Original Article

Clinicopathological features and prognostic analysis of metastatic pulmonary sarcomatoid carcinoma: a SEER analysis

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Background: Pulmonary sarcomatoid carcinoma (PSC) is a rare type of non-small cell lung cancer (NSCLC). Metastases are often detected at the first diagnosis. Despite high rates of distant metastasis, there is insufficient data describing the characteristics of PSC metastasis.

Methods: We performed a Surveillance, Epidemiology, and End Results (SEER) database-based analysis of clinicopathological features and prognosis of distant metastasis in PSC patients. Data queried for this analysis included PSC patients in the database between 2010 and 2016.

Results: A total of 934 patients met the criteria for inclusion in the analysis and included, at the time of diagnosis, 512 (54.8%) patients with metastasis, including bone (n=152; 16.3%), brain (n=108; 11.6%), liver (n=70; 7.5%), lung (n=142; 15.2%) metastases. Binary logistic regression showed that patients with giant cell carcinoma [odds ratio (OR) 4.023, 95% confidence interval (CI): 2.113–7.661, P<0.001] and spindle cell carcinoma (OR 3.151, 95% CI: 1.699–5.843, P<0.001) were associated with metastasis. Log-rank test and Kaplan-Meier plots indicated poor prognosis in metastatic patients [the 1-, 3-, and 5-year overall survival (OS) rates were 14.1%, 5.5%, and 4.8%, respectively]. Multivariable analysis showed younger and chemotherapy as improved prognostic factors of PSC patients with single metastasis site.

Conclusions: The SEER database-based analysis revealed the clinical features of distant metastasis of PSC and showed that different histological types posed distinct metastasis potential. Besides, age and chemotherapy were the independent prognostic factors of PSC patients with single metastasis site.

Keywords: Metastasis; pulmonary sarcomatoid carcinoma (PSC); prognosis; Surveillance, Epidemiology, and End Results (SEER) database; treatment

Submitted Sep 04, 2020. Accepted for publication Nov 20, 2020.
doi: 10.21037/jtd-20-2826
View this article at: http://dx.doi.org/10.21037/jtd-20-2826

Introduction

Lung cancer is the leading cause of death among cancer patients, with non-small cell lung cancer (NSCLC) accounting for 80–85% of the cases (1). However, pulmonary sarcomatoid carcinoma (PSC), a rare type of NSCLC, that has been estimated to represent less than 1% of all lung cancer (2-4), exhibits a high degree of malignancy and comprises nearly half of distant metastasis (5-8), and poor prognosis (8-11). Further, PSC is common among older men and smokers (7,12). Although clinical features of PSC and imaging examination have certain characteristics, additional pathological and immunohistochemical examinations are required for accurate diagnosis (13). Nevertheless, there have been few

previous reports in the literature describing the distribution and characteristics of PSC metastasis, despite high rate of distant metastasis, prompting the need for additional analyses. The Surveillance, Epidemiology, and End Results (SEER) database of survival data from population-based cancer registries encompass 35% of the American population. The SEER database documented data on PSC since 1975 and PSC metastasis sites in bone, brain, liver, and lung since 2010. The aim of the current study was to analyze the characteristics of metastatic PSC patients using SEER analysis.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/jtd-20-2826).

Methods

Patients

This database study used SEER-18 Dataset consisting of 18 cancer registries across the United States. Patients with PSC diagnosed between 2010 and 2016 were included in this study. Data were extracted using the SEER*Stat software (version 8.3.6) of the National Cancer Institute. Diagnosed cases were identified by the specific codes of the International Classification of Diseases for Oncology, 3rd edition (ICD-O) under which pleomorphic carcinoma (8022/3), spindle cell carcinoma (8032/3), giant cell carcinoma (8031/3), carcinosarcoma (8980/3) and pulmonary blastoma (8972/3) are grouped under the term PSC (9). Variables including sex, age of diagnosis, race, primary lesion, tumor size, stage, metastatic site, histological type, differentiation grade, marital status, surgery, radiotherapy, chemotherapy, survival time, and vital status were extracted from the SEER database. We categorized the age of diagnosis (≥60 or >60 years old), metastasis stage (metastasis or non-metastasis), marital status (married or single), and coded tumor size (T1-2 or T3-4).

Statistical analysis

Demographic and tumor characteristics were summarized with descriptive statistics. Comparisons of categorical variables were performed using the Chi square and Fisher's exact probability test. The metastasis correlation factors were compared by binary logistics regression analysis showing odds ratio (OR) and 95% confidence intervals (CI). For overall survival (OS), univariate associations of all cohorts were evaluated using the Cox proportional hazard model and log-rank test. Log-rank P values and Kaplan-Meier plots were used to compare the survival difference of variables. When calculating the OS rate, the value of missing time point was replaced by the previous non-deleted time point survival rate. Cox proportional hazards model was used for identifying risk factors of prognosis with single-site metastasis patients and included univariate and multivariate analyses, with hazard ratio (HR) and 95% CI. All statistical analyses were performed using SPSS version 23.0 (IBM Inc. Chicago, IL, USA). A two-sided P value less than 0.05 was considered as statistically significant.

Ethics

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This was an open database study that involved no identifiable information for individuals throughout the analysis, and therefore, Institutional Review Board of the Disciplines of Excellence and West China Hospital, Sichuan University (ZYGD18021) (1.3.5 Project) consent for this database analysis was waived.

Results

A total of 3,665 cases of PSC, diagnosed between 1975 and 2016, were identified in the SEER database. The absence of metastatic sites data prior to 2010 in the SEER database resulted in the exclusion of 2,705 patients, and 26 patients were further excluded due to missing and inconsistent data on metastasis status. Finally, 934 cases were considered for final analysis (*Figure 1*).

Demographic analysis revealed a higher number of males (n=551; 59.0%) compared to females (n=383; 41.0%), showing a 1.5:1 distribution. The mean and median age for the whole group were 68.9±11.5 and 70±17 years, respectively. The population was distributed into 512 (54.8%) cases of metastatic disease and 422 (45.2%) cases of non-metastatic disease and a between-group comparison of the clinical features is shown in *Table 1*. Data on distant lymph node or other site metastases were missing and therefore, not included. The common metastatic sites included bone (n=152, 16.3%), brain (n=108, 11.6%), liver (n=70, 7.5%), and lung (n=142, 15.2%). Clinicopathological features of patients with different sites of distant metastases are listed in *Table 2*.

Univariate analysis showed that a significantly higher

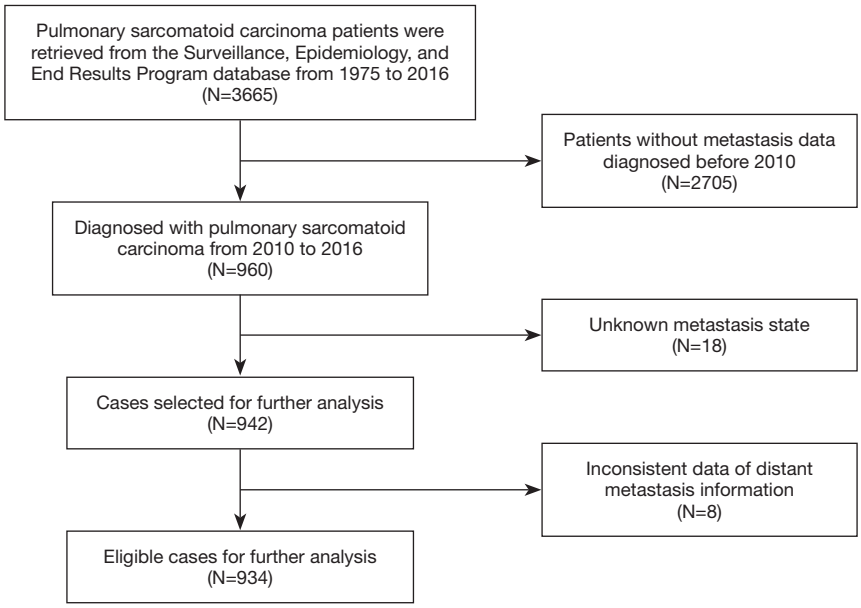

Figure 1 Data disposition.

Table 1 Comparison of clinicopathological characteristics between non-metastasis and metastasis PSC patients of the overall cohort

Variable	Non-metastasis, N (%)	Metastasis, N (%)	P value
Gender			0.083
Male	236 (55.9)	315 (61.5)	
Female	186 (44.1)	197 (38.5)	
Age			0.474
≤60 years	93 (22.0)	123 (24.0)	
>60 years	329 (78.0)	389 (76.0)	
Race			0.023
Other (American Indian/AK Native, Asian/Pacific Islander)	22 (5.2)	31 (6.1)	
White	357 (84.8)	400 (78.1)	
Black/African American	42 (10.0)	81 (15.8)	
Primary site			0.598
Main bronchus	12 (3.0)	16 (3.8)	
Upper lobe, lung	246 (61.2)	244 (58.4)	
Middle lobe, lung	20 (5.0)	24 (5.7)	
Lower lobe, lung	116 (28.9)	130 (31.1)	
Overlapping lesion of lung	8 (2.0)	4 (1.0)	
Tumor size			0.030
T1–2	162 (50.2)	149 (41.9)	
T3–4	161 (49.8)	207 (58.1)	

Table 1 (*continued*)

Table 1 (*continued*)

Variable	Non-metastasis, N (%)	Metastasis, N (%)	P value
Histology			<0.001
Pleomorphic carcinoma	171 (40.5)	131 (25.6)	
Giant cell carcinoma	43 (10.2)	110 (21.5)	
Spindle cell carcinoma, NOS	103 (24.4)	175 (34.2)	
Pulmonary blastoma	18 (4.3)	5 (1.0)	
Carcinosarcoma, NOS	87 (20.6)	91 (17.8)	
Grade			0.278
Well differentiated or moderately differentiated	7 (2.5)	2 (0.9)	
Poorly differentiated	203 (73.6)	159 (71.3)	
Undifferentiated; anaplastic	66 (23.9)	62 (27.8)	
Married status			0.249
Married	217 (54.3)	283 (58.1)	
Single	183 (45.8)	204 (41.9)	
Surgery			<0.001
No	137 (32.7)	457 (89.6)	
Yes	282 (67.3)	53 (10.4)	
Radiation			<0.001
None/unknown	309 (73.2)	299 (58.4)	
Yes	113 (26.8)	213 (41.6)	
Chemotherapy			0.939
None/unknown	252 (59.7)	307 (60.0)	
Yes	170 (40.3)	205 (40.0)	

PSC, pulmonary sarcomatoid carcinoma.

proportion of PSC patients were of the white race than that of black/African American and other races (P=0.023) in both metastasis and non-metastasis groups (*Table 1*). Significantly higher number of large tumors (T3-4) were noted in the metastatic group (P=0.030). For histological types, the proportions of pleomorphic carcinoma patients in the non-metastasis group and spindle cell carcinoma patients in the metastasis group were significantly more than the other types (P<0.001). While the number of metastatic PSC patients who received surgical treatment was small (P<0.001), the proportion who received radiotherapy in the metastasis group was significantly higher compared to non-metastatic patients (P<0.001). The analysis of different metastatic sites (*Table 2*) showed a significant reduction in the number of patients without surgery for bone (P=0.001) or lung (P=0.010) metastases. The proportion of patients with bone (P=0.002) or brain (P<0.001) metastases receiving radiotherapy was significantly higher than those who did not have radiotherapy. The proportions of patients with brain metastases who were younger than 60 years of age (P<0.001), and those with pleomorphic carcinoma and giant cell carcinoma (P=0.001) were higher compared to patients without brain metastases. In addition, the proportion of white patients with lung metastases was significantly higher than that of other races (P=0.024).

Risk factors associated with metastasis were analyzed by binary logistics regression, which showed that patients with giant cell carcinoma (OR 4.023, 95% CI: 2.113–7.661, P<0.001) and spindle cell carcinoma (OR 3.151, 95% CI: 1.699–5.843, P<0.001) (*Table 3*) were more significantly

Table 2 Clinical features of different metastasis sites of PSC

Feature	Bone, N (%)		P	Brain, N (%)		P	Liver, N (%)		P	Lung, N (%)		P
	No	Yes		No	Yes		No	Yes		No	Yes	
Gender			0.114			0.161			0.282			0.203
Male	204 (59.0)	101 (66.4)		245 (63.0)	60 (55.6)		256 (60.4)	47 (67.1)		207 (59.3)	93 (65.5)	
Female	142 (41.0)	51 (33.6)		144 (37.0)	48 (44.4)		168 (39.6)	23 (32.9)		142 (40.7)	49 (34.5)	
Age (years)			0.263			<0.001			0.519			0.208
≤60	89 (25.7)	32 (21.1)		78 (20.1)	42 (38.9)		100 (23.6)	19 (27.1)		90 (25.8)	29 (20.4)	
>60	257 (74.3)	120 (78.9)		311 (79.9)	66 (61.1)		324 (76.4)	51 (72.9)		259 (74.2)	113 (79.6)	
Race			0.269			0.160			0.880			0.024
Other (American Indian/AK Native, Asian/Pacific Islander)	19 (5.5)	11 (7.2)		24 (6.2)	7 (6.5)		26 (6.1)	4 (5.7)		22 (6.3)	8 (5.6)	
White	265 (76.6)	122 (80.3)		308 (79.2)	77 (71.3)		328 (77.4)	56 (80.0)		261 (74.8)	121 (85.2)	
Black/African American	62 (17.9)	19 (12.5)		57 (14.7)	24 (22.2)		70 (16.5)	10 (14.3)		66 (18.9)	13 (9.2)	
Primary site			0.536			0.870			0.602			0.876
Main bronchus	11 (3.8)	5 (4.1)		13 (4.1)	3 (3.3)		15 (4.3)	1 (1.7)		12 (4.1)	4 (3.6)	
Upper lobe, lung	165 (57.5)	72 (59.0)		182 (57.2)	58 (63.0)		207 (59.3)	31 (53.4)		168 (56.8)	70 (63.1)	
Middle lobe, lung	19 (6.6)	4 (3.3)		19 (6.0)	4 (4.3)		20 (5.7)	3 (5.2)		18 (6.1)	6 (5.4)	
Lower lobe, lung	88 (30.7)	41 (33.6)		100 (31.4)	27 (29.3)		103 (29.5)	23 (39.7)		95 (32.1)	30 (27.0)	
Overlapping lesion of lung	4 (1.4)	0 (0.0)		4 (1.3)	0 (0.0)		4 (1.1)	0 (0.0)		3 (1.0)	1 (0.9)	
Tumor size (mm)			0.056			0.689			0.976			0.186
T1–2	94 (38.5)	52 (49.5)		115 (42.3)	31 (39.7)		128 (42.1)	18 (41.9)		111 (43.4)	33 (35.5)	
T3–4	150 (61.5)	53 (50.5)		157 (57.7)	47 (60.3)		176 (57.9)	25 (58.1)		145 (56.6)	60 (64.5)	
Histology			0.753			0.001			0.512			0.090
Pleomorphic carcinoma	89 (25.7)	39 (25.7)		89 (22.9)	38 (35.2)		108 (25.5)	16 (22.9)		95 (27.2)	27 (19.0)	
Giant cell carcinoma	75 (21.7)	32 (21.1)		78 (20.1)	31 (28.7)		92 (21.7)	14 (20.0)		79 (22.6)	28 (19.7)	
Spindle cell carcinoma, NOS	112 (32.4)	56 (36.8)		149 (38.3)	18 (16.7)		140 (33.0)	30 (42.9)		107 (30.7)	61 (43.0)	
Pulmonary blastoma	3 (0.9)	2 (1.3)		4 (1.0)	1 (0.9)		4 (0.9)	1 (1.4)		3 (0.9)	2 (1.4)	
Carcinosarcoma, NOS	67 (19.4)	23 (15.1)		69 (17.7)	20 (18.5)		80 (18.9)	9 (12.9)		65 (18.6)	24 (16.9)	

Table 2 (*continued*)

Table 2 (*continued*)

Feature	Bone, N (%)		P	Brain, N (%)		P	Liver, N (%)		P	Lung, N (%)		P
	No	Yes		No	Yes		No	Yes		No	Yes	
Grade			0.511			0.134			0.706			0.713
Well differentiated or Moderately differentiated	1 (0.7)	1 (1.5)		2 (1.2)	0 (0.0)		2 (1.0)	0 (0.0)		2 (1.2)	0 (0.0)	
Poorly differentiated	105 (70.5)	50 (74.6)		117 (68.4)	39 (83.0)		137 (71.4)	19 (79.2)		113 (69.8)	41 (75.9)	
Undifferentiated; anaplastic	43 (28.9)	16 (23.9)		52 (30.4)	8 (17.0)		53 (27.6)	5 (20.8)		47 (29.0)	13 (24.1)	
Married status			0.471			0.888			0.529			0.337
Married	187 (57.0)	89 (60.5)		213 (57.7)	62 (58.5)		233 (57.4)	40 (61.5)		187 (56.5)	84 (61.3)	
Single	141 (43.0)	58 (39.5)		156 (42.3)	44 (41.5)		173 (42.6)	25 (38.5)		144 (43.5)	53 (38.7)	
Surgery			0.001			0.249			0.333			0.010
No	297 (86.3)	147 (96.7)		344 (88.7)	99 (92.5)		376 (88.9)	64 (92.8)		303 (87.1)	134 (95.0)	
Yes	47 (13.7)	5 (3.3)		44 (11.3)	8 (7.5)		47 (11.1)	5 (7.2)		45 (12.9)	7 (5.0)	
Radiation			0.002			<0.001			0.055			0.150
None/unknown	216 (62.4)	72 (47.4)		256 (65.8)	31 (28.7)		239 (56.4)	48 (68.6)		194 (55.6)	89 (62.7)	
Yes	130 (37.6)	80 (52.6)		133 (34.2)	77 (71.3)		185 (43.6)	22 (31.4)		155 (44.4)	53 (37.3)	
Chemotherapy			0.698			0.733			0.899			0.579
None/unknown	209 (60.4)	89 (58.6)		234 (60.2)	63 (58.3)		251 (59.2)	42 (60.0)		211 (60.5)	82 (57.7)	
Yes	137 (39.6)	63 (41.4)		155 (39.8)	45 (41.7)		173 (40.8)	28 (40.0)		138 (39.5)	60 (42.3)	

PSC, pulmonary sarcomatoid carcinoma.

Table 3 Binary logistic regression of factors associated with distant metastases in PSC

Variable	P	Odds ratio	95% CI for OR
Gender			
Male	Reference		
Female	0.348	0.795	0.492–1.283
Age (years)			
≤60	Reference		
>60	0.503	0.828	0.477–1.439
Tumor size (mm)			
T1–2	Reference		
T3–4	0.355	1.239	0.787–1.949
Married status			
Married	Reference		
Single	0.633	0.892	0.557–1.427
Race			
Other (American Indian/AK Native, Asian/Pacific Islander)	Reference		
White	0.756	0.850	0.305–2.372
Black/African American	0.297	1.903	0.568–6.377
Primary site			
Main bronchus	Reference		
Upper lobe, lung	0.355	0.518	0.129–2.085
Middle lobe, lung	0.643	0.670	0.123–3.654
Lower lobe, lung	0.398	0.541	0.130–2.250
Overlapping lesion of lung	0.523	0.513	0.067–3.963
Histology			
Pleomorphic carcinoma	Reference		
Giant cell carcinoma	<0.001	4.023	2.113–7.661
Spindle cell carcinoma, NOS	<0.001	3.151	1.699–5.843
Pulmonary blastoma	0.979	1.034	0.089–12.001
Carcinosarcoma, NOS	0.325	1.363	0.736–2.524
Grade			
Undifferentiated; anaplastic	Reference		
Poorly differentiated	0.430	0.489	0.083–2.888
Well differentiated or moderately differentiated	0.884	1.039	0.625–1.727

PSC, pulmonary sarcomatoid carcinoma.

Table 4 1-y OS and median survival time of PSC patients

Group	Number (%)	1-year OS (%)	Median survival time (95 CI)
No metastasis	422 (45.2)	58.2	19 (13.879–24.121)
Metastasis	512 (54.8)	14.1	2 (1.633–2.367)
Single site	192 (20.6)	12.1	3 (2.373–3.627)
Multiple sites	106 (11.3)	3.6	2 (1.642–2.358)
Blank	214 (23.0)	–	–

PSC, pulmonary sarcomatoid carcinoma.

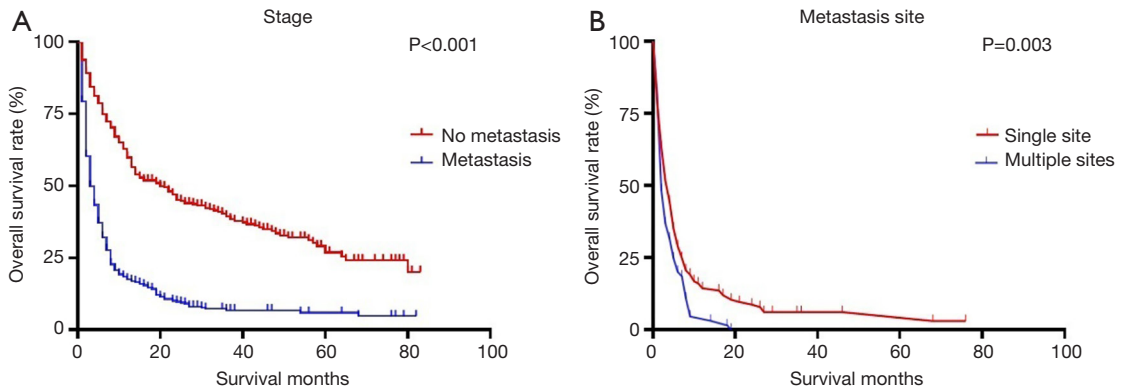

Figure 2 Kaplan-Meier overall survival curves for different metastasis states of PSC. PSC, pulmonary sarcomatoid carcinoma.

likely to associated with metastasis than patients with pleomorphic carcinoma. The 1-year OS rate and median survival time for PSC patients were summarized in *Table 4*. The survival curves of the non-metastases and metastases groups were analyzed using Kaplan-Meier plots. The 1-, 3-, and 5-year OS rates in the non-metastases group (58.2%, 38.3%, and 26.1%, respectively) were significantly higher (P<0.001) compared to that of the metastases group (14.1%, 5.5%, and 4.8%, respectively) (*Figure 2*). The 1-year OS rate and median time of single- and multi-site metastases showed statistical significance (P=0.003) (*Figure 2*).

Significant prognostic factors (age, primary site, grade, radiation and chemotherapy) of patients with single metastasis site identified in the univariate analysis were included as input variables for the Cox proportional hazard model. Multivariate analysis showed that patients aged >60 years of age (HR 1.874, 95% CI: 1.018–3.450, P=0.044) showed a worse prognosis whereas chemotherapy (HR 0.308, 95% CI: 0.175–0.541, P<0.001) showed improved prognosis (*Table 5*). Survival curve with a significant log-rank P value (P<0.05) were depicted in *Figure 3*.

Discussion

Despite a high rate of distant PSC metastasis, the paucity of studies describing its clinicopathological characteristics necessitated a SEER-based analysis, which revealed factors related to metastasis and prognosis in patients with advanced metastasis in addition to clinical characteristics that may provide a reference for clinicians who are keen on developing personalized examination protocols.

Demographics of the study population showed that 80% of the PSC patients were white with an average age similar to that reported previously (3,4,14). Our comparative analysis of non-metastasis and the metastasis groups showed an association between metastasis and large tumor size and spindle cell carcinoma, but there were no statistical differences in gender, age, primary site, grade, or marital status. In agreement with previous reports (5-7), we found a total distant metastatic rate of 54.8%. However, the distant metastasis rates of different sites found in our study are novel findings that have not been reported previously.

The analysis of clinical characteristics of PSC metastatic site showed that compared to spindle cell carcinoma, pleomorphic and giant cell carcinomas were more likely

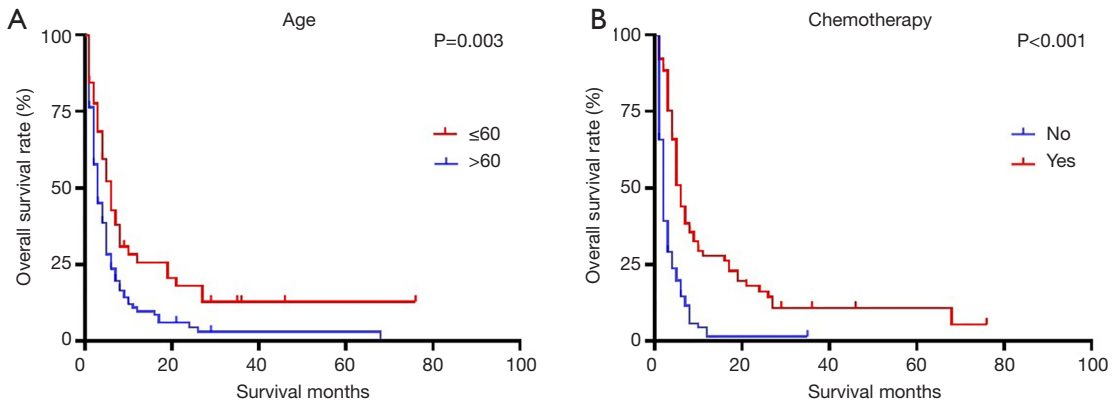

Figure 3 Survival curves demonstrating the effects of independent prognostic factors on the overall survival rate of PSC patients with single metastasis site. PSC, pulmonary sarcomatoid carcinoma.

Table 5 Survival analysis for PSC patients with single metastasis site

Variable	Univariate analysis			Multivariate analysis		
	Median OS (mo)	1-years OS (%)	P	Hazard ratio	95% CI	P
Gender						
Male	2	10.4		–	–	–
Female	4	14.8	0.372	–	–	–
Age (years)						
≤60	5	21.9		Reference		
>60	2	8.1	0.003	1.874	1.018–3.450	0.044
Tumor size (mm)						
T1-T2	3	13.2		–	–	–
T3-T4	3	14.3	0.910	–	–	–
Married status						
Married	3	12.3		–	–	–
Single	2	13.4	0.652	–	–	–
Race						
Other (American Indian/AK Native, Asian/Pacific Islander)	3	12.7		–	–	–
White	3	11.6		–	–	–
Black/African American	4	15.2	0.572	–	–	–
Primary site						
Main bronchus	2	0		Reference		
Upper lobe, lung	4	18.1		0.483	0.176–1.327	0.158
Middle lobe, lung	2	0		1.119	0.295–4.253	0.868
Lower lobe, lung	3	11.2		0.664	0.230–1.914	0.448
Overlapping lesion of lung	1	0	0.032	–	–	–

Table 5 (*continued*)

Table 5 (*continued*)

Variable	Univariate analysis			Multivariate analysis		
	Median OS (mo)	1-years OS (%)	P	Hazard ratio	95% CI	P
Histology						
Pleomorphic carcinoma	3	13.3		–	–	–
Giant cell carcinoma	3	10.7		–	–	–
Spindle cell carcinoma, NOS	3	10.6		–	–	–
Pulmonary blastoma	0	0		–	–	–
Carcinosarcoma, NOS	3	14.1	0.237	–	–	–
Grade						
Undifferentiated; anaplastic	2	4.8		Reference	–	–
Poorly differentiated	5	16.8		1.188	0.144–9.787	0.872
Well differentiated or moderately differentiated	2	0	0.008	0.845	0.463–1.543	0.584
Surgery						
No	3	11.8		–	–	–
Yes	5	15.9	0.086	–	–	–
Radiation						
No	2	7.0		Reference		
Yes	4	16.8	0.003	0.843	0.496–1.432	0.528
Chemotherapy						
No	1	1.1		Reference		
Yes	6	27.5	<0.001	0.308	0.175–0.541	<0.001

to be associated with brain metastasis. Besides, there was a higher proportion of patients younger than 60 years old with brain metastases in our study, suggesting that clinicians may consider more comprehensive brain tests for these clinical populations. Furthermore, binary logistic regression revealed that the occurrence of metastasis positively correlated with giant cell and spindle cell carcinomas, such that these carcinomas were potentially more metastatic than pleomorphic carcinomas. Therefore, our findings warrant a comprehensive metastasis-related image examination in these patients. Previous studies failed to capture a correlation between pathological types and metastasis due to the small sample sizes.

The 1-year OS log-rank test showed favorable prognosis of single metastasis site over multiple sites in PSC patients. Furthermore, the significantly lower survival rate of the metastases group compared to that of the non-metastases group is in concordance with rates reported in the literature (5,15-17). As previously reported (11,12), age was an independent prognostic factor in this study, older patients showed poor prognosis. We found that chemotherapy could significantly improve prognosis whereas radiotherapy did not, though a recent study showed that systemic chemotherapy alone did not improve survival of PSC patients (2). Further, despite an improved prognosis of metastatic PSC with chemotherapy, survival time remained short with a median survival time of only six months after chemotherapy, which may be associated with high rate of resistance to conventional first-line therapy (18). Though, tumor size, marital status, and histological type affected OS of PSC patients, as previously reported (8,10,12,16,17,19), these factors did not significantly affect PSC patients with single-site metastasis. Together, these findings suggest that clinicians should consider chemotherapy for PSC patients with single metastasis site in the absence of other treatment options, despite short

survival time after chemotherapy.

A comprehensive understanding of PSC along with rapid development of gene editing and immunotherapy in recent years, has opened several avenues for patients with advanced disease. While the SEER database lacked information on PSC related gene mutations, *KRAS*, *ALK*, *EGFR*, *MET*, and *BRAF* are common mutations in PSC reported previously (20-24). In addition, high PD-L1 expression in some PSC patients has been reported (25,26). As well, targeted therapy or immunotherapy has significantly improved prognosis of several cases (23,24,27), and may become the mainstream treatment option for PSC patients in the future.

To the best of our knowledge, this is the first SEER-based study that focused on metastatic PSC patients. However, there are several limitations in this retrospective study that should be acknowledged. First, though the common metastatic sites included in the SEER database were the bone, brain, liver and lung, metastases in the heart (28,29), duodenum (30), gingiva (31), and skin (32-34) have been reported, but not included in the SEER database, thereby underestimating the sample size in this study. Second, metastatic data retrieved from the SEER database were from 2010 to 2016, which may not provide sufficient follow-up time. Third, missing data on distant lymph node or other site metastases in SEER database precluded their inclusion in our analysis. We propose multicenter prospective studies in the future to overcome these limitations.

Conclusions

The SEER-based analysis revealed the clinical features of distant metastasis of PSC and showed that different histological types posed distinct metastasis potential. Besides, age and chemotherapy were the independent prognostic factors of PSC patients with single metastasis site.

Acknowledgments

The authors thank investigators and institutions involved in these studies and all patients whose data comprised the SEER Database.

Funding: This work was supported by the Natural Science Foundation of China (81602025), and 1.3.5 Project for Disciplines of Excellence and West China Hospital, Sichuan University (ZYGD18021).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/jtd-20-2826

Peer Review File: Available at http://dx.doi.org/10.21037/jtd-20-2826

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jtd-20-2826). LXL serves as an unpaid editorial board member of *Journal of Thoracic Disease* from Aug 2019–Jul 2021. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This was an open database study that involved no identifiable information for individuals throughout the analysis, and therefore, Institutional Review Board of the Disciplines of Excellence and West China Hospital, Sichuan University (ZYGD18021) (1.3.5 Project) consent for this database analysis was waived.

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Cite this article as: Xiao C, Yang X, Hao J, Guo C, Pu Q, Liu L. Clinicopathological features and prognostic analysis of metastatic pulmonary sarcomatoid carcinoma: a SEER analysis. J Thorac Dis 2021;13(2):893-905. doi: 10.21037/jtd-20-2826