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Association of Mohs Micrographic Surgery vs Wide Local Excision With Overall Survival Outcomes for Patients With Melanoma of the Trunk and Extremities

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IMPORTANCE Although previous database studies suggest that Mohs micrographic surgery (MMS) treatment is associated with improved overall survival (OS) for head and neck melanomas, outcomes for trunk and extremity (T&E) tumors have not been adequately evaluated.

OBJECTIVE To assess survival outcomes for patients with melanomas of the T&E treated with MMS vs wide local excision (WLE).

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study examined deidentified data from the National Cancer Database between 2004 and 2015. Inclusion criteria for the analysis included diagnosis of trunk, upper extremity, or lower extremity melanoma; known Breslow depth; removal by MMS or WLE; and known last date of survival status.

MAIN OUTCOMES AND MEASURES Five-year all-cause mortality (ACM) rates.

RESULTS A total of 188 862 in situ and invasive melanomas were included in the analysis (MMS, 2.3%; WLE, 97.7%); the mean (SD) age of patients included was 58.8 (16.0) years, and 52.7% were male. Multivariate analysis demonstrated no OS difference among trunk (WLE hazard ratio [HR], 1.097; 95% CI, 0.950-1.267; $P = .21$), upper extremity (WLE HR, 1.013; 95% CI, 0.872-1.176; $P = .87$), lower extremity (WLE HR, 0.934; 95% CI, 0.770-1.134; $P = .49$), or combined T&E (WLE HR, 1.031; 95% CI, 0.941-1.130; $P = .51$) tumors. Factors associated with increased risk of ACM on multivariate analysis of all tumors included increasing age (HR, 1.043; 95% CI, 1.042-1.044; $P < .001$), no insurance or nonprivate insurance (none: HR, 1.921 [95% CI, 1.782-2.071]; Medicaid: HR, 2.410 [95% CI, 2.242-2.591]; Medicare: HR, 1.237 [95% CI, 1.194-1.281]; other government insurance: HR, 1.279 [95% CI, 1.117-1.465]; $P < .001$ for all), positive surgical margins (HR, 1.609; 95% CI, 1.512-1.712; $P < .001$), a Charlson-Deyo comorbidity score greater than 0 (Charlson-Deyo score of 1: HR, 1.340; 95% CI, 1.295-1.385; $P < .001$; Charlson-Deyo score of ≥ 2: HR, 2.044; 95% CI, 1.934-2.159; $P < .001$), tumor ulceration (HR, 2.175; 95% CI, 2.114-2.238; $P < .001$), and increasing Breslow depth (HR, 1.002 [per 0.1 mm]; $P < .001$). Female sex (HR, 0.698; 95% CI, 0.680-0.716; $P < .001$) and nonnodular subtype (lentigo maligna/lentigo maligna melanoma: HR, 0.743; 95% CI, 0.686-0.805; $P < .001$; superficial spreading: HR, 0.739; 95% CI, 0.710-0.769; $P < .001$; other subtype: HR, 0.817; 95% CI, 0.790-0.845; $P < .001$; nodular: HR, 1 [reference]) were associated with improved OS.

CONCLUSIONS AND RELEVANCE This cohort study of patients surgically treated for melanomas of the trunk and/or extremities found that, compared with WLE, MMS was not associated with significantly different OS for T&E melanomas.

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Supplemental content

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The use of Mohs micrographic surgery (MMS) for the treatment of cutaneous melanoma remains controversial. Despite recent guidelines that have deemphasized its use,[1,2] use of MMS for treatment of melanoma in the United States continues to increase.[3] This trend may be explained by the robust and expanding body of data supporting its safety and efficacy for both in situ and invasive disease.[4-11]

Our group recently published retrospective data from the National Cancer Database (NCDB) demonstrating that MMS is associated with improved overall survival (OS) for head and neck (H&N) melanomas.[5] Similar NCDB data demonstrated that MMS was associated with a modest improvement in OS relative to wide margin excision for stage I tumors classified by the *American Joint Committee on Cancer Staging Manual*, 8th edition, across all anatomic sites.[4] To our knowledge, all previous database and population-based study designs focused on early-stage melanomas and/or those of the H&N.[4,5,7-9,11] It remains unclear if there is a survival advantage to MMS when it is used for the treatment of all-stage melanomas of the trunk and extremity (T&E). The purpose of the present study was to determine if there are differences in survival outcomes among patients with all-stage in situ and invasive melanoma of the T&E treated with MMS compared with wide local excision (WLE).

Methods

To assess for differences in all-cause mortality (ACM) between MMS and WLE, data from the NCDB from 2004 through 2015 were analyzed in SPSS, version 26 (IBM). Our methods are similar to those described previously.[5] For brevity, only differences in methodology will be discussed.

For the present study, we analyzed all-stage melanomas of the trunk, upper extremities (including the shoulders), or lower extremities (including the hips). Of note, the NCDB does not provide a unique distinction for acral and nail unit melanomas. A total of 202 600 individuals met initial inclusion criteria. Individuals with missing covariate demographic data were subsequently excluded (n = 13 738).

Selected covariates were largely identical to our previous study.[5] The only variable not included from our previous analysis was medical facility type, as data were missing for more than 20% of participants. A sensitivity analysis was performed including only invasive melanomas. Statistical analysis was otherwise identical to that described previously.[5]

The NCDB is a joint project of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society. The CoC's NCDB and the hospitals participating in the CoC NCDB are the source of the deidentified data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors. This study was exempt from institutional review board approval owing to its use of deidentified data collected from a publicly available database.

Key Points

Question Is Mohs micrographic surgery vs wide local excision associated with improved overall survival for trunk and extremity (T&E) melanomas?

Findings This cohort study of 188 862 cases of in situ and invasive T&E melanomas from the National Cancer Database between 2004 and 2015 did not demonstrate a difference in overall survival among T&E melanomas treated with Mohs micrographic surgery vs wide local excision.

Meaning Mohs micrographic surgery may be considered a reasonable treatment option for select T&E melanomas; the absence of a survival benefit for Mohs micrographic surgery supports current US practice patterns, where wide local excision is the predominant treatment for T&E melanomas.

Results

A total of 188 862 cases of in situ and invasive T&E melanoma from the NCDB were included in the present analysis. Detailed demographic data are summarized in **Table 1**. The mean (SD) age of patients included was 58.8 (16.0) years, and 52.7% were male. Treatment with WLE (97.7%) was more commonly used than treatment with MMS (2.3%). Overall tumor characteristics were fairly similar between anatomic sites, although there was a higher proportion of lentigo maligna or lentigo maligna melanoma tumors treated on the upper extremities (upper extremities, 4.7%; trunk, 2.4%; lower extremities, 1.4%). Rates of MMS use were similar between anatomic subgroups (trunk, 2.2%; upper extremity, 2.5%; lower extremity, 2.3%).

By the Kaplan-Meier estimator, MMS treatment was associated with increased 5-year OS for all T&E tumors (MMS, 86.1%; WLE, 82.9%; $P < .001$). However, the multivariate Cox model showed no overall difference in ACM among trunk (WLE hazard ratio [HR], 1.097; 95% CI, 0.950-1.267; $P = .21$), upper extremity (WLE HR, 1.013; 95% CI, 0.872-1.176; $P = .87$), lower extremity (WLE HR, 0.934; 95% CI, 0.770-1.134; $P = .49$), or combined T&E (WLE HR, 1.031; 95% CI, 0.941-1.130; $P = .51$) melanomas treated with MMS or WLE (**Tables 2** and **3**). No statistically significant difference in OS was observed at any site when only invasive tumors were included.

Factors associated with increased risk of ACM on multivariate analysis of all tumors included increasing age (HR, 1.043; 95% CI, 1.042-1.044; $P < .001$), nonprivate insurance (Table 2), positive surgical margins (HR, 1.609; 95% CI, 1.512-1.712; $P < .001$), a Charlson-Deyo comorbidity score greater than 0 (Charlson-Deyo score of 1: HR, 1.340; 95% CI, 1.295-1.385; $P < .001$; Charlson-Deyo score of ≥2: HR, 2.044; 95% CI, 1.934-2.159; $P < .001$), tumor ulceration (HR, 2.175; 95% CI, 2.114-2.238; $P < .001$), and increasing Breslow depth (HR, 1.002 [per 0.1 mm]; $P < .001$). Female sex (HR, 0.698; 95% CI, 0.680-0.716; $P < .001$) and nonnodular subtype (lentigo maligna/lentigo maligna melanoma: HR, 0.743; 95% CI, 0.686-0.805; $P < .001$; superficial spreading: HR, 0.739; 95% CI, 0.710-0.769; $P < .001$; other subtype: HR, 0.817; 95% CI, 0.790-0.845; $P < .001$; nodular: HR, 1 [reference]) were associated

Table 1. Characteristics of the Study Population by Tumor Location

Characteristic	No. (%)			
			Extremity	
	All cases	Trunk	Upper	Lower
No. treated	188 862	79 314	63 115	46 433
Age, mean (SD), y	58.8 (16.0)	57.5 (15.8)	61.7 (15.6)	56.8 (16.5)
Sex				
Male	99 448 (52.7)	52 239 (65.9)	33 387 (52.9)	13 822 (29.8)
Female	89 414 (47.3)	27 075 (34.1)	29 728 (47.1)	32 611 (70.2)
Race				
White	184 330 (97.6)	77 699 (98.0)	61 879 (98.0)	44 752 (96.4)
Other	4523 (2.4)	1615 (2.0)	1236 (2.0)	1681 (3.6)
Insurance				
Private	112 334 (59.5)	49 137 (62.0)	33 823 (53.6)	29 374 (63.3)
None	4704 (2.5)	2177 (2.7)	1390 (2.2)	1137 (2.4)
Medicaid	4292 (2.3)	1812 (2.3)	1234 (2.0)	1246 (2.7)
Medicare	65 696 (34.8)	25 438 (32.1)	26 012 (41.2)	14 246 (30.7)
Other government insurance	1836 (1.0)	750 (0.9)	656 (1.0)	430 (0.9)
Surgery type				
MMS	4413 (2.3)	1767 (2.2)	1595 (2.5)	1051 (2.3)
WLE	184 449 (97.7)	77 547 (97.8)	61 520 (97.5)	45 382 (97.7)
Margins reported				
Negative	185 265 (98.1)	77 982 (98.3)	61 875 (98.0)	45 408 (97.8)
Positive	3597 (1.9)	1332 (1.7)	1240 (2.0)	1025 (2.2)
Ulceration				
No	156 060 (82.6)	65 848 (83.0)	52 435 (83.1)	37 777 (81.4)
Yes	32 802 (17.4)	13 466 (17.0)	10 680 (16.9)	8656 (18.6)
Charlson-Deyo score				
0	166 339 (88.1)	69 972 (88.2)	54 874 (86.9)	41 493 (89.4)
1	18 786 (9.9)	7853 (9.9)	6776 (10.7)	4157 (9.0)
≥2	3737 (2.0)	1489 (1.9)	1465 (2.3)	783 (1.7)
Tumor type				
Nodular	18 776 (9.9)	7737 (9.8)	6896 (10.9)	4143 (8.9)
Other	96 373 (51.0)	39 210 (49.4)	32 056 (50.8)	25 107 (54.1)
LM/LMM	5475 (2.9)	1910 (2.4)	2935 (4.7)	630 (1.4)
Superficial spreading	68 238 (36.1)	30 457 (38.4)	21 228 (33.6)	16 553 (35.6)
Breslow depth, mean (SD), per 0.1 mm	1.40 (1.83)	1.40 (1.87)	1.41 (1.81)	1.41 (1.78)

Abbreviations: LM, lentigo maligna; LMM, lentigo maligna melanoma; MMS, Mohs micrographic surgery; WLE, wide local excision.

with improved OS. Multivariate analysis by anatomic subgroup demonstrated similar findings (Table 3). Treatment group characteristics are provided in the eTable of the Supplement.

Discussion

Multivariate analysis of all-stage in situ and invasive T&E melanomas from the NCDB demonstrated no difference in OS between tumors treated with MMS and those treated with WLE. This finding is unsurprising, given existing data. Cheraghlou and colleagues[4] reported an OS benefit for MMS when it is used in treatment of stage I tumors, classified by the *American Joint Committee on Cancer Staging Manual*, 8th edition, across all anatomic sites; however, subgroup analysis demonstrated that this benefit was only observed for H&N tumors. Their findings are consistent with those presented herein and by our group previously.[5]

Factors associated with increased risk of mortality on multivariate analysis of all T&E melanomas included age, male sex, nonprivate insurance, positive surgical margins, tumor ulceration, Charlson-Deyo comorbidity score greater than 0, nodular subtype, and Breslow depth. It is noteworthy that medical facility type was not included in this model, as previous data suggest that treatment at high-volume academic centers is associated with improved long-term patient survival.[12]

There are several features of cutaneous H&N melanoma that may explain why MMS is associated with improved survival at this site, but not the T&E.[5] Head and neck tumors more commonly present with subclinical spread, making clinical margin delineation challenging.[13] National Comprehensive Cancer Network guidelines currently recommend WLE

Table 2. Univariate and Multivariate Cox Regression Analysis of 5-Year All-Cause Mortality for All Participants

	Univariate		Multivariate	
Characteristic	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age	1.056 (1.055-1.057)	<.001	1.043 (1.042-1.044)	<.001
Sex				
Male	1 [Reference]		1 [Reference]	
Female	0.560 (0.546-0.575)	<.001	0.698 (0.680-0.716)	<.001
Race				
White	1 [Reference]		1 [Reference]	
Other	1.148 (1.064-1.239)	<.001	1.071 (0.992-1.156)	.078
Insurance				
Private	1 [Reference]		1 [Reference]	
None	2.472 (2.294-2.664)	<.001	1.921 (1.782-2.071)	<.001
Medicaid	3.188 (2.967-3.425)	<.001	2.410 (2.242-2.591)	<.001
Medicare	3.738 (3.638-3.839)	<.001	1.237 (1.194-1.281)	<.001
Other government insurance	1.814 (1.584-2.077)	<.001	1.279 (1.117-1.465)	<.001
Surgery type				
MMS	1 [Reference]		1 [Reference]	
WLE	1.266 (1.155-1.386)	<.001	1.031 (0.941-1.130)	.507
Margins				
Negative	1 [Reference]		1 [Reference]	
Positive	2.449 (2.302-2.605)	<.001	1.609 (1.512-1.712)	<.001
Ulceration				
No	1 [Reference]		1 [Reference]	
Yes	4.335 (4.229-4.443)	<.001	2.175 (2.114-2.238)	<.001
Charlson-Deyo score				
0	1 [Reference]		1 [Reference]	
1	2.030 (1.964-2.099)	<.001	1.340 (1.295-1.385)	<.001
≥2	3.849 (3.645-4.065)	<.001	2.044 (1.934-2.159)	<.001
Tumor type				
Nodular	1 [Reference]		1 [Reference]	
Other	0.388 (0.376-0.400)	<.001	0.817 (0.790-0.845)	<.001
LM/LMM	0.385 (0.357-0.416)	<.001	0.743 (0.686-0.805)	<.001
Superficial spreading	0.259 (0.250-0.269)	<.001	0.739 (0.710-0.769)	<.001
Breslow depth, per 0.1 mm	1.003 (1.003-1.003)	<.001	1.002 (1.002-1.002)	<.001

Abbreviations: HR, hazard ratio; LM, lentigo maligna; LMM, lentigo maligna melanoma; MMS, Mohs micrographic surgery; WLE, wide local excision.

(1-2-cm margins) universally for the treatment of all invasive melanoma; however, the guidelines state that "margins may be modified to accommodate individual anatomic or functional considerations."[2] Narrower-than-recommended margins are commonly taken around specialty site melanomas,[14] a practice that, although not evidence based, is endorsed by current guidelines.[2] Melanomas of the H&N or special sites are associated with 9.1% (0%-16%) positive margin and 9.9% (2.6%-49%) local recurrence rates compared with 1.7% positive margin (0%-2.2%) and 1.7% local recurrence (0.8%-12.4%) rates for T&E tumors when treated with WLE.[14] Therefore, it is unsurprising that a significant survival benefit has been observed for tumors treated with MMS on the H&N, but not the T&E.[4,5,9]

Limitations

As with any database project, there are likely contributing variables not captured by the database, and misclassification of variables is possible. Furthermore, there were baseline dissimilarities and size imbalances between the 2 treatment groups. It is possible that, due to the small number of patients in the MMS treatment group, the study was not powered sufficiently to identify a statistically significant survival difference if one exists. The NCDB is a hospital-based database, so findings may not be representative of other treatment settings. Finally, certain technique-specific data were not included in the database, including immunohistochemistry use and histologic processing technique.

Conclusions

In contrast with previous database studies of H&N melanoma, this analysis of 188 862 cases of T&E melanoma from the NCDB did not demonstrate a difference in OS between MMS or WLE treatments. These findings add to the existing body of evidence demonstrating that WLE is not associated with a greater survival benefit than MMS for treatment of cutaneous melanoma.

Table 3. Univariate and Multivariate Cox Regression Analysis of 5-Year All-Cause Mortality by Tumor Location

	Trunk				Extremities							
					Upper				Lower			
	Univariate		Multivariate		Univariate		Multivariate		Univariate		Multivariate	
Characteristic	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age	1.050 (1.048-1.051)	<.001	1.038 (1.036-1.040)	<.001	1.066 (1.064-1.068)	<.001	1.052 (1.050-1.055)	<.001	1.061 (1.059-1.063)	<.001	1.045 (1.042-1.048)	<.001
Sex												
Male	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Female	0.560 (0.536-0.585)	<.001	0.784 (0.750-0.820)	<.001	0.570 (0.545-0.595)	<.001	0.706 (0.676-0.738)	<.001	0.532 (0.504-0.561)	<.001	0.656 (0.622-0.692)	<.001
Race												
White	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Other	0.903 (0.786-1.038)	.153	1.015 (0.883-1.167)	.836	0.871 (0.742-1.022)	.091	1.035 (0.881-1.215)	.674	1.794 (1.605-2.006)	<.001	1.125 (1.004-1.260)	.042
Insurance												
Private	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
None	2.419 (2.182-2.682)	<.001	1.793 (1.615-1.989)	<.001	2.490 (2.159-2.871)	<.001	2.228 (1.930-2.572)	<.001	2.478 (2.097-2.927)	<.001	1.792 (1.515-2.119)	<.001
Medicaid	3.129 (2.823-3.469)	<.001	2.397 (2.160-2.661)	<.001	2.929 (2.534-3.387)	<.001	2.382 (2.060-2.756)	<.001	3.663 (3.190-4.207)	<.001	2.319 (2.016-2.667)	<.001
Medicare	3.305 (3.177-3.439)	<.001	1.270 (1.206-1.339)	<.001	3.994 (3.805-4.193)	<.001	1.217 (1.145-1.293)	<.001	4.460 (4.210-4.725)	<.001	1.213 (1.124-1.310)	<.001
Other government insurance	1.497 (1.209-1.854)	<0.001	1.094 (0.883-1.355)	.412	2.039 (1.627-2.556)	<.001	1.410 (1.124-1.767)	.003	2.247 (1.701-2.968)	<.001	1.589 (1.202-2.100)	.001
Surgery type												
MMS	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
WLE	1.326 (1.148-1.532)	<.001	1.097 (0.950-1.267)	.208	1.249 (1.077-1.450)	.003	1.013 (0.872-1.176)	.868	1.190 (0.981-1.444)	.077	0.934 (0.770-1.134)	.492
Margins												
Negative	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Positive	2.436 (2.205-2.692)	<.001	1.706 (1.543-1.886)	<.001	2.053 (1.838-2.292)	<.001	1.520 (1.361-1.699)	<.001	3.140 (2.808-3.511)	<.001	1.565 (1.398-1.752)	<.001
Ulceration												
No	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Yes	4.551 (4.384-4.725)	<.001	2.378 (2.276-2.484)	<.001	3.638 (3.485-3.797)	<.001	1.855 (1.767-1.947)	<.001	5.273 (5.002-5.557)	<.001	2.310 (2.174-2.454)	<.001
Charlson-Deyo score												
0	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
1	1.950 (1.853-2.052)	<.001	1.304 (1.239-1.373)	<.001	1.935 (1.830-2.046)	<.001	1.340 (1.267-1.418)	<.001	2.346 (2.185-2.519)	<.001	1.412 (1.314-1.517)	<.001
≥2	3.575 (3.277-3.900)	<.001	1.991 (1.823-2.173)	<.001	3.757 (3.441-4.101)	<.001	2.114 (1.935-2.309)	<.001	4.558 (4.053-5.126)	<.001	2.061 (1.830-2.320)	<.001
Tumor type												
Nodular	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Other	0.354 (0.338-0.371)	<.001	0.809 (0.769-0.852)	<.001	0.422 (0.400-0.445)	<.001	0.809 (0.765-0.856)	<.001	0.411 (0.385-0.440)	<.001	0.838 (0.780-0.900)	<.001
LM/LMM	0.353 (0.310-0.401)	<.001	0.729 (0.639-0.833)	<.001	0.419 (0.376-0.466)	<.001	0.736 (0.657-0.824)	<.001	0.362 (0.285-0.459)	<.001	0.731 (0.574-0.931)	.011
Superficial spreading	0.256 (0.243-0.270)	<.001	0.755 (0.712-0.801)	<.001	0.292 (0.275-0.311)	<.001	0.738 (0.689-0.790)	<.001	0.217 (0.199-0.235)	<.001	0.677 (0.619-0.741)	<.001
Breslow depth, per 0.1 mm	1.003 (1.003-1.003)	<.001	1.002 (1.002-1.002)	<.001	1.003 (1.003-1.003)	<.001	1.002 (1.001-1.002)	<.001	1.003 (1.003-1.003)	<.001	1.002 (1.002-1.002)	<.001

Abbreviations: HR, hazard ratio; LM, lentigo maligna; LMM, lentigo maligna melanoma; MMS, Mohs micrographic surgery; WLE, wide local excision.

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Acquisition, analysis, or interpretation of data: Demer, Hanson, Liszewski.
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