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DATABASE ANALYSIS

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Clinical Features and Prognosis of Merkel Cell Carcinoma in Elderly Patients

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Background: Merkel cell carcinoma (MCC) occurs primarily among elderly patients over 70 years old, but the ability to predict the prognosis of these elderly patients is poor. This population-based study aimed to identify prognostic risk factors for elderly patients with MCC.

Material/Methods: The survival and disease information of MCC patients age 65 years or older was downloaded from the SEER database, and all data were split into 2 groups based on age 80 years, with overall survival and MCC-specific survival as the main outcome indicators.

Results: Application of the inclusion criteria yielded 1973 patients with MCC, of whom 55.6% were age 65–80 years. Among them, 1258 were males, accounting for 63.8%. In survival analysis, factors that were significantly correlated with overall survival and MCC-specific survival were N stage, M stage, liver metastasis, and lymph node surgery.

Conclusions: We provide epidemiological insights into Merkel cell carcinoma in elderly patients and confirmed that patients receiving lymph node surgery have better outcomes. To the best of our knowledge, this is the first study to show that the occurrence of liver metastasis is associated with poor prognosis. Our results will help strengthen monitoring of the liver condition of elderly patients and to perform necessary lymph node surgery within the patient's tolerance.

MeSH Keywords: Carcinoma, Merkel Cell • Prognosis • Survival Analysis

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Background

As a type of cutaneous tumor, Merkel cell carcinoma (MCC) generally occurs in areas with sun damage and is characterized by neuroendocrine tumors [1,2]. The typical manifestations are painless, rapidly growing skin nodules [3]. Pathologically, because the tumor cells are of the same size and immature, they can be misdiagnosed as "blastoma" type lymphoma, enamel melanoma, or metastatic cancer, especially oat cell carcinoma of the lung. The annual incidence rate is about 0.01/100 000, mostly in whites, and rarely in blacks [4,5]. The age at onset is widely distributed (7 to 104 years), mainly in the elderly, and less than 5% of patients are under 50 years old [6]. Studies have shown that the overall survival of MCC is negatively affected by older age, and age is an independent predictor of patient prognosis, with a gap between the outcomes of young and elderly patients [7]. Therefore, it is not accurate to infer the prognosis of elderly patients based on studies of patients of all ages, and research is needed to explore this in elderly patients.

MCC occurs mostly in the elderly population, but the prognostic significance of MCC in elderly patients has not been well evaluated. This study systematically summarized the information on MCC in the Surveillance, Epidemiological and End Results (SEER) database, calculated the survival rate and prognostic risk factors of elderly patients, and had assessed the implications for MCC treatment.

Material and Methods

In this study, patient clinicopathological and demographic data were obtained by installing SEER * stat software and following SEER guidelines. Due to the focus on elderly patients, the study population included only patients age 65 years or older, divided into a younger (65–80) group and an older (>80) group, with 80 years of age as the boundary. We obtained research data from the SEER database with reference number 16760-Nov2018 and agreed not to disclose any personal identity, screening for patients with clear survival information, histological type (ICD-0-3) for Merkel cell carcinoma (8247), and site recode for other non-epithelial skin disease.

The clinicopathological parameters included age, sex, marital status, race, tumor size, TNM staging, distant metastasis (bone, brain, liver, lung, lung), primary site, primary site surgery, regional nodes examined, regional nodes positive, radiation, chemotherapy, and lymph node surgery. The primary sites included face/head/neck, trunk, upper and lower extremities, and other areas. We examined records on regional lymph nodes that have been excised and subjected to pathological examination. "Regional nodes positive" means that the lymph nodes have been confirmed by pathology to contain metastasis.

The main variables were screened in the SEER database, all shown as categorical variables, and the comparison was performed using the Pearson chi-square test. MCC-specific survival (MSS) and overall survival (OS) were the main outcome indicators, and the difference was calculated by log-rank test and visualized through the Kaplan-Meier curve. Multivariate Cox proportional analysis was applied to calculate the independent risk factors for the prognosis of elderly MCC patients, expressed as a significant hazard ratio and a 95% confidence interval. All statistical analyses were considered to be statistically significant with a 2-sided $P < 0.05$ and were performed using Statistical Analysis System (SAS) software (Cary, NC), SPSS version 22.0 statistical package (IBM, NY), and GraphPad Prism 8 (San Diego, California).

Ethics approval

This article does not cover human participants and animal studies, and does not disclose any personal information, so formal consent was not required. Furthermore, the authors obtained permission to access data from the SEER database (Reference Number 16760-Nov2018).

Results

Clinical characteristics

Information on 9370 MCC patients was downloaded and screened from the SEER database, and 1973 patients were included according to the inclusion criteria, of which 1258 were males, accounting for 63.8%. The average age was 79.1 years; 55.6% of patients were 65–80 years old, and 44.4% were over 80 years of age. Table 1 summarizes the general characteristics distribution of elderly MCC patients. In patients aged 65–80, the primary tumors were mostly located in the upper extremities and lower extremities (47.6%). In patients over 80 years old, MCC occurred mostly in the face/head/neck (52.6%).

In terms of treatment measures, the ratios of patients undergoing primary site surgery were similar in both groups. However, more than half of the patients >80 years of age had no lymph node surgery (55.5%) and no regional nodes examined (57.4%), compared with 27.3% and 29.7%, respectively, of patients age 65–80. For distant metastasis, the risk of metastasis in the younger group was lower than in patients >80 years of age, and the rates of bone metastasis (1.5% *vs.* 1.1%), liver metastasis (1.7% *vs.* 1.6%), and lung metastasis (1.3% *vs.* 0.9%) were higher in patients over 80 years old.

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Table 1. General characteristics of elderly patients with Merkel cell carcinoma.

Variables	Age 65–80 years		Age >80 years		P value
Race					0.899
White	1056	(96.2%)	838	(95.8%)	
Black	14	(1.3%)	11	(1.3%)	
Other	25	(2.3%)	22	(2.5%)	
Unknown	3	(0.3%)	4	(0.5%)	
Sex					0.031
Male	723	(65.8%)	535	(61.1%)	
Female	375	(34.2%)	340	(38.9%)	
Marital status					<0.001
Single	314	(28.6%)	379	(43.3%)	
Married	721	(65.7%)	424	(48.5%)	
Unknown	63	(5.7%)	72	(8.2%)	
Primary site					<0.001
Face/head/neck	401	(36.5%)	460	(52.6%)	
Trunk	107	(9.7%)	87	(9.9%)	
Upper and lower extremities	523	(47.6%)	305	(34.9%)	
Other	67	(6.1%)	23	(2.6%)	
Tumor size					<0.001
No mass/tumor found	71	(6.5%)	19	(2.2%)	
1–10 mm	338	(30.8%)	247	(28.2%)	
11–20 mm	311	(28.3%)	279	(31.9%)	
21–30 mm	168	(15.3%)	148	(16.9%)	
31–40 mm	85	(7.7%)	66	(7.5%)	
41–50 mm	55	(5.0%)	44	(5.0%)	
>50 mm	64	(5.8%)	62	(7.1%)	
Unknown	6	(0.5%)	10	(1.1%)	
T stage					<0.001
T0	66	(6.0%)	17	(1.9%)	
T1	642	(58.5%)	513	(58.5%)	
T2	291	(26.5%)	240	(27.4%)	
T3	55	(5.0%)	50	(5.7%)	
T4	44	(4.0%)	55	(6.3%)	
N stage					0.005
N0	696	(63.4%)	610	(69.7%)	
N1	371	(33.8%)	236	(27.0%)	
N2	31	(2.8%)	29	(3.3%)	
M stage					0.101
M0	1043	(95.0%)	816	(93.3%)	
M1	55	(5.0%)	59	(6.7%)	
Primary site surgery					0.119
No	110	(10.0%)	111	(12.7%)	

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Table 1 continued. General characteristics of elderly patients with Merkel cell carcinoma.

Variables	Age				P value
	65–80 years		>80 years		
Yes	987	(89.9%)	764	(87.3%)	
Unknown	1	(0.1%)	0		
Scope regional lymph node surgery					<0.001
None	300	(27.3%)	486	(55.5%)	
Regional lymph nodes removed	305	(27.8%)	173	(19.8%)	
Sentinel lymph node biopsy	393	(35.8%)	163	(18.6%)	
Sentinel lymph node biopsy+regional lymph nodes removed	91	(8.3%)	43	(4.9%)	
Unknown	9	(0.8%)	10	(1.1%)	
Regional nodes examined					<0.001
No	326	(29.7%)	502	(57.4%)	
Yes	770	(70.1%)	372	(42.5%)	
Unknown	2	(0.2%)	1	(0.1%)	
Regional nodes positive					<0.001
No	422	(38.4%)	167	(19.1%)	
Yes	347	(31.6%)	205	(23.4%)	
No nodes examined	326	(29.7%)	502	(57.4%)	
Unknown	3	(0.3%)	1	(0.1%)	
Radiation					<0.001
No	481	(43.8%)	536	(61.3%)	
Yes	617	(56.2%)	339	(38.7%)	
Chemotherapy					<0.001
No/unknown	950	(86.5%)	831	(95.0%)	
Yes	148	(13.5%)	44	(5.0%)	
Bone metastasis					0.003
No	1085	(98.8%)	851	(97.3%)	
Yes	12	(1.1%)	13	(1.5%)	
Unknown	1	(0.1%)	11	(1.3%)	
Brain metastasis					0.013
No	1095	(99.7%)	863	(98.6%)	
Yes	1	(0.1%)	1	(0.1%)	
Unknown	2	(0.2%)	11	(1.3%)	
Liver metastasis					0.004
No	1079	(98.3%)	849	(97.0%)	
Yes	18	(1.6%)	15	(1.7%)	
Unknown	1	(0.1%)	11	(1.3%)	
Lung metastasis					0.002
No	1087	(99.0%)	852	(97.4%)	
Yes	10	(0.9%)	11	(1.3%)	
Unknown	1	(0.1%)	12	(1.4%)	

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Table 2. Survival rates of Merkel cell cancer patients stratified by age.

Variables	Age		P value
	65–80 years	>80 years	
Overall survival			<0.001
1-year OS (95% CI)	84.8% (82.6%–87.0%)	67.8% (64.7%–70.9%)	
3-year OS (95% CI)	63.0% (59.9%–66.1%)	39.2% (35.7%–42.7%)	
5-year OS (95% CI)	54.8% (51.1%–58.5%)	24.7% (20.6%–28.8%)	
Median OS (months)	66.0	25.0	
MCC-specific survival			0.087
1-year MSS (95% CI)	92.6% (91.0%–94.2%)	89.8% (87.6%–92.0%)	
3-year MSS (95% CI)	81.9% (79.2%–84.6%)	80.3% (77.0%–83.6%)	
5-year MSS (95% CI)	80.1% (77.2%–83.0%)	76.2% (71.3%–81.1%)	
Median MSS (months)	69.7	66.9	

OS – overall survival; MSS – MCC-specific survival.

Survival analysis

Of the 1973 patients, 969 (49.1%) died, of which 301 (15.3%) died from MCC. Of the 1098 patients age 65–80, 419 (38.2%) died, of which 168 (15.3%) died from MCC. Of the 875 patients over the age of 80, 550 (62.9%) died, of which 133 (15.2%) died from MCC.

Patients age 65–80 years and >80 years had a significant difference in overall survival, but no significant difference in MCC-specific survival. As shown in Table 2, the one-, three-, and five-year overall survival rates of patients 65–80 years were 84.8%, 63.0%, and 54.8%, and the 1-, 3-, and 5-year overall survival rates of patients >80 years were 67.8%, 39.2%, 24.7%, respectively. MCC-specific survival differed slightly by age. The 1-, 3-, and 5-year MCC-specific survival rates of patients 65–80 years were 92.6%, 81.9%, and 80.1%, and those of patients >80 years of age were 89.8%, 80.3%, and 76.2%, respectively.

Similar trends were observed to be stratified by primary site and age. Face/head/neck, trunk, and upper and lower extremities all showed that overall survival rates were higher in patients aged 65–80, and the difference in MCC-specific survival was not significant (Figure 1).

When the data were stratified by tumor size and age, the overall survival rate of patients aged 65–80 years was better in all groups except those with tumor size >50 mm. In addition to patients with tumor sizes of 40–50 mm and >50 mm, the differences in MCC-specific survival between the other groups were not significant (Figure 2).

In the multivariate analysis (Table 3), factors significantly related to overall survival included age, sex, primary site, scope of lymph node surgery, tumor size, N stage, M stage, liver metastasis, and radiation. Factors significantly connected with worse overall survival included age >80 years (HR=1.714), N1 staging (HR=2.178), N2 staging (HR=1.804), M1 staging (HR=1.967), and liver metastasis (HR=1.883). Female sex (HR=0.660), the primary site on the trunk (HR=0.847), radiation (HR=0.725), regional lymph nodes removed (HR=0.449), sentinel lymph node biopsy (HR=0.327), and sentinel lymph node biopsy (SLNB)+regional lymph nodes removed (HR=0.343) were associated with better overall survival of patients.

In contrast to overall survival, multivariate survival analysis showed that age had no significant association with MCC-specific survival (P=0.945). Similar to overall survival, the factors significantly related to MCC-specific survival included N1 staging (HR=4.335), N2 staging (HR=4.500), M1 staging (HR=2.951), liver metastasis (HR=2.790), regional lymph nodes removed (HR=0.138), sentinel lymph node biopsy (HR=0.089), and SLNB+regional lymph nodes removed (HR=0.090).

Discussion

In this study, we included 1973 elderly patients selected according to the inclusion criteria. A total of 1098 patients were aged 65–80, and 875 were over 80 years of age. Older patients in the 2 groups had a higher overall survival risk, but there was no significant reduction in MCC-specific survival. This may be due to the fact that aging leads to more natural deaths, so the overall survival of patients over 80 years old is worse, and there is no statistical gap in MCC-specific survival between the 2 groups. In addition to tumor staging, we screened for significant correlations with overall survival and MCC-specific survival, including liver metastasis, regional

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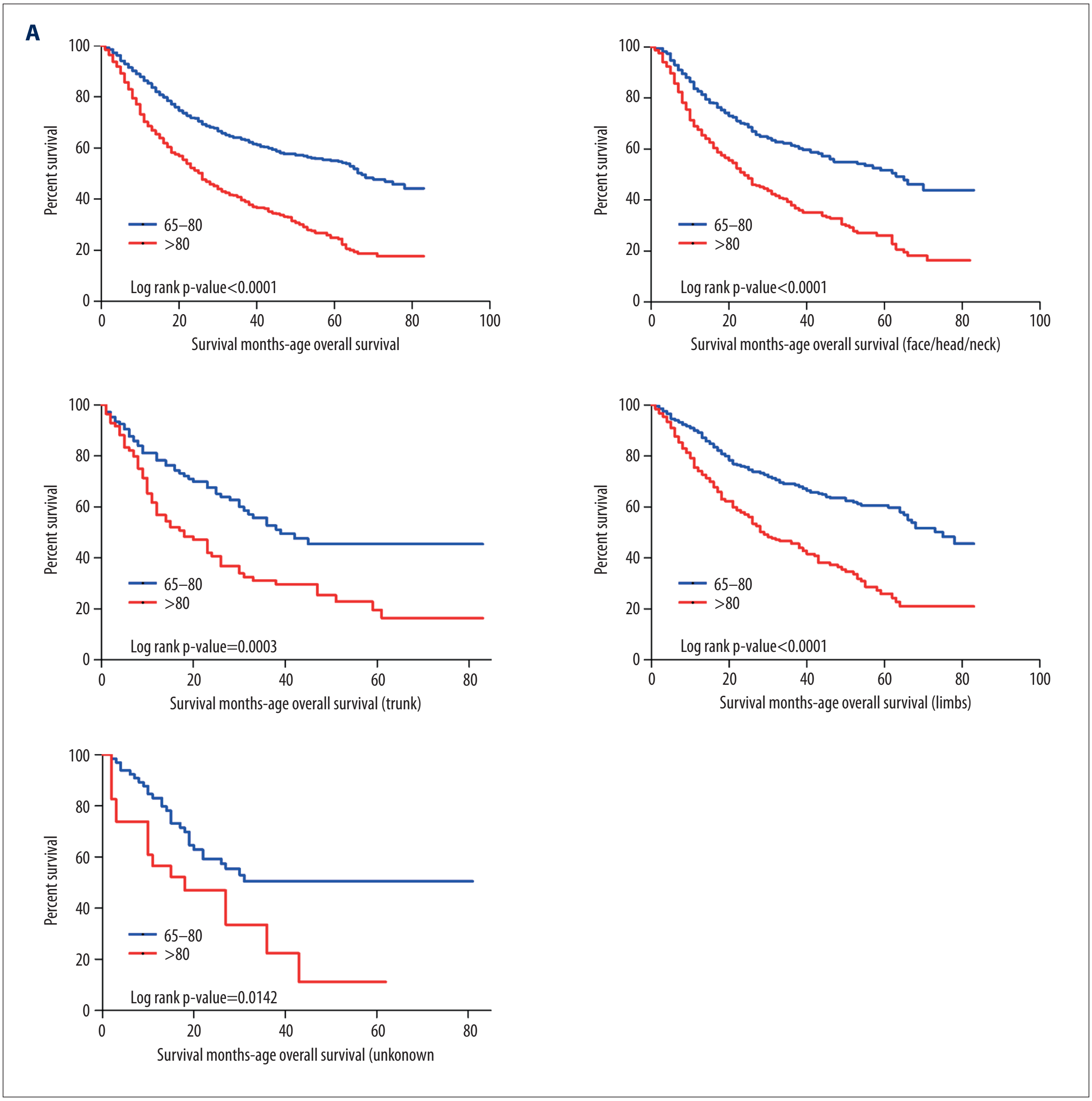
lymph nodes removed, and SLNB. To the best of our knowledge, this is the first population study to focus on factors associated with MCC prognosis in elderly patients, and previous studies did not suggest that the occurrence of liver metastasis was associated with poor prognosis.

As the second most common cause of skin tumor deaths, lymph node metastasis of MCC can occur in the early stages of the disease, with a high occult metastasis rate [8–10]. As the disease progresses and metastasizes to distant lymph nodes and organs, the disease is no longer localized and the patient's risk of death increases dramatically [11,12]. In our data, there were 33 patients with liver metastasis, of which 32 died. The 5-year OS was 76% for patients with localized lesions and pathology confirmed no lymph node metastasis, 39% in patients with regional lymph node metastasis, and only 18% in patients with distant metastasis [13]. The 5-year OS of localized MCC is 54–63.8%, and when infiltrated into deep skin structures such as fascia, muscle, cartilage, or bone, the 5-year survival rate decreased by 26% to 40.3% [14], which is consistent with our results.

There have been reports in the literature that the overall survival rate is associated with the pathological results of SLNB, and the recurrence rate in the SLNB-positive group was 2-fold higher than in the negative group [15]. A meta-analysis by



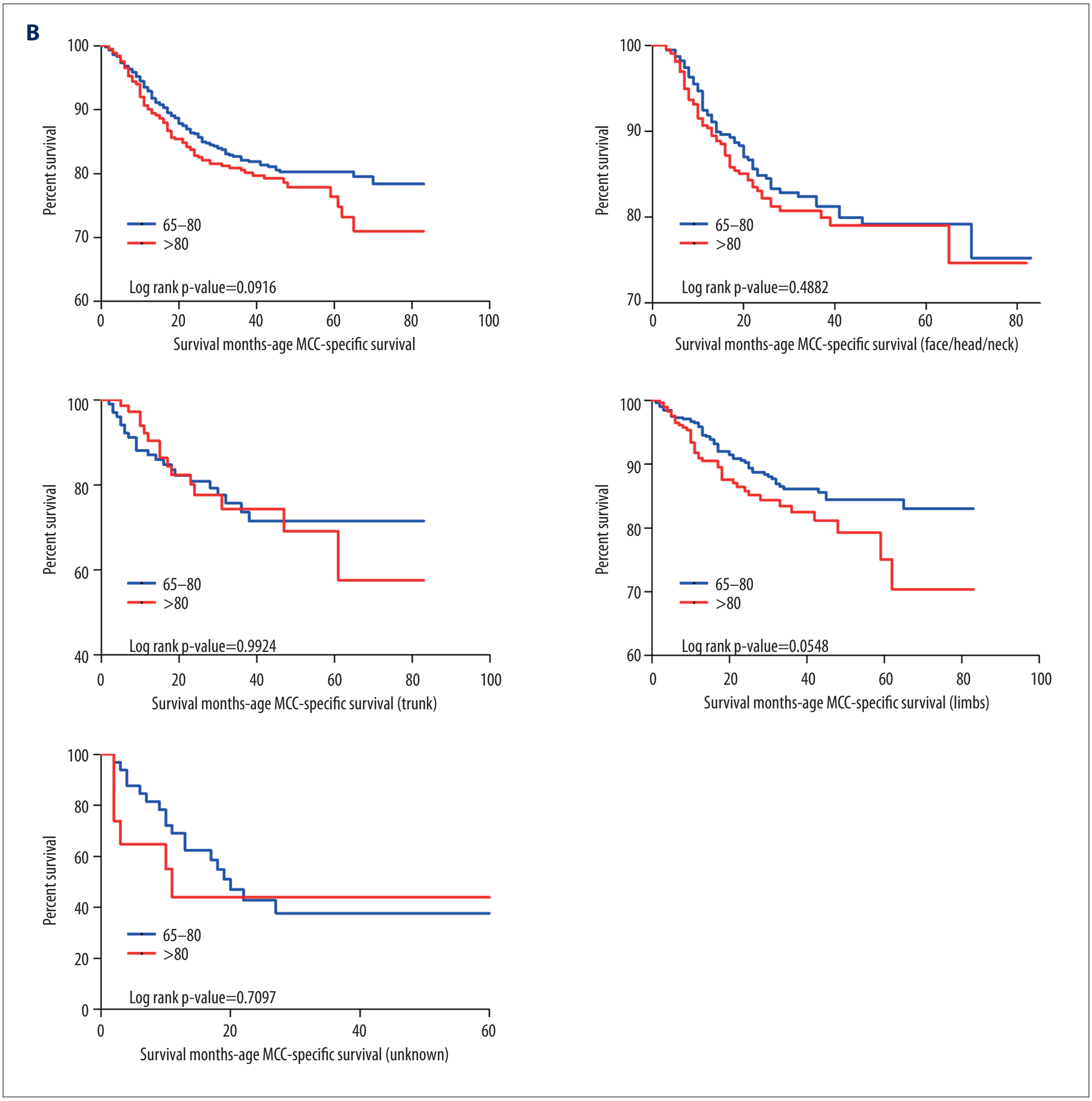
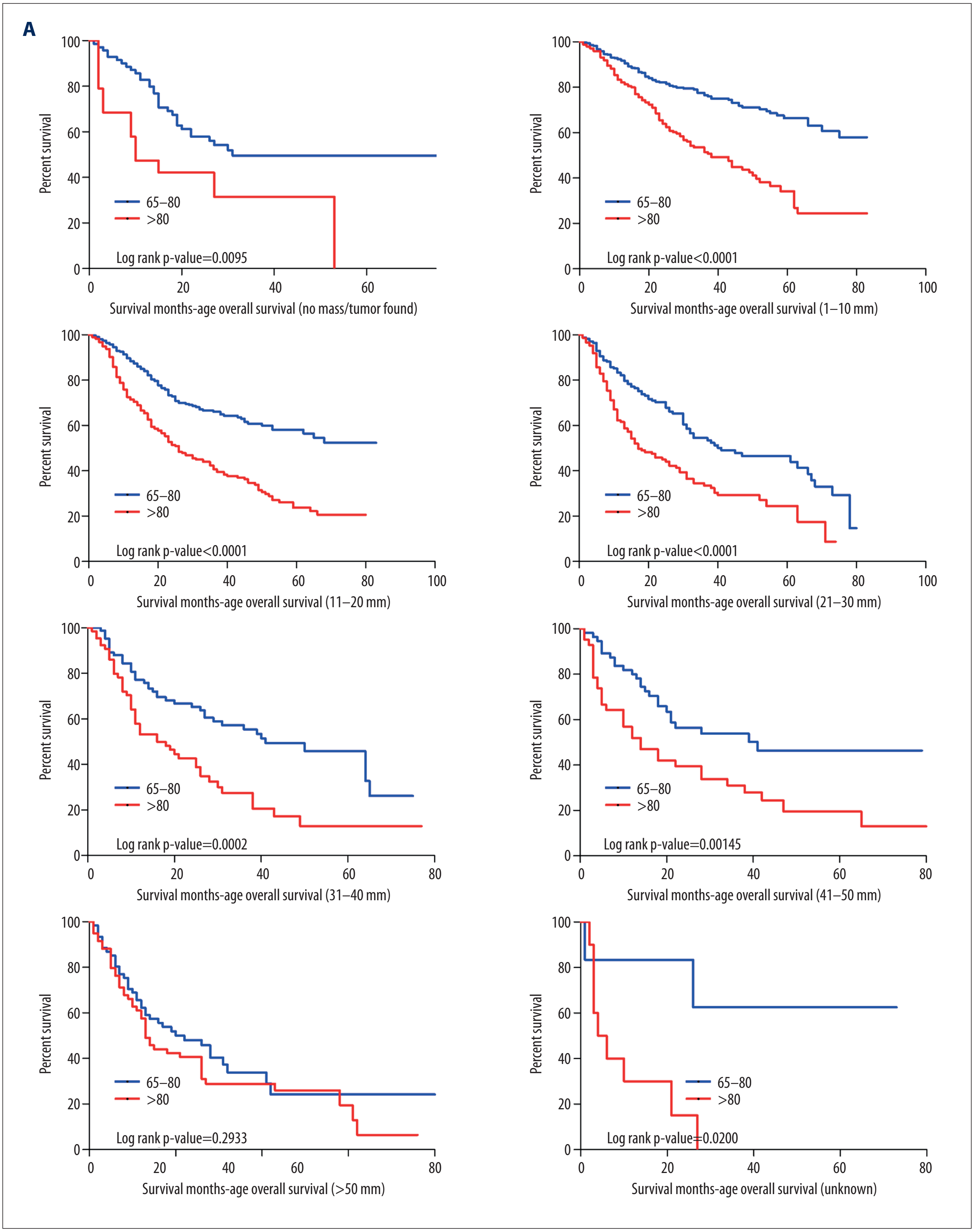


Figure 1. (**A**) Overall survival (OS) stratified by age and primary site. (**B**) MCC-specific survival (MSS) stratified by age and primary site.

Sadeghi et al. confirmed that SLNB can provide prognostic information on overall survival and disease-specific survival [16]. Early biopsy can identify patients with positive lymph nodes, which is of great significance for the early implementation of radiotherapy and immunotherapy to improve the prognosis of MCC patients. In our results, SLNB was associated with reduced OS (HR=0.327) and MCC-specific survival (HR=0.089) risks in older patients. In addition to the impact of the surgery itself, it should be noted that, considering the characteristics of elderly patients, patients who choose to receive biopsy or surgery generally have better physical conditions and tolerance to surgical trauma. Moreover, as the basis of tumor staging, SLNB status can help guide the diagnosis and subsequent treatment of patients. Therefore, assessment of the effect of the surgery itself on the prognosis needs to be independent of these factors and clarified by a rigorously controlled prospective study. In our results, the surgical group, including SLNB and regional lymph node removed, had better survival. However, for elderly patients, it is necessary to evaluate the patient's physical condition and to assess the patient's tolerance to weigh the advantages and disadvantages. Within the patient's tolerance range, minimizing the patient's tumor burden requires the experience and continuous exploration of clinicians.



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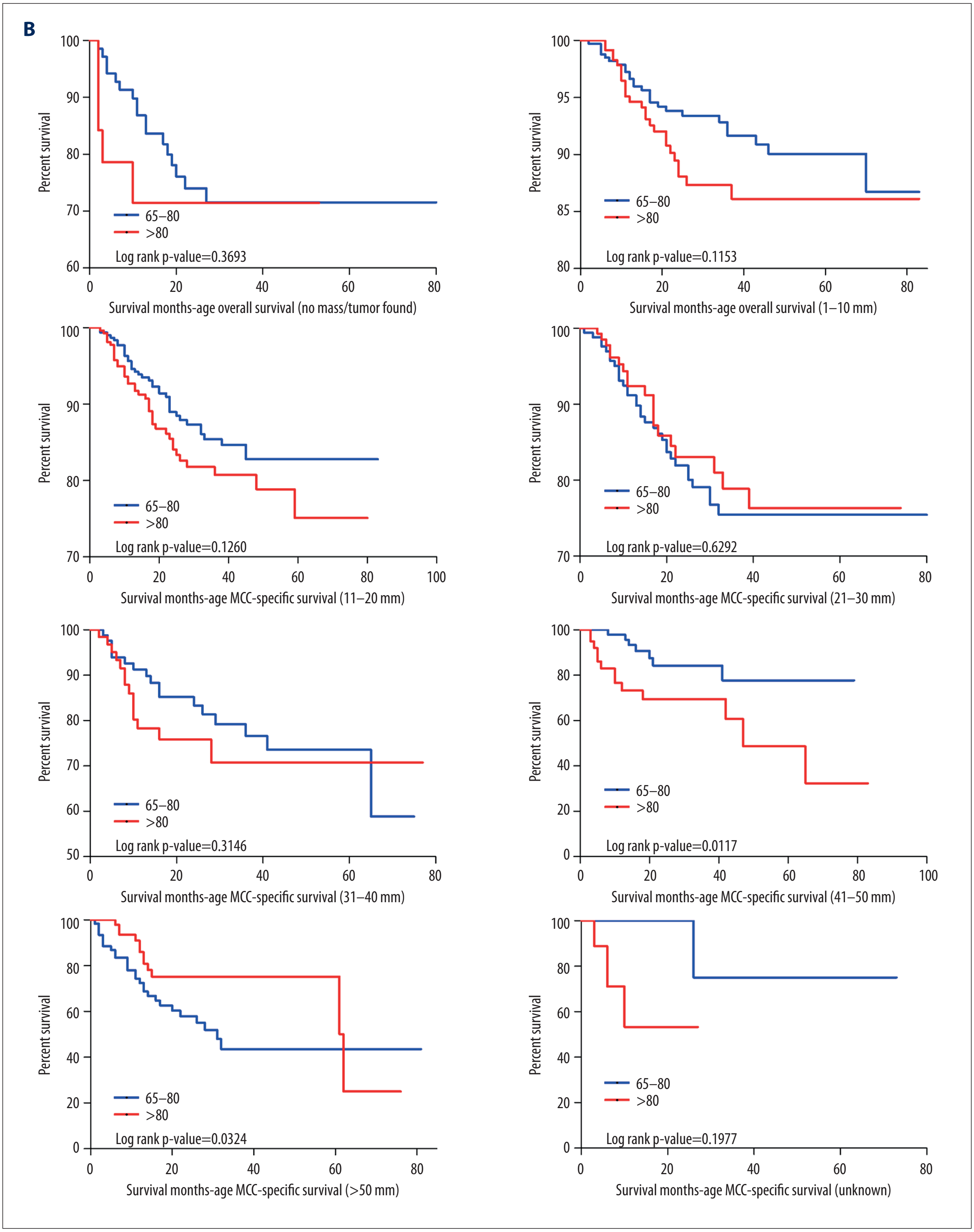

Figure 2. (**A**) Overall survival (OS) stratified by tumor size and age. (**B**) MCC-specific survival (MSS) stratified by tumor size and age.

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Table 3. Univariate and multivariate survival analysis of elderly patients with Merkel cell carcinoma.

Variables	Overall survival				MCC-specific Survival			
	Univariable		Multivariable		Univariable		Multivariable	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Age								
65–80	Reference		Reference		Reference		Reference	
>80	2.096 (1.845–2.381)	<0.001	1.714 (1.489–1.973)	<0.001	1.219 (0.970–1.531)	0.089	1.009 (0.782–1.302)	0.945
Race								
White	Reference		Reference		Reference		Reference	
Black	0.856 (0.543–1.348)	0.502	0.760 (0.479–1.205)	0.243	1.118 (0.554–2.256)	0.756	1.157 (0.561–2.388)	0.693
Other	0.208 (0.029–1.479)	0.117	0.195 (0.027–1.396)	0.104	–	0.937	–	0.808
Unknown	–	–	–	–	–	–	–	–
Sex								
Male	Reference				Reference		Reference	
Female	0.713 (0.622–0.818)	<0.001	0.660 (0.567–0.768)	<0.001	0.702 (0.548–0.899)	0.005	0.786 (0.597–1.034)	0.086
Marital status								
Single	Reference		Reference		Reference		Reference	
Married	0.840 (0.646–1.092)	0.193	0.906 (0.693–1.183)	0.468	0.649 (0.379–1.113)	0.116	0.739 (0.424–1.288)	0.286
Unknown	–	–	–	–	–	–	–	–
Primary site								
Face/head/neck	Reference		Reference		Reference		Reference	
Trunk	0.727 (0.632–0.836)	<0.001	0.847 (0.728–0.986)	0.032	0.742 (0.574–0.960)	0.023	0.770 (0.580–1.022)	0.070
Upper and lower extremities	1.049 (0.777–1.416)	0.756	0.832 (0.438–1.580)	0.574	1.893 (1.235–2.901)	0.003	1.368 (0.488–3.833)	0.551
Other	–	–	–	–			–	–
Tumor size								
No mass/tumor found	Reference		Reference		Reference		Reference	
1–10 mm	0.553 (0.402–0.761)	<0.001	0.400 (0.164–0.976)	0.044	0.277 (0.170–0.453)	<0.001	0.624 (0.086–4.556)	0.642
11–20 mm	0.803 (0.588–1.097)	0.168	0.557 (0.229–1.355)	0.197	0.452 (0.284–0.719)	0.001	0.959 (0.132–6.943)	0.967
21–30 mm	1.067 (0.772–1.475)	0.693	0.559 (0.187–1.677)	0.300	0.610 (0.373–0.998)	0.049	1.133 (0.107–11.949)	0.918
31–40 mm	1.189 (0.833–1.696)	0.341	0.535 (0.176–1.628)	0.271	0.820 (0.478–1.406)	0.470	1.303 (0.121–13.989)	0.827
41–50 mm	1.198 (0.814–1.765)	0.360	0.559 (0.182–1.719)	0.310	0.877 (0.485–1.585)	0.664	1.639 (0.151–17.830)	0.685
>50 mm	1.692 (1.185–2.415)	0.004	0.705 (0.225–2.213)	0.550	1.535 (0.921–2.558)	0.100	1.786 (0.160–19.936)	0.637
Unknown	1.796 (0.930–3.467)	0.081	0.577 (0.173–1.929)	0.372	1.306 (0.452–3.778)	0.622	0.944 (0.077–11.634)	0.964

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Table 3 continued. Univariate and multivariate survival analysis of elderly patients with Merkel cell carcinoma.

Variables	Overall survival				MCC-specific Survival			
	Univariable		Multivariable		Univariable		Multivariable	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
T stage								
T0	Reference		Reference		Reference		Reference	
T1	0.691 (0.502–0.951)	0.023	2.236 (0.722–6.929)	0.163	0.347 (0.221–0.546)	<0.001	1.778 (0.185–17.069)	0.618
T2	1.126 (0.813–1.561)	0.474	2.622 (0.723–9.510)	0.143	0.650 (0.409–1.035)	0.070	1.351 (0.102–17.876)	0.820
T3	1.604 (1.092–2.355)	0.016	2.484 (0.648–9.524)	0.185	1.421 (0.831–2.429)	0.199	2.099 (0.148–29.773)	0.584
T4	1.576 (1.070–2.323)	0.021	2.628 (0.763–9.045)	0.126	1.038 (0.582–1.852)	0.898	1.555 (0.125–19.390)	0.732
Unknown	–	–	–	–	–	–	–	–
N stage								
N0	Reference		Reference		Reference		Reference	
N1	1.823 (1.598–2.079)	<0.001	2.178 (1.654–2.869)	<0.001	3.567 (2.813–4.524)	<0.001	4.335 (2.812–6.684)	<0.001
N2	2.251 (1.632–3.104)	<0.001	1.804 (1.231–2.643)	0.002	5.365 (3.371–8.539)	<0.001	4.500 (2.553–7.931)	<0.001
Unknown	–	–	–	–	–	–	–	–
M stage								
M0	Reference		Reference		Reference		Reference	
M1	4.397 (3.569–5.415)	<0.001	1.967 (1.458–2.653)	<0.001	8.056 (5.979–10.854)	<0.001	2.951 (1.915–4.548)	<0.001
Primary site surgery								
No	Reference		Reference		Reference		Reference	
Yes	0.535 (0.448–0.640)	<0.001	0.917 (0.720–1.169)	0.485	0.437 (0.325–0.588)	<0.001	1.128 (0.720–1.767)	0.600
Unknown	1.634 (0.229–11.684)	0.625	1.683 (0.188–15.043)	0.642	–	0.936	–	0.930
Scope regional lymph node surgery								
None	Reference		Reference		Reference		Reference	
Regional lymph nodes removed	0.904 (0.778–1.050)	0.187	0.449 (0.209–0.964)	0.040	1.418 (1.094–1.838)	0.008	0.138 (0.027–0.699)	0.017
Sentinel lymph node biopsy	0.382 (0.320–0.456)	<0.001	0.327 (0.151–0.712)	0.005	0.412 (0.293–0.580)	<0.001	0.089 (0.017–0.461)	0.004
Sentinel lymph node biopsy+regional lymph nodes removed	0.607 (0.465–0.794)	<0.001	0.343 (0.154–0.765)	0.009	0.814 (0.512–1.294)	0.384	0.090 (0.017–0.484)	0.005
Unknown	1.195 (0.657–2.174)	0.559	0.894 (0.464–1.720)	0.736	2.048 (0.837–5.011)	0.117	1.265 (0.429–3.727)	0.670
Regional nodes examined								
No	Reference		Reference		Reference		Reference	
Yes	0.619 (0.545–0.702)	<0.001	1.479 (0.682–3.209)	0.322	0.963 (0.686–1.087)	0.211	5.510 (0.952–28.868)	0.073

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Table 3 continued. Univariate and multivariate survival analysis of elderly patients with Merkel cell carcinoma.

Variables	Overall survival				MCC-specific Survival			
	Univariable		Multivariable		Univariable		Multivariable	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Unknown	2.127 (0.530–8.536)	0.287	–	0.906	3.791 (0.529–27.160)	0.185	–	0.888
Regional nodes positive								
No	Reference		Reference		Reference		Reference	
Yes	2.789 (2.317–3.358)	<0.001	0.961 (0.690–1.339)	0.815	4.662 (3.285–6.615)	<0.001	0.723 (0.414–1.262)	0.253
No nodes examined	2.797 (2.346–3.334)	<0.001	–	0.925	2.930 (2.056–4.176)	<0.001	–	–
Unknown	2.371 (0.588–9.562)	0.225	–	0.906	5.152 (0.708–37.493)	0.105	–	0.893
Radiation								
No	Reference		Reference		Reference		Reference	
Yes	0.727 (0.640–0.825)	<0.001	0.725 (0.630–0.834)	<0.001	1.025 (0.817–1.285)	0.833	0.943 (0.732–1.215)	0.650
Chemotherapy								
No/unknown	Reference		Reference		Reference		Reference	
Yes	1.929 (1.609–2.312)	<0.001	1.178 (0.936–1.482)	0.164	3.273 (2.493–4.298)	<0.001	1.072 (0.755–1.522)	0.697
Bone metastasis								
No	Reference		Reference		Reference		Reference	
Yes	4.505 (2.945–6.893)	<0.001	0.822 (0.478–1.414)	0.479	9.004 (5.239–15.477)	<0.001	1.082 (0.530–2.208)	0.829
Unknown	3.667 (2.075–6.483)	<0.001	0.309 (0.017–5.632)	0.428	5.123 (2.115–12.411)	<0.001	–	0.950
Brain metastasis								
No	Reference		Reference		Reference		Reference	
Yes	10.389 (2.585–41.749)	0.001	4.384 (0.956–20.113)	0.057	34.582 (8.510–140.539)	<0.001	4.062 (0.717–23.013)	0.113
Unknown	3.594 (2.079–6.214)	<0.001	4.322 (0.582–32.101)	0.153	4.482 (1.851–10.854)	0.001	–	0.948
Liver metastasis								
No	Reference		Reference		Reference		Reference	
Yes	7.016 (4.905–10.034)	<0.001	1.883 (1.176–3.015)	0.008	14.114 (8.867–22.466)	<0.001	2.790 (1.476–5.274)	0.002
Unknown	3.716 (2.102–6.569)	<0.001	–	–	5.257 (2.170–12.737)	<0.001	–	–
Lung metastasis								
No	Reference		Reference		Reference		Reference	
Yes	3.866 (2.422–6.172)	<0.001	0.913 (0.524–1.592)	0.748	6.179 (3.174–12.028)	<0.001	0.843 (0.369–1.925)	0.685
Unknown	3.858 (2.231–6.671)	<0.001	1.448 (0.188–11.169)	0.722	5.094 (2.629–13.261)	<0.001	3.937 (0.455–34.061)	0.213

HR – hazard ratio; CI – confidence interval.

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MCC patients have been reported to have increased risk of secondary malignancy, especially in immunosuppressed patients [10]. In addition, MCC patients were also found to have an increased risk of complicated malignant blood diseases [17,18]. Liver metastasis secondary to MCC has also been reported [19], especially in immunosuppressed patients [20]. Among distant metastases, only liver metastasis was correlated with OS (HR=1.883) and MCC-specific survival (HR=2.790). For elderly patients, liver metastasis significantly increased the risk of death. Due to the lack of specificity in diagnosis of metastatic lesions, it is necessary to differentiate the diagnosis from primary liver cancer, liver abscess, and other liver metastases. Therefore, in clinical practice, it is important to closely monitor changes in liver function and CT and MRI imaging.

This study analyzed the prognosis of elderly patients with MCC and screened independent predictors of survival in elderly patients. However, there are some limitations. First, this was a retrospective study, and there may be some bias. Patients who underwent lymph nodes surgical intervention had a reduced risk of survival. Due to the characteristics of the elderly population, it is difficult to rule out the fact that in addition to the effects of the surgery itself, the elderly patients who choose the surgery are the patients who are more tolerant of surgical trauma and have better general physical condition. Second, we lacked general patient information, such as family history, presence or absence of underlying diseases, smoking history, and specific chemoradiotherapy regimens administered, which could have affected our results. To better understand MCC, these limitations should be addressed in future research.

Conclusions

Despite these limitations, this study provides epidemiological insights into Merkel cell carcinoma in elderly patients and confirmed that patients receiving lymph node surgery have better outcomes. This is the first study to show that liver metastasis is associated with poor prognosis. There is a need to strengthen monitoring of the liver condition of elderly patients and to perform necessary lymph node surgery within the patient's tolerance.

Conflict of interest

None.

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