Mohs micrographic surgery reduces the need for a repeat surgery for primary Merkel cell carcinoma when compared to wide local excision: A retrospective cohort study of a commercial insurance claims database

To the Editor: Merkel cell carcinoma (MCC) is an aggressive cutaneous neuroendocrine tumor with high rates of local recurrence and distant metastasis. Although wide local excision (WLE) is the standard of care for primary MCC, Mohs micrographic surgery (MMS) is often used for cases requiring tissue preservation, with multiple retrospective studies demonstrating comparable outcomes with respect to margin status, overall survival, and MCC-specific death.[1] Here, we aimed to examine whether surgical modality for primary early-stage MCC correlates with the utilization pattern of subsequent interventions, such as sentinel lymph node biopsy (SLNB), adjuvant therapies, and additional surgeries.

We conducted a retrospective cohort study utilizing the MarketScan Commercial Database (IBM) for insured US adults (2011-2017) to compare the use of SLNB, radiation, chemotherapy, and re-excisions following WLE or MMS. Index cases in patients aged ≥18 years were identified with a previously validated algorithm[2] pairing a Current Procedure Terminology (CPT) code for WLE or MMS with an International Classification of Diseases (ICD) code for MCC (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/znpn529ysp/1). Collected data included demographics, tumor characteristics, comorbidities, and treatment modalities. Statistical analyses to calculate odds ratios (ORs) and 95% CIs were performed using GraphPad Prism v9.1.1.

Seven hundred fifty-five patients with MCC were identified during the study period. Forty-four patients with nodal and/or distant metastatic disease were excluded from the analysis.

Among the 711 patients with early-stage MCC, 60 (8.4%) underwent MMS and 695 (91.6%) underwent WLE. Statistically significant factors associated with MMS as the initial surgical procedure included older age ($P = .0017$), history of immunosuppression ($P = .0008$, OR = 2.46, 95% CI: 1.43-4.15), and tumors located on the face ($P < .0001$, OR = 10.05, 95% CI: 4.57-23.7), scalp and neck ($P = .0003$, OR = 5.95, 95% CI: 2.19-15.9), or genital area ($P = .013$, OR = 5.08, 95% CI: 1.75-15.3) (Table I).

With respect to subsequent procedures, MMS-treated patients were less likely to undergo SLNB (OR = 0.18, 95% CI: 0.09-0.34) or repeat surgery ($P = .0119$, OR = 0.32, 95% CI: 0.14-0.79) than those who received WLE. There were no differences in the utilization of adjuvant radiation, chemotherapy/immunotherapy, and the average number of chemotherapeutic agents (Table II).

Our findings suggest that MMS as an initial surgical treatment may be associated with fewer subsequent procedures, such as re-excision or SLNB. Although our study lacks stage-specific data, the majority of early-stage MCC has previously been reported to be stage I disease with comparable outcomes by the 2 surgical approaches in these patients.[1,3] Potential explanations for fewer SLNBs following MMS include the greater use of MMS for head and neck tumors and the impracticality of performing SLNB during the same MMS procedure visit.[4] We also show no differences in radiation utilization based on the type of procedure, a contrasting finding to prior reports of adjuvant radiation more likely after MMS.[5] These discordant findings may be due to radiation being reserved for advanced/metastatic disease and/or because of narrower surgical margins in MMS. Lastly, our study cohort does not capture uninsured or publicly insured patients. Nevertheless, our study describes real-world patterns of health care utilization following the surgical treatment of early-stage MCC.

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Table I. Patient demographics and tumor characteristics that would predict the surgical choice for primary Merkel cell carcinoma, IBM MarketScan Commercial Database, 2011-2017

	Total	MMS	WLE	*P* value*	Odds ratio (95% CI)
n (%)	711 (100)	60 (8.4)	651 (91.6)		
Mean age at diagnosis (range, SD)	72.8 (20-99, 12.6)	77.7 (57-99, 11.1)	72.4 (20-98, 12.7)	.0017	
Age group, *n* (%)					
18-34	3 (0.4)	0	3 (0.5)	.0118†	
35-44	6 (0.8)	0	6 (0.9)		
45-54	43 (6.0)	0	43 (6.6)		
55-64	152 (21.4)	10 (16.7)	142 (21.8)		
65 and older	507 (71.3)	50 (83.3)	457 (70.2)		
Sex, *n* (%)					
Male	440 (61.9)	41 (68.3)	399 (61.3)	.2824	
Female	271 (38.1)	19 (31.7)	252 (38.7)		
Region, *n* (%)					
Northeast	139 (19.5)	14 (23.3)	125 (19.2)	.7026	
North Central	197 (27.7)	14 (23.3)	183 (28.1)		
South	237 (33.3)	18 (30.0)	219 (33.6)		
West	125 (17.6)	12 (20.0)	113 (17.4)		
Unknown	13 (1.8)	2 (3.3)	11 (1.7)		
Urban, *n* (%)					
Yes	587 (82.6)	50 (83.3)	537 (82.5)	.8689	
No or unknown	124 (17.4)	10 (16.7)	114 (17.5)		
Tumor location, *n* (%)					
Face	209 (29.4)	37 (61.7)	172 (26.4)	<.0001	10.05 (4.57-23.7)
Scalp and neck	62 (8.7)	7 (11.7)	55 (8.4)	.0003	5.95 (2.19-15.9)
Genital	51 (7.2)	5 (8.3)	46 (7.1)	.0129	5.08 (1.75-15.3)
Trunk and extremity	334 (47.0)	7 (11.7)	327 (50.2)		1
Two sites	27 (3.8)	0	27 (4.1)		
Unspecified	28 (3.9)	4 (6.7)	24 (3.7)		
History of immunosuppression, *n* (%)‡					
Yes	199 (28.0)	28 (46.7)	171 (26.3)	.0008	2.46 (1.43-4.15)
No	512 (72.0)	32 (53.3)	480 (73.7)		

MMS, Mohs micrographic surgery; *WLE*, wide local excision.
*Fisher's exact test was used to detect differences in groups with $n \leq 5$.
†The χ^2 test for trend was performed.
‡Immunosuppression includes HIV, solid organ transplantation, and hematologic malignancies (plasma cell disorders, leukemia, lymphoma, and Hodgkin's disease).

Table II. Utilization pattern of other diagnostic and therapeutic procedures in MCC patients treated with MMS or WLE

	Total (*n* = 711)	MMS (*n* = 60)	WLE (*n* = 651)	*P* value*	Odds ratio (95% CI)
Sentinel lymph node biopsy, *n* (%)					
No	338 (47.5)	49 (81.7)	289 (44.4)	<.0001	0.18 (0.09-0.34)
Yes	373 (52.5)	11 (18.3)	362 (55.6)		
Repeat surgery, *n* (%)					
No	563 (79.2)	55 (91.7)	508 (78.0)	.0119	0.32 (0.14-0.79)
Yes	148 (20.8)	5 (8.3)	143 (22.0)		
Type of repeat procedure, *n* (%)					
WLE	141 (95.3)	1 (20)	140 (97.9)		
MMS	7 (4.7)	4 (80)	3 (2.1)		
Radiation, *n* (%)					
No	396 (55.7)	38 (63.3)	358 (55.0)	.21	
Yes	315 (44.3)	22 (36.7)	293 (45.0)		

Continued

Table II. Cont'd

	Total ($n = 711$)	MMS ($n = 60$)	WLE ($n = 651$)	*P* value*	Odds ratio (95% CI)
Chemotherapy, *n* (%)					
No	632 (88.9)	57 (95.0)	575 (88.3)	.13	
Yes	79 (11.1)	3 (5.0)	76 (11.7)		
No. of chemotherapies and immunotherapies received†					
1	9	1	8		
2	46	2	44		
3	9	0	9		
4	2	0	2		
5	3	0	3		
6	1	0	1		
Average no. of chemotherapies and immunotherapies received†	2.24	1.67	2.27	.29	

MCC, Merkel cell carcinoma; *MMS*, Mohs micrographic surgery; *WLE*, wide local excision.
*Fisher's exact test was used to detect differences in groups with $n \leq 5$.
†Chemotherapy and immunotherapy agents were identified using the J codes and include cisplatin, carboplatin, etoposide, topotecan, cyclophosphamide, doxorubicin, vincristine, pembrolizumab, nivolumab, and avelumab (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/znpn529ysp/1).

Key words: chemotherapy; MarketScan database; Merkel cell carcinoma; Mohs micrographic surgery; radiation; sentinel lymph node biopsy; wide local excision.

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Conflict of interest

None disclosed.

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