though not significantly.

There were 63 local recurrences overall (29 [4.6%] in the wide group and 34 [6.1%] in the narrow group), 22 regional relapses (12 [1.9%] in the wide group and 10 [1.8%] in the narrow group), and 21 distant metastases (11 [1.8%] in the wide group and 10 [1.8%] in the narrow group), which were followed by 21 melanoma-related deaths. Distant metastasis and MSM only occurred in the ALM and SSM subtypes (6 of 81 [7.4%] and 15 of 855 [1.8%] patients, respectively) and in 14 of 21 (66.7%) patients with Breslow thickness greater than 0.4 mm and mitotic rate greater than 1/mm^2.

Association Analyses

The results of the univariable and multivariable Fine-Gray models for MSM and CCI of local recurrence are shown in **Table 2**. In the MSM univariable models, all covariates but excision margin width and regression were associated with worse MSM. On multivariable analysis, Breslow thickness greater than 0.4 mm (sHR for 0.6 vs 0.4 mm, 2.42; 95% CI, 1.59-3.68; $P < .001$) and mitotic rate greater than 1/mm^2 (sHR of single increment, 3.35; 95% CI, 2.59-4.32; $P < .001$) were significantly associated with worse MSM. In the CCI of local recurrence univariable mod-

Table 1. Observed and Weighted Clinicopathological Characteristics of the 1179 Patients With T1a Melanoma, According to Excision Margins (5 vs 10 mm)

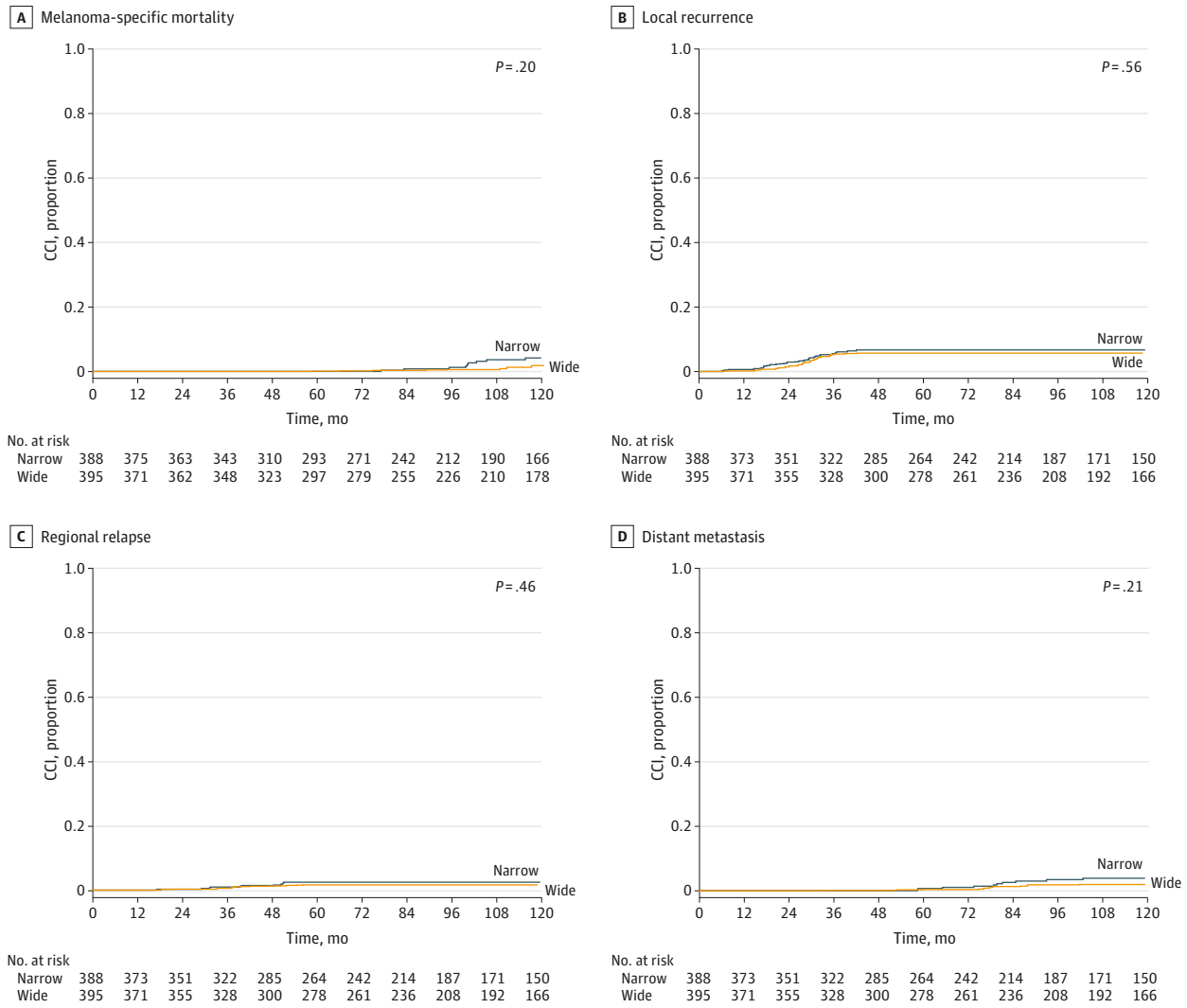
	Observed				Weighted			
	No. (%)				No. (%)			
	Overall (N = 1179)	10-mm margins (n = 626)	5-mm margins (n = 553)	SMD	Overall (N = 784.5)	10-mm margins (n = 396.0)	5-mm margins (n = 388.5)	SMD
Sex								
Female	610 (51.7)	309 (49.4)	301 (54.4)	0.102	406.1 (51.8)	206.5 (52.1)	199.6 (51.4)	0.015
Male	569 (48.3)	317 (50.6)	252 (45.6)		378.4 (48.2)	189.5 (47.9)	188.9 (48.6)	
Age, median (IQR), y	50.0 (39.5-63.0)	52.0 (40.0-64.0)	49.0 (39.0-61.0)	0.148	50.0 (39.6-62.9)	50.0 (39.0-63.0)	50.0 (40.0-62.0)	0.016
Site of primary melanoma								
Head and face	997 (84.6)	534 (85.3)	463 (83.7)	0.077	656.5 (83.7)	329.7 (83.3)	326.8 (84.1)	0.024
Genitals, periumbilical, perineal	72 (6.1)	40 (6.4)	32 (5.8)		47.4 (6.0)	24.3 (6.1)	23.2 (6.0)	
Acral	110 (9.3)	52 (8.3)	58 (10.5)		80.6 (10.3)	42.0 (10.6)	38.6 (9.9)	
Melanoma subtype								
LMM	193 (16.4)	110 (17.6)	83 (15.0)	0.111	117.9 (15.0)	59.0 (14.9)	58.9 (15.2)	0.015
SM	50 (4.2)	22 (3.5)	28 (5.1)		28.2 (3.6)	14.3 (3.6)	13.9 (3.6)	
SSM	855 (72.5)	455 (72.7)	400 (72.3)		584.2 (74.5)	294.6 (74.4)	289.6 (74.5)	
ALM	81 (6.9)	39 (6.2)	42 (7.6)		54.2 (6.9)	28.0 (7.1)	26.2 (6.7)	
VGP								
Absent	620 (52.6)	296 (47.3)	324 (58.6)	0.228	435.0 (55.5)	216.4 (54.6)	218.7 (56.3)	0.033
Present	559 (47.4)	330 (52.7)	229 (41.4)		349.5 (44.5)	179.6 (45.4)	169.9 (43.7)	
Breslow thickness, median (IQR), mm	0.5 (0.3-0.5)	0.5 (0.4-0.6)	0.4 (0.3-0.5)	0.711	0.4 (0.3-0.5)	0.5 (0.3-0.5)	0.4 (0.3-0.5)	0.031
Clark level								
2	594 (50.4)	310 (49.5)	284 (51.4)	0.043	407.7 (52.0)	204.2 (51.6)	203.5 (52.4)	0.026
3	426 (36.1)	228 (36.4)	198 (35.8)		284.3 (36.2)	143.5 (36.2)	140.8 (36.3)	
4	159 (13.5)	88 (14.1)	71 (12.8)		92.5 (11.8)	48.3 (12.2)	44.2 (11.4)	
Mitoses per mm^2								
0	1038 (88.0)	536 (85.6)	502 (90.8)	0.252	694.7 (88.6)	346.2 (87.4)	348.5 (89.7)	0.192
1	80 (6.8)	48 (7.7)	32 (5.8)		55.6 (7.1)	32.1 (8.1)	23.5 (6.0)	
2	41 (3.5)	33 (5.3)	8 (1.4)		21.7 (2.8)	14.4 (3.6)	7.4 (1.9)	
3	14 (1.4)	9 (1.4)	8 (1.4)		9.9 (1.3)	3.3 (0.8)	6.6 (1.7)	
4	3 (0.3)	0	3 (0.5)		2.6 (0.3)	0	2.6 (0.7)	
TILs								
Absent	949 (80.5)	498 (79.6)	451 (81.6)	0.055	633.8 (80.8)	320.1 (80.8)	313.7 (80.7)	0.004
Nonbrisk	187 (15.9)	103 (16.4)	84 (15.2)		124.4 (15.9)	62.6 (15.8)	61.9 (15.9)	
Brisk	43 (3.6)	25 (4.0)	18 (3.3)		26.3 (3.3)	13.3 (3.4)	12.9 (3.3)	
LVI								
Absent	1168 (99.1)	615 (98.2)	553 (100)	0.189	779.1 (99.3)	390.6 (98.6)	388.5 (100)	0.166
Present	11 (0.9)	11 (1.8)	0		5.4 (0.7)	5.4 (1.4)	0	
Regression								
Absent	855 (72.5)	466 (74.4)	389 (70.3)	0.092	571.5 (72.9)	289.2 (73.0)	282.4 (72.7)	0.008
Present	324 (27.5)	160 (25.6)	164 (29.7)		212.9 (27.1)	106.8 (27.0)	106.1 (27.3)	

Abbreviations: ALM, acral lentiginous melanoma; LMM, lentigo maligna melanoma; LVI, lymphovascular invasion; SM, Spitz melanoma; SMD, standardized mean difference; SSM, superficial spreading melanoma; TIL, tumor infiltrating lymphocyte; VGP, vertical growth phase.

els, only the LMM subtype was associated with worse CCI of local recurrence. On multivariable analysis, ALM vs SSM subtype (sHR, 2.81; 95% CI, 1.14-6.94) and LMM vs SSM subtype (sHR, 4.09; 95% CI, 2.26-7.42; $P < .001$) and Breslow thickness greater than 0.4 mm (sHR for 0.6 vs 0.4 mm, 1.69; 95% CI, 1.07-2.67; $P = .03$) were significantly associated with worse CCI of local recurrence.

The results of the univariable and multivariable Cox models for overall survival and disease-free survival are shown in **Table 3**. In the overall survival univariable models, all covariates but excision margin width and regression were associated with overall survival. In the multivariable model, VGP (HR, 4.99; 95% CI, 1.74-14.27; $P = .003$) and mitotic rate (HR of single increment, 1.97; 95% CI, 1.39-2.79; $P < .001$) were associated

Figure 1. Crude Cumulative Incidence (CCI) Curves of Melanoma-Specific Mortality, Local Relapse, Regional Relapse, and Distant Metastasis According to Excision Margin Width (Wide vs Narrow) in Patients With T1a Melanomas Close to Critical Structures



with overall survival. On univariable analysis, all covariates but excision margin width were associated with disease-free survival. On multivariable analysis, LMM subtype (HR, 2.11; 95% CI, 1.21-3.70; $P = .04$), VGP (HR, 1.74; 95% CI, 1.09-2.78; $P = .02$), and mitotic rate (HR, 1.58; 95% CI, 1.25-2.00; $P < .001$) were associated with worse disease-free survival.

Wound Closure and Reconstructive Surgery

In 227 of the 1179 (19.3%) patients, more than 1 reexcision was performed to achieve a histologic clearance margin of 5 or 10 mm. Reexcisions were similar in the 2 groups: 159 of 1179 patients (13.5%) underwent 2 reexcisions (77 of 626 [12.3%] in the wide group and 82 of 553 [14.8%] in the narrow group); 61 of 1179 patients (5.2%) needed 3 reexcisions (27 of 626 [4.3%] in the wide group and 34 of 553 [6.1%] in the narrow group); and 7 of 1179 (0.6%) had 4 reexcisions (3 of 626 [0.5%] in the wide group and 4 of 553 [0.7%] in the narrow group).

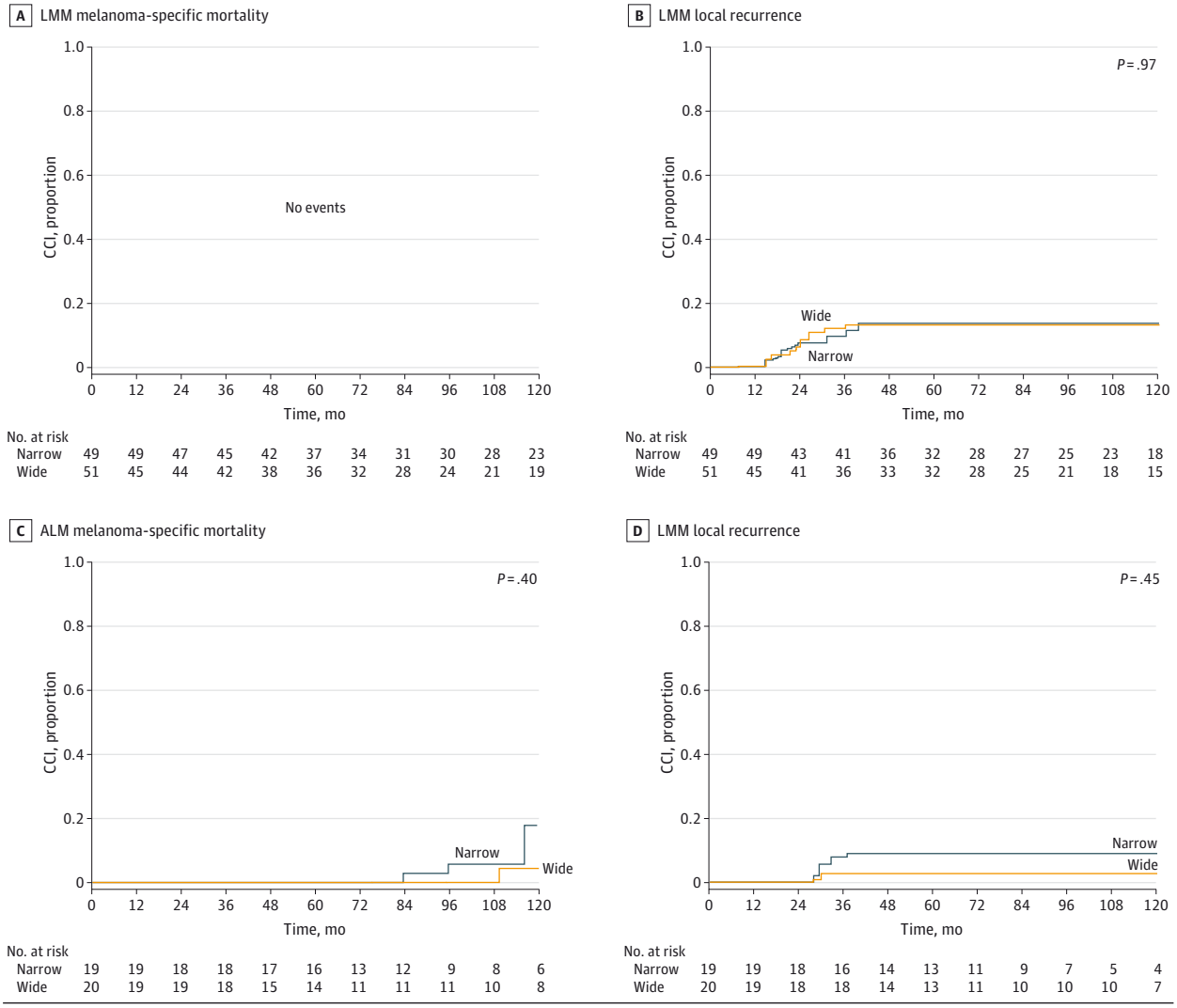
Among the 952 patients (80.7%) who had no reexcisions, the final surgical margins to obtain histopathologic clearance were 5 mm and 10 mm for the narrow and wide groups, respectively. In the 227 patients (19.3%) who underwent more than 1 reexcision, the final surgical margins were up to 10 mm and 15 mm, respectively.

Of the 626 patients in the wide group, 434 (69.3%) underwent linear repair, and 192 (30.7%) required flap or graft reconstruction. Of the 553 patients in the narrow group, 491 (88.8%) underwent linear repair, and 62 (11.2%) required flap or graft reconstruction. The difference in flap or graft reconstruction frequency between groups was significant (odds ratio, 0.29; 95% CI, 0.21-0.39; $P < .001$).

Discussion

The main finding of this cohort study was that treating primary T1a melanomas with WLE with 5-mm margins, instead of 10 mm as recommended by the guidelines,[1-3] was not significantly associated with MSM, CCI of local recurrence, over-

Figure 2. Crude Cumulative Incidence (CCI) Curves of Melanoma-Specific Mortality and Local Relapse in Lentigo Maligna Melanoma (LMM) and Acral Lentiginous Melanoma (ALM) According to Excision Margin Width (Wide vs Narrow) in Patients With T1a Melanomas Close to Critical Structures



all survival, or disease-free survival. In the multivariable models applied to our series, we observed that Breslow thickness greater than 0.4 mm and mitotic rate greater than 1/mm^2 were associated with MSM. Excision margin width was not significantly associated with MSM (P = .29), but the estimated sHR of 0.59 and its 95% CI of 0.22-1.58 had an imprecise margin. This evidence, combined with the underlying point estimates of CCI of MSM (1.8% [95% CI, 0.8%-4.2%] and 4.2% [95% CI, 2.2%-7.9%] in the wide and narrow groups, respectively) should be discussed with patients before surgery. Although the absence of events in LMM and SM types prevented us from estimating the association of melanoma subtype with MSM, the simple frequencies in the associated subtypes (ALM, 7.4% of patients; SSM, 1.8% of patients) and their strict correlation with distant metastases is a potential indication of a subtype association. It is also noteworthy that the higher incidence of local recurrence in the LMM and SM subtypes was unrelated to MSM and distant metastasis (no event). This result is reflected in the overall survival rate, where LMM and SM had the better outcomes, albeit not significant in multivariable analysis. The worse association for VGP (HR, 4.99) is related to its association with high mitotic rate. In disease-free survival, we observed a melanoma subtype association led by CCI of local recurrence and a mitotic rate outcome led by its association with MSM. Breslow thickness greater than 0.4 mm showed the most consistent worse association throughout the outcomes. The role of mitotic rate as a significant variable was also found in a study by Evans et al[18] that analyzed 71 235 patients (79.0% with stage I melanoma) and showed that mitotic rate may be independently associated with survival for localized melanoma.

It is noteworthy that among patients with ALM in our series, those with narrow margins did not have a significantly higher incidence of MSM and local recurrence (Figure 2). In a large case-control (local recurrence and no local recurrence) study of T1 melanomas, MacKenzie Ross et al[19] found that a higher local recurrence rate was significantly associated with specific melanoma subtypes. They suggested surgical mar-

Table 2. Results of the Weighted Univariable and Multivariable Fine-Gray Models for Melanoma-Specific Mortality and Local Recurrence

	Melanoma-specific mortality				Local recurrence			
	Univariable		Multivariable		Univariable		Multivariable	
Covariate	sHR (95% CI)	*P* value[a]	sHR (95% CI)	*P* value[a]	sHR (95% CI)	*P* value[a]	sHR (95% CI)	*P* value[a]
Melanoma subtype								
ALM vs SSM	NA	NA	NA	NA	2.03 (0.83-4.98)	<.001	2.81 (1.14-6.94)	<.001
LMM vs SSM	NA		NA		3.60 (1.99-6.51)		4.09 (2.26-7.42)	
SM vs SSM	NA		NA		2.16 (0.65-7.14)		3.00 (0.94-9.65)	
Present vs absent VGP	4.07 (1.35-12.23)	.01	1.10 (0.45-2.72)	.97	1.11 (0.65-1.89)	.70	0.99 (0.56-1.77)	.98
Breslow thickness, mm[b]								
0.4 vs 0.2	0.42 (0.08-2.30)	<.001	0.70 (0.07-7.59)	<.001	1.63 (0.70-3.84)	.18	2.06 (0.84-5.04)	.03
0.6 vs 0.4	6.02 (3.28-11.06)		2.42 (1.59-3.68)		1.39 (0.94-2.07)		1.69 (1.07-2.67)	
1 vs 0 mitoses/mm^2	4.16 (3.24-5.35)	<.001	3.35 (2.59-4.32)	<.001	0.17 (0.03-0.95)	.04	0.16 (0.03-0.81)	.03
Present vs absent regression	0.87 (0.29-2.64)	.81	1.02 (0.39-2.67)	.17	0.33 (0.14-0.78)	.01	0.29 (0.12-0.68)	.004
Wide vs narrow excision margins	0.51 (0.20-1.27)	.15	0.59 (0.22-1.58)	.29	0.84 (0.49-1.44)	.53	0.83 (0.48-1.44)	.50

Abbreviations: ALM, acral lentiginous melanoma; LMM, lentigo maligna melanoma; NA, not applicable; sHR, subdistribution hazard ratio; SM, Spitz melanoma; SSM, superficial spreading melanoma; VGP, vertical growth phase.

[a] By weighted Gray test.

[b] Modeled as restricted cubic spline. Values represent the beginning and end of the most pending part of the curve between the log (hazard) of the event and the values of the variable.

Table 3. Results of the Weighted Univariable and Multivariable Cox Models for Overall and Disease-Free Survival

	Overall survival				Disease-free survival			
	Univariable models		Multivariable model		Univariable models		Multivariable model	
Covariate	HR (95% CI)	*P* value[a]	HR (95% CI)	*P* value[a]	HR (95% CI)	*P* value[a]	HR (95% CI)	*P* value[a]
Melanoma subtype								
ALM vs SSM	3.66 (1.50-8.95)	.02	1.47 (0.56-3.87)	.74	2.34 (1.23-4.45)	.03	1.58 (0.81-3.09)	.04
LMM vs SSM	0.42 (0.09-2.01)		0.55 (0.11-2.74)		1.70 (0.98-2.93)		2.11 (1.21-3.70)	
SM vs SSM	0.84 (0.09-8.36)		0.82 (0.08-8.64)		1.71 (0.63-4.70)		1.77 (0.64-4.91)	
Present vs absent VGP	7.53 (2.79-20.30)	<.001	4.99 (1.74-14.27)	.003	2.29 (1.48-3.55)	<.001	1.74 (1.09-2.78)	.02
Breslow thickness, mm[b]								
0.4 vs 0.2	0.53 (0.19-1.51)	<.001	0.55 (0.18-1.71)	.40	1.08 (0.58-2.03)	<.001	1.29 (0.66-2.51)	.21
0.6 vs 0.4	3.27 (2.06-5.21)		1.31 (0.71-2.42)		2.09 (1.53-2.87)		1.37 (0.94-2.00)	
1 vs 0 mitoses/mm^2	2.85 (2.16-3.74)	<.001	1.97 (1.39-2.79)	<.001	1.94 (1.60-2.36)	<.001	1.58 (1.25-2.00)	<.001
Present vs absent regression	0.48 (0.18-1.30)	.15	0.65 (0.23-1.82)	.41	0.50 (0.28-0.88)	.02	0.52 (0.29-0.92)	.03
Wide vs narrow excision margins	0.82 (0.40-1.67)	.58	0.88 (0.41-1.90)	.75	0.82 (0.54-1.26)	.37	0.85 (0.55-1.30)	.46

Abbreviations: ALM, acral lentiginous melanoma; HR, hazard ratio; LMM, lentigo maligna melanoma; SM, Spitz melanoma; SSM, superficial spreading melanoma; VGP, vertical growth phase.

[a] By Wald test.

[b] Modeled as restricted cubic spline. Values represent the beginning and end of the most pending part of the curve between the log (hazard) of the event and the values of the variable.

gins of 1 cm or greater (where possible) to reduce the risk of local recurrence, especially in cases of desmoplastic melanoma, ALM, and LMM.[19] Our series included few patients with ALM (6.9%) and none with desmoplastic melanoma, consistent with these subtypes being rarely diagnosed at an early stage.[20,21]

With regard to the secondary aim of our study, we found that 62 patients (11.2%) in the narrow group and 192 (30.7%) in the wide group required reconstructive surgery. This difference was significant ($P < .001$) and suggests that narrower margins may reduce infection, poor healing, scarring, and mental issues often occurring with excisions close to critical structures. Rawlani et al[22] retrospectively examined 5-year recurrence-free survival in 79 melanomas (60% ≤ 1-mm thick) of the head and neck treated with reduced margins where the recommended margins might have increased the risk of functional or cosmetic defects. They found that excision margin reduction was not associated with increased local recurrence rates.

Lau et al[23] investigated a series of stage IA melanomas treated with standard 10-mm excision margins and found self-reported postoperative morbidities in 25% of patients. This rather high proportion suggests that the need for 10-mm excision margins should be reevaluated, particularly for lesions close to critical structures.

Recently, the melanoma guidelines have recommended the use of microscopically controlled surgery to spare tissue and improve margin control.[24,25] In a large retrospective study of keratinocyte carcinomas and melanomas (in situ and invasive) occurring on the head and neck and treated with Mohs micrographic surgery, Fix et al[26] showed that melanomas had a higher risk of local recurrence and more frequently required reconstructive surgery than keratinocyte carcinomas. However, in a retrospective analysis, Beal et al[27] showed that in T1 head-and-neck melanomas treated with Mohs micrographic surgery, all recurrence rates were very low (0.51%). Furthermore, Rzepecki et al[28] showed that melanomas at critical structures carried higher risks (approximately 10%) of positive excision margins and the likelihood of reconstruction after conventional excision with postoperative margin assessment. They emphasized the need to develop guidelines with indications for Mohs micrographic surgery in melanomas at critical structures, as this technique allows complete tumor removal before reconstruction. Another study of various skin tumors (including lentiginous melanomas) showed that complete circumferential peripheral and deep margin assessment allowed complete control of resection margins and enabled skin-sparing resections with low recurrence rates.[29] Because our series showed a high rate of positive margins (19.3%) needing flap or graft reconstruction (with additional expenses and higher risks of morbidity and anxiety), we delayed reconstruction in these patients until we achieved pathological clear margins of 5 mm and 10 mm in the narrow and wide groups, respectively. Our findings confirmed that Mohs micrographic surgery and complete circumferential peripheral and deep margin assessment can be alternative procedures to conventional surgery with postoperative margin assessment, particularly in selected melanoma subtypes such as LMM and ALM. Furthermore, our study showed a high percentage of the SSM subtype in the head and face regions, which may be associated with the relatively young average age of our cohort.

Strengths and Limitations

The main strength of this study is that it comprised a large series of patients with a long follow-up. The study's limitations are that it was retrospective and that the wide and narrow groups were defined by patient decisions to accept or refuse the guideline recommendations. This definition of patients groups could be a source of bias, particularly in terms of the strength of physician accounts of the possible aesthetic and functional sequelae of wide excision. Another limitation is that the histopathological review was not centralized, although all slides were reviewed according to a common protocol.[9]

Conclusions

In this cohort study, WLE with narrow (5-mm) margins in primary pT1a melanomas was not associated with worse outcomes but was associated with significantly fewer reconstructive surgeries. Because this association was found in melanomas of the head and neck, acral, and genital sites, there is no plausible reason why it could not be extrapolated to other locations. The findings also support the need for prospective randomized clinical trials to definitively answer the important question about appropriate excision margins for T1a melanoma.

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