Improved overall survival of melanoma of the head and neck treated with Mohs micrographic surgery versus wide local excision

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Background: Optimal surgical management for melanoma of the head and neck remains controversial.

Objective: Assess outcomes for melanomas of the head and neck treated with Mohs micrographic surgery (MMS) versus wide local excision (WLE) from the National Cancer Database.

Methods: Head and neck melanoma data from the National Cancer Database from years 2004-2015 were analyzed.

Results: In total, 50,397 cases of head and neck melanoma were reviewed; 3510 (7%) were treated with MMS and 46,887 (93%) with WLE. After controlling for potential confounding variables, patients treated with MMS were more likely than patients treated with WLE to survive after 5 years (hazard ratio [HR] 1.181, 95% confidence interval [CI] 1.083-1.288; $P < .001$). Factors associated with a statistically significant survival disadvantage included male sex (HR 1.287, 95% CI 1.242-1.357; $P = 0$), tumor ulceration (HR 1.687, 95% CI 1.616-1.760; $P = 0$), and positive surgical margins (HR 1.395, 95% CI 1.306-1.490; $P = 0$). Patient survival was inversely proportional to tumor Breslow depth.

Limitations: Database study, limited number of MMS treated melanomas.

Conclusion: MMS is a valid treatment option for melanoma of the head and neck; National Cancer Database data suggests that MMS might confer a survival benefit over WLE. (J Am Acad Dermatol 2020;82:149-55.)

Key words: melanoma; Mohs micrographic surgery; NCDB.

The optimal surgical management for melanoma of the head and neck remains controversial.[1] The National Comprehensive Cancer Network currently recommends wide local excision (WLE) universally for all cutaneous melanomas and recommends that more exhaustive histologic margin assessment be considered for larger lesions of melanoma in situ or those of the lentigo maligna subtype.[2] Both the National Comprehensive Cancer Network and American Academy of Dermatology currently recommend that the surgical margins for melanoma in situ be 0.5-1 cm.[2,3] These wider margins replace the previous recommendation of 0.5-cm margins for melanoma in situ, likely because of historically high rates of recurrence, particularly for melanomas in the head and neck region.[4-8]

Melanoma of the head and neck has a higher propensity for amelanotic spread, consequently determination of clinically clear margins can be particularly challenging.[4] In addition, these areas have increased cosmetic and functional importance

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and reduced tissue reservoirs relative to trunk and extremity sites, often leading surgeons to take narrower-than-recommended margins in an effort to preserve cosmetic and functional outcomes.[9,10] These unique challenges have led some clinicians to favor Mohs micrographic surgery (MMS), a technique that enables for both a tissue-sparing approach and examination of 100% of the surgical margins to confirm tumor clearance. However, while multiple groups have published positive retrospective experience with margin-controlled surgeries, including MMS, for melanoma of the head and neck, these techniques have been de-emphasized in recent guidelines.[1,3,11,12]

Currently, there are no prospective clinical studies comparing MMS and WLE for treatment of melanoma.[13] However, multiple database and population-based studies have consistently demonstrated that there is no survival disadvantage for patients with melanoma treated with MMS relative to WLE.[14-16] In this study, we sought to examine data from the National Cancer Database (NCDB) to determine if there are differences in outcomes in patients with melanoma of the head and neck treated with WLE compared with MMS.

CAPSULE SUMMARY

- Treatment of melanoma of the head and neck remains controversial.
- Examination of the National Cancer Database 2004-2015 data set demonstrates improved survival for patients undergoing Mohs micrographic surgery versus those undergoing wide local excision, even when correcting for a variety of tumor-specific factors.

METHODS

Data from the 2004-2015 NCDB data set were analyzed in SPSS (IBM, Armonk, NY) and SAS (Cary, NC). The NCDB is a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. It is the largest clinical registry worldwide, with >1500 participating hospitals, it is estimated that ~70% of all new cancer diagnoses in the United States are captured by the database each year.[17] The Commission on Cancer NCDB and the hospitals participating in the database 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.

Covariates were selected on the basis of similar epidemiologic models.[15,18,19] The analysis was limited to melanomas of the head and neck in individuals >18 years of age at the time of diagnosis. There was a total of 104,016 cases. Individuals with missing data for ≥1 covariate were excluded from the analysis (n = 53,619), leaving a final sample size of 50,397. Where appropriate, covariates were condensed into combined categories. Breslow depth was treated as a continuous variable in regression models. The NCDB only provides disease-specific mortality for individuals in the initial 90 days after their cancer diagnosis; however, it provides ongoing all-cause mortality for all individuals. Thus, when evaluating 5-year mortality, only all-cause mortality data was able to be assessed. To control for medical comorbidities, the Charlson/Deyo score was used; an increasing Charlson/Deyo score represents more comorbidities. Mohs surgery was defined by the NCDB coding system, which was determined by the participating Commission on Cancer hospitals, as 1 of 3 variables: Mohs surgery not otherwise specified, Mohs with ≤1-cm margins, or Mohs with >1-cm margin. These were condensed into 1 combined Mohs category for simplicity.

Differences in descriptive baseline characteristics were assessed by the χ^2 or t test. The level of significance was set at $P = .05$.

To assess for differences between tumors treated with Mohs versus non-Mohs surgery, a Cox proportional hazard model was fit to assess 5-year all-cause mortality. As a quality-control measure, each covariate was plotted to ensure the proportional hazard assumption was not violated. To further investigate the factors associated with differences in all-cause mortality between Mohs and non-Mohs cases, the covariates in the initial Cox model were kept, and the model was rerun by Breslow depth and separately by tumor histologic subtype.

RESULTS

In total, 104,016 cases of head and neck melanomas were identified from the NCDB 2004-2015 data set. Of these, 50,397 met inclusion criteria and were included in the final analysis. Demographic data for treatment groups is outlined in Table I. Overall, 7% (3510/50,397) of melanomas were treated with MMS, and 93% (46,887/50,397) were treated with WLE. Most of the study population were white (98.2%) men (74.10%) with a Charlson/Deyo comorbidity score of 0 (84.6%). The mean age of the study population was 68.7 years. These characteristics did not vary significantly between treatment groups. Although more patients

Abbreviations used:

CI: confidence interval
HR: hazard ratio
MMS: Mohs micrographic surgery
NCDB: National Cancer Database
WLE: wide local excision

(50.98%) were treated at an academic facility, a much higher percentage of patients in the MMS group (73.79%) than the WLE group (49.27%) were treated at academic institutions. Overall, the most common tumor type was designated as other (51.18%); however, patients treated with MMS did have a higher percentage of lentigo maligna and lentigo maligna melanoma subtypes than patients treated with WLE (36.38% MMS vs 16.19% WLE). The vast majority of patients from both treatment groups did not exhibit tumors with ulceration (92.68% MMS and 81.18% WLE) or have positive surgical margins (95.36% MMS and 94.93% WLE). However, the mean Breslow depth of MMS-treated tumors (0.8 mm) was thinner than that of WLE-treated tumors (1.7 mm).

With regard to the primary outcome, on both univariate and multivariate analysis, patients with melanomas of the head and neck treated with MMS had a significantly ($P < .001$) higher overall survival 5 years after melanoma diagnosis than those treated with WLE as depicted in the Kaplan-Meier survival curve in Fig 1 (hazard ratio [HR] 1.181, 95% confidence interval [CI] 1.083-1.288). Factors that were associated with a statistically significant survival disadvantage ($P < .05$) on both univariate and multivariate analysis included older age, male sex, nonprivate insurance, tumor

Table I. Characteristics of the study population by surgery type

Characteristic	Mohs micrographic surgery, n (%)	Wide local excision, n (%)	Overall, n (%)
Age, y, mean	68.7	69.8	68.7
Sex			
Male	2484 (70.77)	34,862 (74.35)	37,346 (74.10)
Female	1026 (29.23)	12,025 (26.65)	13,051 (25.90)
Race			
White	3437 (97.92)	46,054 (98.22)	49,491 (98.20)
Nonwhite	73 (2.08)	833 (1.78)	906 (1.80)
Facility type			
Academic	2590 (73.79)	23,100 (49.27)	25,690 (50.98)
Comprehensive community cancer program	682 (19.43)	16,747 (35.72)	17,429 (34.58)
Community cancer program	70 (1.99)	2462 (5.25)	2532 (5.02)
Integrated network	168 (4.79)	4578 (9.76)	4746 (9.42)
Charlson/Deyo comorbidity status			
0	3134 (89.29)	39,504 (84.25)	42,638 (84.60)
1	304 (8.66)	6030 (13.51)	6334 (12.57)
≥2	72 (2.05)	1353 (2.89)	1425 (2.83)
Tumor type			
Nodular	115 (3.28)	5003 (10.67)	5118 (10.16)
Other	1647 (46.92)	24,145 (51.50)	25,792 (51.58)
LM or LMM	1277 (36.38)	7591 (16.19)	8868 (17.60)
Superficial spreading	471 (13.42)	10,148 (21.64)	10,619 (21.07)
Mean Breslow depth, mm	0.8	1.7	1.62
Ulceration			
No	3253 (92.68)	38,062 (81.18)	41,315 (81.98)
Yes	257 (7.32)	8825 (18.82)	9082 (18.02)
Surgical margins			
Negative	3347 (95.36)	44,508 (94.93)	47,855 (94.96)
Positive	163 (4.64)	2379 (5.07)	2542 (5.04)
Insurance status			
Private insurance	1280 (36.47)	18,475 (39.40)	19,755 (39.20)
Not insured	46 (1.31)	699 (1.49)	745 (1.48)
Medicaid	32 (0.91)	622 (1.33)	654 (1.30)
Medicare	2082 (59.32)	26,631 (56.80)	28,713 (56.97)
Other government	70 (1.99)	460 (0.98)	530 (1.05)

LM, Lentigo maligna; *LMM*, lentigo maligna melanoma.

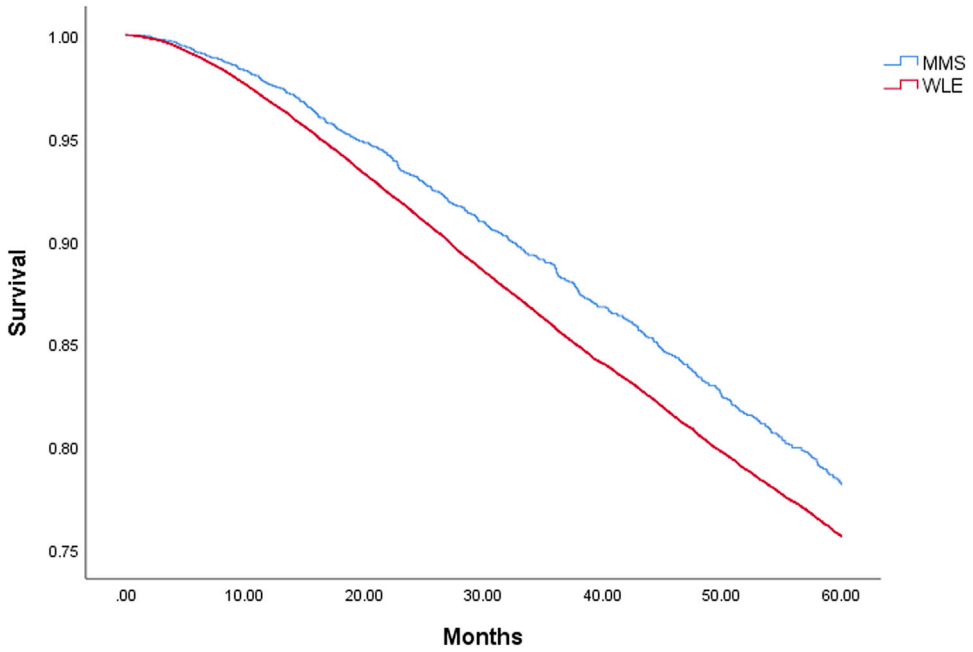

Fig 1. Kaplan-Meier survival curve for patient overall survival. *MMS*, Mohs micrographic surgery; *WLE*, wide local excision.

ulceration, positive surgical margins, a higher Charlson/Deyo comorbidity score and nodular histologic subtype (Table II). Treatment at an academic facility was associated with worse outcomes on univariate analysis but, after correcting for confounding variables, was actually found to have better outcomes than any other facility type on multivariate analysis. Similarly, white race was found to be associated with worse outcomes on univariate analysis (HR 0.816, 95% CI 0.705-0.946), and although this trend persisted on multivariate analysis, the result was no longer significant (HR 0.936, 95% CI 0.808-1.085).

When evaluating by tumor Breslow depth on both univariate and multivariate analyses, patients with melanomas of the head and neck treated with MMS had no significant survival disadvantage at any given T score compared with those treated with WLE (Table III). Patients with invasive melanomas of a Breslow depth of 0.01-0.74 were found to have a statistically significant ($P < .05$) survival advantage when treated with MMS over WLE; this finding was true on both univariate (HR 1.29, 95% CI 1.14-1.47) and multivariate (HR 1.164, 95% CI 1.03-1.32) analyses.

With regard to tumor histologic subtype (Table IV), on univariate analysis, treatment of superficial spreading melanoma (HR 1.37, 95% CI 1.17-1.62) and lentigo maligna or lentigo maligna melanoma (HR 1.44, 95% CI 1.13-1.84) with MMS was associated with a statistically significant survival benefit compared with WLE. There was no significant difference between treatment types for nodular melanoma. Although these trends remained on multivariate analysis, the results were not significant.

DISCUSSION

Our analysis of head and neck melanomas from the NCDB demonstrated an overall 5-year survival advantage at all time points for patients with tumors treated with MMS over WLE. Furthermore, this survival benefit was maintained even after correcting for a wide variety of tumor-specific factors. The covariates in our study that were independently associated with increased risk are concordant with previous studies, lending support for the validity of our model.[15,18]

On multivariate analysis, the survival benefit only remained significant for patients with melanomas <0.74 mm. However, there was a trend toward improved survival for T1b-T3 tumors. We hypothesize this finding might have been the result of having a low overall number of deeper, higher-risk tumors treated with MMS, making it difficult to obtain a statistically significant result, especially given the relatively poorer prognosis of deeper melanomas.

Of note, a higher percentage of melanomas at academic institutions were treated by MMS (73.79%) than WLE (49.27%), and on multivariate analysis, treatment at an academic institution over any other

Table II. Univariate and multivariate regression analysis showing 5-year post melanoma diagnosis mortality risk factors for the overall study population

Characteristic	Univariate, HR (95% CI)	*P* Value	Multivariate, HR (95% CI)	*P* value
Age	1.060 (1.059-1.062)	0	1.055 (1.053-1.057)	0
Sex				
Male	1 (Reference)		1 (Reference)	
Female	0.719 (0.688-0.751)	0	0.779 (0.737-0.805)	0
Race				
White	1 (Reference)		1 (Reference)	
Nonwhite	0.816 (0.705-0.946)	.007	0.936 (0.808-1.085)	.379
Facility type				
Academic	1 (Reference)		1 (Reference)	
Comprehensive community cancer program	0.902 (0.833-0.976)	.011	1.087 (1.044-1.131)	0
Community cancer program	0.752 (0.696-0.814)	0	1.288 (1.190-1.393)	0
Integrated network	0.833 (0.804-0.969)	.009	1.072 (1.006-1.141)	.032
Charlson/Deyo comorbidity status				
0	1 (Reference)		1 (Reference)	
1	1.678 (1.599-1.761)	0	1.312 (1.250-1.377)	0
≥2	2.827 (2.612-3.059)	0	1.981 (1.830-2.145)	0
Tumor type				
Nodular	1 (Reference)		1 (Reference)	
Other	0.530 (0.504-0.558)	0	0.831 (0.788-0.876)	0
LM or LMM	0.375 (0.351-0.401)	0	0.701 (0.652-0.754)	0
Superficial spreading	0.468 (0.441-0.497)	0	0.905 (0.849-0.965)	.002
Breslow depth	1.002 (1.002-1.002)	0	1.001 (1.001-1.001)	0
Ulceration				
No	1 (Reference)		1 (Reference)	
Yes	2.747 (2.644-2.854)	0	1.687 (1.616-1.760)	0
Surgical margins				
Negative	1 (Reference)		1 (Reference)	
Positive	1.900 (1.779-2.028)	0	1.395 (1.306-1.490)	0
Surgery type				
Mohs micrographic surgery	1 (Reference)		1 (Reference)	
Wide local excision	1.529 (1.405-1.665)	0	1.181 (1.083-1.288)	0
Insurance status				
Private insurance	1 (Reference)		1 (Reference)	
Not insured	1.779 (1.517-2.087)	0	1.604 (1.367-1.882)	0
Medicaid	2.679 (2.304-3.114)	0	2.001 (1.720-2.328)	0
Medicare	2.661 (2.547-2.780)	0	1.062 (1.008-1.118)	.230
Other government	1.570 (1.278-1.928)	0	1.077 (0.876-1.324)	.483

CI, Confidence interval; *HR*, hazard ratio; *LM*, lentigo maligna; *LMM*, lentigo maligna melanoma.

Table III. Univariate and multivariate regression analysis showing 5-year post melanoma diagnosis mortality risk by Breslow depth for tumors treated by wide local excision versus Mohs micrographic surgery

Breslow depth, mm	Univariate, HR (95% CI)	*P* Value	Multivariate, HR (95% CI)	*P* Value
0	1.19 (0.81-1.73)	.376	0.985 (0.65-1.50)	.944
0.01-0.74	1.29 (1.14-1.47)	<.001	1.164 (1.03-1.32)	.019
0.75-1.00	1.06 (0.78-1.44)	.708	1.05 (0.77-1.44)	.756
1.01-2.00	1.03 (0.82-1.29)	.822	1.13 (0.90-1.41)	.314
2.01-4.00	0.98 (0.77-1.26)	.880	1.09 (0.85-1.40)	.490
≥4.01	1.01 (0.80-1.29)	.910	1.00 (0.79-1.28)	.972

CI, Confidence interval; *HR*, hazard ratio.

Table IV. Univariate and multivariate regression analysis showing 5-year post melanoma diagnosis mortality risk by tumor histologic subtype for tumors treated by wide local excision versus Mohs micrographic surgery

Subtype	Univariate, HR (95% CI)	*P* Value	Multivariate, HR (95% CI)	*P* Value
Nodular	0.87 (0.65-1.15)	.318	0.89 (0.67-1.18)	.414
Superficial spreading	1.37 (1.17-1.62)	<.001	1.10 (0.93-1.30)	.253
LM or LMM	1.44 (1.13-1.84)	.003	1.28 (1.004-1.63)	.046

CI, Confidence interval; *HR*, hazard ratio; *LM*, lentigo maligna; *LMM*, lentigo maligna melanoma.

facility type was associated with improved survival. A similar finding was recently published by Cheraghlou et al in an evaluation of all melanomas from the NCDB; this group found that facility case volume was significantly associated with improved patient survival and within high-volume facilities, academic affiliation was further associated with better outcomes.[20] Although there are likely a number of contributing factors responsible for this finding, it is possible that higher utilization of MMS at academic institutions might be 1 of these factors.

Several previous reports have shown reduced rates of melanoma recurrence and equivalent survival outcomes for tumors treated with MMS over WLE; however, many of these investigations were small, single-center retrospective studies.[4,21,22] A more recent analysis of the Survival, Epidemiology, and End Results database demonstrated no difference in long-term survival for patients with melanomas treated with MMS versus WLE.[15,23] Likewise, a population-based study from Canada demonstrated no survival disadvantage for Mohs when compared with WLE for melanoma of the head and neck.[14] Despite this existing data demonstrating equivalent or improved outcomes for patients with melanomas treated with MMS, our analysis revealed that MMS was only utilized for 7% of all head and neck melanomas from the NCDB. This percentage is similar to previously reported MMS utilization values.[15,19]

Although recent guidelines have de-emphasized MMS and margin-controlled surgeries as a treatment modality for head and neck melanoma, the weight of retrospective evidence suggesting a significant benefit with regard to minimizing local recurrence, preserving vital anatomic structures, and the findings from multiple database and population-based studies demonstrating no survival disadvantage all support the notion that MMS and complete-margin examination surgeries should be considered for the treatment of melanomas of the head and neck.

There are inherent limitations to this database study; specifically, there are patient-specific factors not captured by the database that could potentially influence outcomes. Also, technique-specific data that could provide a more thorough comparison between MMS and WLE (ie, the use of immunohistochemistry for MMS, inclusion of modified Mohs or slow Mohs techniques) are not provided in the database. In addition, there were a significant proportion of patients lost to follow-up or missing data; it is possible that inclusion of these patients might have affected study outcomes. Last, the number of melanomas treated with MMS compared with WLE was limited.

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