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Factors associated with time to treatment for Merkel cell carcinoma



To the Editor: Merkel cell carcinoma (MCC) is a rare, aggressive skin cancer.¹ Although early treatment is critical for improving survival, little is known regarding factors associated with time from diagnosis to definitive surgical treatment (TTDS) for MCC.¹ Our

primary objective was to investigate factors associated with delays in treatment for patients with MCC.

In this retrospective review of the National Cancer Database from 2004 through 2015, patients with MCC were included, and patients with excisional biopsy as definitive treatment were excluded.² Univariate analyses compared sociodemographic characteristics, stage/grade at diagnosis, primary site, and time to treatment by race. Multivariable logistic regression evaluated TTDS differences by sociodemographic characteristics/primary site. Multivariable linear regression determined the unique contribution (in days) of each sociodemographic/disease characteristic to TTDS. Analyses were performed in SAS 9.4 (SAS Institute), and $P < .05$ was considered significant.

Of the 26,237 patients with MCC identified, 1766 (6.73%) were Black (Table I). More Black than non-Hispanic White (NHW) patients presented with later-stage, poorly differentiated/undifferentiated, anaplastic, and truncal MCC ($P < .001$). TTDS was greater for Black patients (58.9 days) than for NHW patients (46.3 days; $P < .05$). Time to radiation was 18.9 days longer for Black than NHW patients ($P < .001$), and time to chemotherapy did not differ by race ($P = .1453$). Black patients lived closer to the hospital (23.2 miles) than NHW patients (41.7 miles; $P < .05$). TTDS was longer for Black than NHW patients for stages I to III ($P < .05$), but not stage IV ($P = .1319$) MCC (Supplemental Table I; available via Mendeley at <https://doi.org/10.17632/pv6dp9kn3g.1>). Racial differences persisted for private insurance and Medicare ($P < .01$), but not for Medicaid ($P = .8986$) or uninsured patients ($P = .7510$).

After controlling for socioeconomic characteristics, stage, and primary site, Black race was

Table I. Sociodemographic characteristics of sample*

Characteristics	White	Black
Total number of patients	24,471	1766
Age, y, n (%)		
<30	649 (2.65)	181 (10.25)
30-39	1105 (4.52)	308 (17.44)
40-49	1763 (7.20)	356 (20.16)
50-59	3043 (12.44)	343 (19.42)
60-69	4811 (19.66)	278 (15.74)
70-79	6551 (26.77)	185 (10.48)
80+	6549 (26.76)	115 (6.51)
Sex, n (%)		
Male	14,718 (60.14)	817 (46.26)
Female	9753 (39.86)	949 (53.74)
Stage at diagnosis, n (%)		
0	213 (0.87)	7 (0.40)
I	6552 (26.77)	211 (11.95)
II	2512 (10.27)	139 (7.87)

Continued

Table I. Cont'd

Characteristics	White	Black
III	3606 (14.74)	79 (4.47)
IV	1015 (4.15)	57 (3.23)
Unknown/not applicable	10,573 (43.21)	1273 (72.08)
Grade at diagnosis, n (%)		
Well differentiated	984 (4.02)	135 (7.64)
Moderately differentiated	807 (3.30)	95 (5.38)
Poorly differentiated	2010 (8.21)	87 (4.93)
Undifferentiated/anaplastic	807 (3.30)	22 (1.25)
Unknown/not applicable	19,863 (81.17)	1427 (80.80)
Primary site, n (%)		
Lip	310 (1.27)	7 (0.40)
Eyelid	1047 (4.28)	59 (3.34)
External ear	835 (3.41)	35 (1.98)
Other parts of face	5029 (20.55)	143 (8.10)
Scalp and neck	3226 (13.18)	158 (8.95)
Trunk	4854 (19.84)	717 (40.60)
Upper limb and shoulder	4574 (18.69)	261 (14.78)
Lower limb and hip	3181 (13.00)	327 (18.52)
Overlapping lesion of skin	97 (0.40)	10 (0.57)
Other	1318 (5.39)	49 (2.77)
Time to treatment, d, mean (95% CI)		
Time to definitive surgery	46.26 (45.65-46.88)	58.86 (54.87-62.85)
Time to chemotherapy	72.15 (69.70-74.61)	63.60 (54.91-72.29)
Time to radiation	92.49 (91.27-93.72)	111.4 (102.3-120.5)
Time to definitive surgery, d, n (%)		
0-30	12,217 (49.92)	746 (42.24)
31-60	7905 (32.30)	507 (28.71)
61-90	2558 (10.45)	270 (15.29)
More than 90	1791 (7.32)	243 (13.76)
Insurance, n (%)		
Not insured	444 (1.81)	151 (8.55)
Private insurance	8582 (35.07)	846 (47.90)
Medicaid	620 (2.53)	238 (13.48)
Medicare	14,053 (57.43)	455 (25.76)
Other government	277 (1.13)	34 (1.93)
Unknown	495 (2.02)	42 (2.38)
Median household income, n (%)		
<\$38,000	1894 (8.02)	478 (28.10)
\$38,000-\$47,999	3715 (15.74)	301 (17.70)
\$48,000-\$62,999	6524 (27.64)	451 (26.51)
\$63,000+	11,470 (48.60)	471 (27.69)
Distance from hospital, miles		
Mean (95% CI)	41.71 (39.86-43.57)	23.17 (18.52-27.82)
<20, n (%)	15,811 (64.97)	1420 (80.73)
20-39, n (%)	3803 (15.63)	149 (8.47)
40-59, n (%)	1593 (6.55)	78 (4.43)
>60, n (%)	3129 (12.86)	112 (6.37)
Facility location		
New England	1531 (6.774)	42 (3.29)
Middle Atlantic	3911 (17.22)	240 (18.79)
South Atlantic	4657 (20.50)	402 (31.48)
East North Central	3968 (17.47)	249 (19.50)
East South Central	1239 (5.45)	93 (7.28)
West North Central	2026 (8.92)	49 (3.84)
West South Central	1268 (5.58)	113 (8.85)
Mountain	1231 (5.42)	14 (1.10)
Pacific	2886 (12.70)	75 (5.87)

CI, Confidence interval.

* $P < .001$ for all chi-square and t tests except for time to chemotherapy ($P = .1453$).

Table II. Multivariable logistic regression for time to definitive surgery*

Characteristics	Time to definitive surgical treatment, d					
	31-60		61-90		>90	
	aOR (95% CI)	P	aOR (95% CI)	P	aOR (95% CI)	P
Race						
White	Reference	—	Reference	—	Reference	—
Black	1.15 (0.91-1.45)	.245	1.97 (1.48-2.63)	<.0001	2.11 (1.52-2.93)	<.001
Sex						
Male	Reference	—	Reference	—	Reference	—
Female	0.97 (0.89-1.05)	.402	1.12 (0.99-1.26)	.076	0.96 (0.82-1.13)	.627
Age, y						
<30	Reference	—	Reference	—	Reference	—
30-39	0.82 (0.41-1.64)	.306	0.28 (0.12-0.65)	.091	0.56 (0.22-1.47)	.808
40-49	0.98 (0.52-1.85)	.864	0.44 (0.22-0.88)	.789	0.64 (0.27-1.53)	.217
50-59	1.01 (0.54-1.86)	.559	0.39 (0.20-0.76)	.441	0.56 (0.24-1.30)	.665
60-69	0.96 (0.52-1.78)	.992	0.38 (0.20-0.74)	.235	0.55 (0.19-1.02)	.074
70-79	1.03 (0.56-1.92)	.303	0.36 (0.18-0.70)	.087	0.41 (0.18-0.95)	.020
80+	0.95 (0.51-1.77)	.886	0.36 (0.19-0.71)	.099	0.33 (0.14-0.77)	<.0001
Median income						
<\$38,000	Reference	—	Reference	—	Reference	—
\$38,000-47,999	0.91 (0.78-1.07)	.009	1.28 (0.99-1.65)	.363	1.00 (0.74-1.37)	.856
\$48,000-62,999	1.09 (0.94-1.27)	.035	1.29 (1.02-1.65)	.195	1.02 (0.77-1.36)	.977
\$63,000+	1.07 (0.93-1.24)	.101	1.27 (1.01-1.61)	.263	1.05 (0.80-1.38)	.610
Insurance						
Not insured	Reference	—	Reference	—	Reference	—
Private	0.92 (0.64-1.32)	.206	0.73 (0.41-1.29)	.196	1.27 (0.73-2.21)	.879
Medicaid	1.43 (1.06-1.92)	.067	1.31 (0.85-2.02)	.187	2.00 (1.29-3.11)	.014
Medicare	0.97 (0.87-1.08)	.024	0.98 (0.83-1.17)	.773	1.02 (0.82-1.27)	.112
Other government	1.42 (0.98-2.06)	.136	1.05 (0.57-1.95)	.887	1.33 (0.66-2.67)	.784
Unknown	1.09 (0.82-1.46)	.847	1.08 (0.69-1.68)	.742	0.99 (0.56-1.74)	.375
Stage						
I	Reference	—	Reference	—	Reference	—
II	0.86 (0.77-0.95)	<.0001	1.04 (0.89-1.21)	.945	1.41 (1.16-1.70)	<.0001
III	0.89 (0.81-0.98)	<.0001	0.81 (0.69-0.94)	<.0001	1.04 (0.85-1.26)	.919
IV	0.35 (0.29-0.43)	<.0001	0.51 (0.39-0.68)	<.0001	0.81 (0.59-1.12)	.033
Primary site						
Lip	1.25 (0.93-1.68)	.059	0.78 (0.47-1.30)	.630	0.84 (0.46-1.53)	.720
Eyelid	1.39 (1.09-1.78)	.0001	2.12 (1.57-2.87)	<.0001	1.47 (0.99-2.19)	<.0001
External ear	1.40 (1.13-1.74)	<.0001	1.24 (0.90-1.71)	.014	0.81 (0.53-1.24)	.716
Other parts of face	1.28 (1.13-1.46)	<.0001	0.96 (0.79-1.16)	.263	0.83 (0.66-1.05)	.380
Scalp and neck	1.12 (0.96-1.31)	.037	1.19 (0.95-1.48)	.002	0.98 (0.75-1.28)	.028
Trunk	Reference	—	Reference	—	Reference	—
Upper limb/shoulder	1.18 (1.03-1.35)	.0001	0.77 (0.63-0.94)	.171	0.60 (0.47-0.7)	.031
Lower limb/hip	1.07 (0.93-1.24)	.113	0.82 (0.66-1.02)	.509	0.62 (0.47-0.81)	.089
Overlapping lesion	1.35 (0.69-2.66)	.275	1.44 (0.57-3.62)	.235	1.98 (0.78-5.05)	.024
Other	0.12 (0.09-0.17)	<.0001	0.12 (0.07-0.21)	<.0001	0.11 (0.06-0.20)	<.0001

aOR, Adjusted odds ratio.

*Reference time to definitive surgery: 0 to 30 days.

associated with roughly twice the odds of having a TTDS of 61 to 90 (adjusted odds ratio [aOR], 1.97) or longer than 90 days (aOR, 2.11; $P < .001$) (Table II). Eyelid tumors were associated with increased odds of TTDS of 31 to 60 (aOR, 1.39), 61 to 90 (aOR, 2.12), and longer than 90 days (aOR, 1.47; $P < .001$). External ear tumors were associated with increased

odds of TTDS of 31 to 60 (aOR, 1.40) and 61 to 90 days (aOR, 1.24), and primary site on other parts of the face (aOR, 1.28) and scalp/neck (aOR, 1.12) were associated with increased odds of TTDS of 31 to 60 days ($P < .05$). Black race, eyelid lesions, and Medicaid were uniquely associated with 11.1, 6.24, and 12.17 additional days from diagnosis to surgical

treatment, respectively ($P < .01$) (Supplemental Table II; available via Mendeley at <https://doi.org/10.17632/pv6dp9kn3g.1>).

Black patients experience delays in TTDS for MCC that persist for stages I to III MCC and for private insurance/Medicare, despite living closer to the hospital than NHW patients. Medicaid and primary facial MCC are also associated with substantial surgical delays. The 5-year survival of MCC is 64% for local disease, 39% for regional nodal disease, and 18% for metastatic disease.¹ Although we were unable to evaluate the association of TTDS with long-term survival, increased TTDS is associated with worse outcomes for melanoma, breast, and head/neck cancers.³ Increased TTDS in Black patients with MCC may affect racial disparities in MCC outcomes, although time to adjuvant radiation therapy does not affect MCC outcomes.^{4,5} Regardless of the association of treatment delays with survival, racial discrepancies in time to treatment may affect quality of life and comorbidity burden and reflect systemic disparities in health care delivery/quality of care that should be addressed by dermatologists. Variability in TTDS by insurance and primary site underscores the importance of improving access to timely treatment for MCC, which may involve coordination of multiple specialties. Ultimately, better understanding the components underlying disparities in treatment delays is integral to developing interventions to improve MCC outcomes.

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