Original Article

Additional chemotherapy improves survival in stage II–III pulmonary sarcomatoid carcinoma patients undergoing surgery: a propensity scoring matching analysis

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Background: The role of additional chemotherapy in pulmonary sarcomatoid carcinoma (PSC) is controversial. This study aimed to investigate the function of chemotherapy in PSC patients with surgical resection.

Methods: PSC patient information between 2004 to 2016 was extracted from the Surveillance, Epidemiology, and End Results (SEER) database. X-tile software was used to calculate the optimal cut-off value to divide groups. The disease stages were recalculated according to the American Joint Commission on Cancer (AJCC) 8th edition tumor-node-metastasis (TNM) staging system. Propensity score matching (PSM) analysis was conducted to balance the baseline of patients. Kaplan-Meier analysis and Cox proportional hazards analysis were used to evaluate survival outcome.

Results: A total of 865 PSC patients were included in our study. Among them, 611 patients were only operated with surgery, and the 254 others were treated with additional chemotherapy. The median age was 69.0 years (interquartile range, 61.6 to 76.3 years). Kaplan-Meier analysis showed that patients with additional chemotherapy had longer overall survival (OS) and cancer-specific survival (CSS, P<0.05). The median OS and the 1-, 3-, 5-year OS rates were 36.0 months (95% CI: 20.5–51.5 months), 72.7%, 49.6% and 38.5% in the chemotherapy group and 29.0 months (95% CI: 23.6–34.4 months), 63.2%, 44.5% and 37.6% in the non-chemotherapy group, respectively. The OS advantage of chemotherapy was not statistically significant after PSM analysis. Moreover, Cox proportional hazards model showed that chemotherapy was an independent prognosis factor for better OS and CSS. In subgroup of stages II and III, the chemotherapy group had a survival advantage (P<0.05). Patients with young age, female gender, low histology grade, large tumor size and lobectomy surgical resection benefited more from chemotherapy.

Conclusions: Chemotherapy is recommended for stages II and III PSC patients undergoing surgery, especially for those with young age, female gender, low histology grade, large tumor size and lobectomy surgical resection.

Keywords: Chemotherapy; pulmonary sarcomatoid carcinoma (PSC); Surveillance, Epidemiology, and End Results (SEER) database; survival

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Introduction

Pulmonary sarcomatoid carcinoma (PSC) is a rare group of non-small cell lung cancer (NSCLC) and accounts for less than 1% of lung cancer (1). Five subgroups are included in PSC according to the 2015 World Health Organization Classification of Lung Tumors: pleomorphic carcinoma, spindle cell carcinoma, giant cell carcinoma, carcinosarcoma and pulmonary blastoma (2). PSC is an aggressive tumor with a 12.6–34.6% 5-year overall survival (OS) (3-5). Surgery is currently the most popular strategy, especially for PSC at early stages. However, a retrospective research revealed that the median recurrence-free survival after resection was only 6.8 months (6). Chemotherapy combined with surgical resection is a standard treatment for NSCLC patients at stages IIB, IIIA and IIIB (7). No guideline or consensus has been addressed for PSC. Due to the different pathological characteristics and behaviors, the investigation on PSC remains of great importance for individualized therapy.

The benefits of additional chemotherapy on PSC patients undergoing surgery are still controversial. Due to the rarity of PSC, all retrospective studies had limited population and long diagnostic time span (6,8-13). Currently, several open access databases with large patient population are available for cancer researchers. In this study, we investigated the advantage of additional chemotherapy in PSC patients with surgical resection by searching the Surveillance, Epidemiology, and End Results (SEER) database. Propensity score matching (PSM) analysis was used to balance the covariates distribution between treated and untreated groups. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-20-3226).

Methods

Patient and data selection

We extracted the data of patients identified as PSC from 2004 and 2016 in SEER database: incidence-SEER 18 Regs Custom Data (with additional treatment field), Nov 2018 Sub (1975–2016), using the SEER*Stat software (version 8.3.6). Positive histology was defined as PSC: pleomorphic carcinoma, 8,022/3; giant cell and spindle cell carcinoma, 8,030/3; giant cell carcinoma, 8,031/3; spindle cell carcinoma, not otherwise specified (NOS), 8032/3; pseudosarcomatous carcinoma, 8,033/3; pulmonary blastoma, 8972/3; carcinosarcoma, NOS, 8,980/3 (1). Disease primary sites and corresponding ICD-O-3 codes were main bronchus lung, C34.0; upper lobe lung, C34.1; middle lobe lung, C34.2; lower lobe lung, C34.3; over lapping lesion of lung, C34.8; lung NOS, C34.9. The exclusion criteria were as follows: (I) incomplete follow-up; (II) unknown survival month; (III) sources from autopsy only or death certification; (IV) received radiation therapy; (V) did not undergo surgery.

The following variates were collected: age, year at diagnosis, gender, race, grade, histological result, surgery type, tumor size, disease stage and chemotherapy status. Disease stages were adjusted manually based upon the American joint commission on cancer (AJCC) 8th edition tumor-node-metastasis (TNM) staging system (14). The first outcome end point was OS, and the second one was cancer-specific survival (CSS). OS was calculated form the date of diagnosis to death or last follow-up. CSS was identified as the time ranging from the date of diagnosis until the date of death due to cancer.

Statistical analysis

The optimal cut-off values in age, year at diagnosis and tumor size were calculated by X-tile software (version 3.6.1) to divide patients into groups. The association between chemotherapy and clinical demographics or tumor characteristics were analyzed by chi-square tests. The survival curves were depicted by Kaplan-Meier analysis and compared by log-rank test. Univariate and multivariate analyses were performed by the Cox proportional hazards model to identify variates associated with OS and CSS, with 95% confidence intervals (CIs). PSM analysis was conducted to balance the baseline of patients. The covariates included age, gender, race, year of diagnosis, grade, histology, surgery type, tumor size and disease stage. In subgroup analysis, Cox model was used to determine the significant difference in different characteristic and chemotherapy status. All the statistical analyses and PSM analyses were performed by

SPSS (version 25.0) software. Forest plot was drawn up using GraphPad Prism (version 7.0). A lower than 0.05 two-sided P value was considered as statistically significant.

Results

Patient characteristics

A total of 865 patients were included in our study before PSM (*Table 1*). The median age was 69.0 years (interquartile range, 61.6 to 76.3 years). All patients had a median follow-up of 36.1 months (range, 0 to 155 months). The patients receiving additional chemotherapy had younger ages, lower grade tumors, larger tumor sizes and advanced tumors. There was a significant difference in the number of patients receiving chemotherapy between different surgery type groups and year of diagnosis groups (P<0.05). To balance the baseline of patient features between the chemotherapy and non-chemotherapy groups, a one-to-two PSM method was conducted with a caliper of 0.02 and random matching order. After PSM, 213 patients remained in the chemotherapy group and 342 ones were matched in the non-chemotherapy group (*Figure 1*). The numbers of patients receiving chemotherapy in different disease stage groups showed a statistically significant difference (P<0.05). The other variables were all balanced after the PSM analysis (P>0.05; *Table 1*).

Survival analysis

Kaplan-Meier analysis indicated that patients with additional chemotherapy had longer OS and CSS compared with the ones without chemotherapy (P<0.05; *Figure 2A,B*). The median OS and the 1-, 3-, 5-year OS rates were 36.0 months (95% CI: 20.5–51.5 months), 72.7%, 49.6% and 38.5% in the chemotherapy group and 29.0 months (95% CI: 23.6–34.4 months), 63.2%, 44.5% and 37.6% in the non-chemotherapy group, respectively. The median CSS and the 1-, 3-, 5-year CSS rates were 47.0 months (95% CI: 32.2–61.9 months), 74.7%, 52.3% and 41.1% in the chemotherapy group and 29.0 months (95% CI: 24.1–33.9 months), 63.4%, 44.3% and 37.5% in the non-chemotherapy group, respectively. After PSM analysis, the survival advantage of chemotherapy was not significant. The OS and CSS survival curves in the chemotherapy and non-chemotherapy groups in matching cohorts are shown in *Figure 2C,D*.

Multivariate analysis by Cox proportional hazard model showed that chemotherapy was an independently prognostic factor for better OS. Young age, female gender, low histological grade and early disease stage were also associated with prolonged survival (*Table 2*). In the analysis for CSS, old age, late year of diagnosis, large tumor size, advanced disease stage and no chemotherapy were all adverse factors (*Table 3*).

Subgroup analysis

Considering the reduction of selection bias, all subgroup analyses were conducted using the cohorts after PSM. In the stages II and III patients, survival advantage was observed in the chemotherapy group (P<0.05), which was not found in the stages I and IV patients (*Figure 3*). The 5-year OS rates for chemotherapy (yes *vs.* no/unknown) were 52.0% *vs.* 37.6% and 37.0% *vs.* 26.6% in the stages II and III patients. Prolonged survival time was also associated with chemotherapy in pseudosarcomatous carcinoma group. More detailed subgroup analysis in the stage IA, IB, IIA groups showed that chemotherapy benefited stage IIA PSC patients receiving surgery (*Figure 4*). In the analysis for CSS, chemotherapy played a positive role in patients at 65–74 years or with large tumors (>4 cm). Female patients or lobectomy surgery patients might benefit more from additional chemotherapy. Patients with poor differentiation or undifferentiated histology, as well as at stages II and III or pseudosarcomatous carcinoma, were also recommended for chemotherapy. Cox proportional hazard analysis showed that chemotherapy was an independently prognostic factor of OS in patients at 65–74 years, with pseudosarcomatous carcinoma, or at stages II and III. Chemotherapy was also an independently prognostic factor of CSS in patients at ≤74 years, with large tumor (>4 cm), at stages II and III, or with lobectomy surgery. Furthermore, additional chemotherapy independently influence the CSS of female patients or patients with poor differentiation or undifferentiated histology (*Figures 5,6*).

Discussion

As a subtype of NSCLC, PSC has more aggressive behaviors and worse prognosis than conventional NSCLC. The 5-year survival rate of PSC was reported to be from 20.1% to 36.7% (6,15-17). The accurate diagnosis of PSC requires histological examination of large tissues (18). Surgery is a mainstay and important treatment, especially

Table 1 characteristics of patients undergoing surgical resection between chemotherapy group and no/unknown chemotherapy group

Characteristic	Before propensity score matching				After propensity score matching			
	Total, N=865	Chemotherapy (%) N=254	No/unknown chemotherapy (%), N=611	P value	Total N=555	Chemotherapy (%), N=213	No/unknown chemotherapy (%), N=342	P value
Age (years)								
0–64	307	124 (40.4)	183 (59.6)	<0.0001	228	91 (39.9)	137 (60.1)	0.674
65–74	299	96 (32.1)	203 (67.9)		229	88 (38.4)	141 (61.6)	
75+	259	34 (13.1)	225 (86.9)		98	34 (34.7)	64 (65.3)	
Gender								
Male	485	143 (29.5)	342 (70.5)	0.930	312	120 (38.5)	192 (61.5)	0.964
Female	380	111 (29.2)	269 (70.8)		243	93 (38.3)	150 (61.7)	
Race								
White	747	221 (29.6)	526 (70.4)	0.914	482	184 (38.2)	298 (61.8)	0.322
Black	77	21 (27.3)	56 (72.7)		50	17 (34.0)	33 (66.0)	
Others	41	12 (29.3)	29 (70.7)		23	12 (52.2)	11 (47.8)	
Year of diagnosis								
2004–2008	321	81 (25.2)	240 (74.8)	0.040	182	71 (39.6)	110 (60.4)	0.689
2009–2016	544	173 (31.8)	371 (68.2)		373	141 (37.8)	232 (62.2)	
Grade								
III + IV	620	199 (32.1)	421 (67.9)	0.005	419	164 (39.1)	255 (60.9)	0.517
Others	245	55 (22.4)	190 (77.6)		136	49 (36.0)	87 (64.0)	
Histology								
Pleomorphic carcinoma	228	73 (32.0)	155 (68.0)	0.509	147	60 (40.8)	87 (59.2)	0.912
Giant cell and spindle cell carcinoma	13	4 (30.8)	9 (69.2)		7	2 (28.6)	5 (71.4)	
Giant cell carcinoma	78	26 (33.3)	52 (66.7)		57	23 (40.4)	34 (59.6)	
Spindle cell carcinoma, NOS	104	22 (21.2)	82 (78.8)		60	20 (33.3)	40 (66.7)	
Pulmonary blastoma	23	7 (30.4)	16 (69.6)		14	6 (42.9)	8 (57.1)	
Carcinosarcoma, NOS	107	34 (31.8)	73 (68.2)		70	29 (41.4)	41 (58.6)	
Sarcomatoid carcinoma	312	88 (28.2)	224 (71.8)		200	73 (36.5)	127 (63.5)	

Table 1 (*continued*)

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Characteristic	Before propensity score matching				After propensity score matching			
	Total, N=865	Chemotherapy (%) N=254	No/unknown chemotherapy (%), N=611	P value	Total N=555	Chemotherapy (%), N=213	No/unknown chemotherapy (%), N=342	P value
Surgery type								
Sublobular resection	163	28 (17.2)	135 (82.8)	0.001	78	26 (33.3)	52 (66.7)	0.372
Lobectomy	607	188 (31.0)	419 (69.0)		418	166 (39.7)	252 (60.3)	
Pneumonectomy	90	36 (40.0)	54 (60.0)		58	20 (34.5)	38 (65.6)	
Not otherwise specified	5	2 (40.0)	3 (60.0)		1	1 (100.0)	0 (0.0)	
Tumor size								
≤4 cm	419	89 (21.2)	330 (78.8)	<0.0001	60	17 (28.3)	43 (71.7)	0.224
>4 cm	416	156 (37.5)	260 (62.5)		479	189 (39.5)	290 (60.5)	
Non-specific	30	9 (30.0)	21 (70.0)		16	7 (43.8)	9 (56.3)	
Disease stage								
I	299	37 (12.3)	263 (87.7)	<0.0001	170	32 (18.8)	138 (81.2)	<0.0001
II	225	86 (38.2)	139 (61.8)		155	74 (47.7)	81 (52.3)	
III	227	97 (42.7)	130 (57.3)		160	83 (51.9)	77 (48.1)	
IV	87	24 (27.6)	63 (72.4)		54	18 (33.3)	36 (66.7)	
Unknown	27	10 (37.0)	17 (63.0)		16	6 (37.5)	10 (62.5)	

NOS, not otherwise specified.

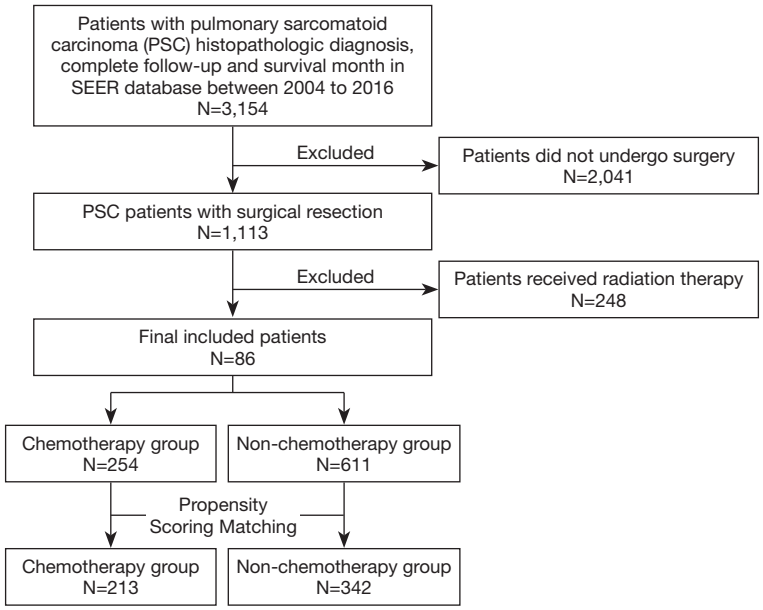

Figure 1 A flow diagram for selection of study population.

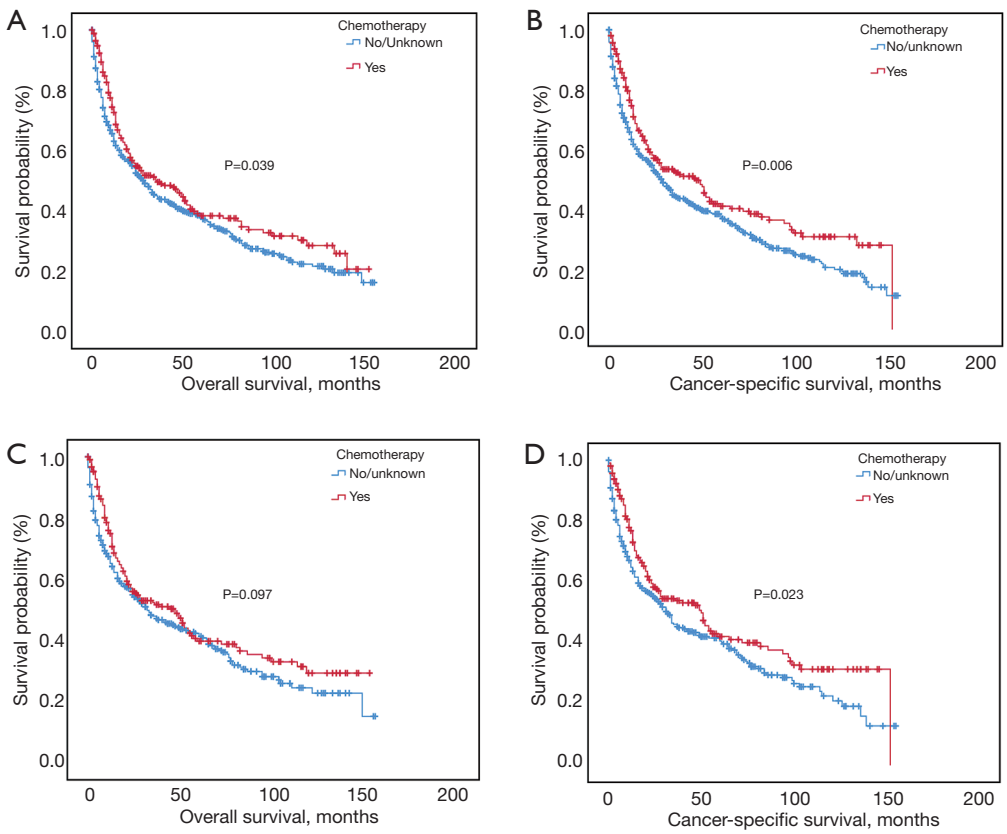

Figure 2 Overall survival and cancer-specific survival of patients according to chemotherapy treatment before (A,B) and after (C,D) PSM. PSM, propensity score matching.

Table 2 Univariate and multivariate Cox proportional Hazard analyses for the overall survival in pulmonary sarcomatoid carcinoma patients before propensity score matching

	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% confidence interval)	P value	Hazard ratio (95% confidence interval)	P value
Age (years)				
0–64	Reference		Reference	
65–74	1.496 (1.208–1.854)	<0.0001	1.648 (1.320–2.057)	<0.0001
75+	2.184 (1.764–2.705)	<0.0001	2.151 (1.714–2.700)	<0.0001
Gender				
Male	Reference		Reference	
Female	0.779 (0.656–0.925)	0.004	0.832 (0.697–0.993)	0.042
Race				
White	Reference			
Black	1.057 (0.789–1.415)	0.712		
Others	1.007 (0.668–1.518)	0.973		
Year of diagnosis				
2004–2008	Reference			
2009–2016	1.112 (0.913–1.329)	0.242		
Grade				
III + IV	Reference		Reference	
Others	0.801 (0.662–0.970)	0.023	0.789 (0.648–0.961)	0.019
Histology				
Pleomorphic carcinoma	Reference			
Giant cell and spindle cell carcinoma	1.397 (0.711–2.746)	0.332		
Giant cell carcinoma	1.095 (0.794–1.509)	0.582		
Spindle cell carcinoma, NOS	0.984 (0.735–1.317)	0.913		
Pulmonary blastoma	0.484 (0.254–0.920)	0.027		
Carcinosarcoma, NOS	0.934 (0.695–1.255)	0.651		
Sarcomatoid carcinoma	1.157 (0.929–1.440)	0.193		
Surgery type				
Sublobular resection	Reference			
Lobectomy	0.692 (0.561–0.854)	0.001		
Pneumonectomy	0.848 (0.618–1.162)	0.304		
Tumor size				
≤4 cm	Reference			
>4 cm	1.403 (1.179–1.668)	<0.0001		

Table 2 (*continued*)

Table 2 (*continued*)

	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% confidence interval)	P value	Hazard ratio (95% confidence interval)	P value
Disease stage				
I	Reference		Reference	
II	1.275 (1.008–1.612)	0.043	1.224 (0.896–1.672)	0.204
III	2.059 (1.648–2.573)	<0.0001	2.135 (1.573–2.898)	<0.0001
IV	5.279 (4.010–6.949)	<0.0001	4.766 (3.524–6.445)	<0.0001
Chemotherapy status				
No/unknown	Reference		Reference	
Yes	0.819 (0.676–0.993)	0.042	0.718 (0.579–0.890)	0.003

NOS, not otherwise specified.

Table 3 Univariate and multivariate Cox proportional hazard analyses for cancer-specific survival in pulmonary sarcomatoid carcinoma patients before propensity score matching

	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% confidence interval)	P value	Hazard ratio (95% confidence interval)	P value
Age (years)				
0–64	Reference		Reference	
65–74	1.463 (1.183–1.809)	<0.0001	1.530 (1.229–1.907)	<0.0001
75+	2.059 (1.663–2.551)	<0.0001	1.980 (1.580–2.482)	<0.0001
Gender				
Male	Reference			
Female	0.812 (0.684–0.965)	0.018		
Race				
White	Reference			
Black	0.926 (0.682–1.258)	0.624		
Others	0.788 (0.498–1.247)	0.309		
Year of diagnosis				
2004–2008	Reference		Reference	
2009–2016	1.454 (1.208–1.749)	<0.0001	1.453 (1.203–1.757)	<0.0001
Grade				
III + IV	Reference			
Others	0.853 (0.707–1.030)	0.098		

Table 3 (*continued*)

Table 3 (*continued*)

	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% confidence interval)	P value	Hazard ratio (95% confidence interval)	P value
Histology				
Pleomorphic carcinoma	Reference			
Giant cell and spindle cell carcinoma	1.144 (0.534–2.449)	0.730		
Giant cell carcinoma	1.082 (0.780–1.501)	0.637		
Spindle cell carcinoma, NOS	1.038 (0.776–1.388)	0.804		
Pulmonary blastoma	0.548 (0.296–1.015)	0.056		
Carcinosarcoma, NOS	0.914 (0.676–1.236)	0.559		
Sarcomatoid carcinoma	1.242 (0.996–1.548)	0.054		
Surgery type				
Sublobular resection	Reference			
Lobectomy	0.645 (0.525–0.793)	<0.0001		
Pneumonectomy	0.694 (0.501–0.962)	0.028		
Tumor size				
≤4 cm	Reference		Reference	
>4 cm	1.389 (1.167–1.652)	<0.0001	1.321 (1.019–1.712)	0.036
Disease stage				
I	Reference		Reference	
II	1.120 (0.886–1.416)	0.344	1.037 (0.757–1.420)	0.823
III	1.8873 (1.502–2.334)	<0.0001	1.886 (1.385–2.567)	<0.0001
IV	4.846 (3.684–6.373)	<0.0001	4.557 (3.374–6.154)	<0.0001
Chemotherapy status				
No/unknown	Reference		Reference	
Yes	0.762 (0.627–0.927)	0.007	0.662 (0.533–0.823)	<0.0001

NOS, not otherwise specified.

for PSC at early stages. Surgical methods include sublobar resection, lobectomy and pneumonectomy. Sublobar resection is composed of segmentectomy and wedge resection. Compared with pneumonectomy, lobectomy has the same therapeutic effects with better preservation of lung functions for NSCLC patients. For elderly patients with early stage NSCLC, sublobar resection achieves equivalent therapeutic outcomes compared with lobectomy. Considerable research has demonstrated that surgery promotes the survival of PSC patients. Retrospective analysis of 69 PSC patients by Lin *et al.* found that good prognosis was associated with complete resection (P<0.05) (11). A more recent study reported that the median OS of PSC patients with complete surgical resection was better than that of PSC patients without surgery [16.4 months (95% CI: 6.1 to not reached] *vs.* 3 months [95% CI: 2.1–5 months)] (6). However, PSC had a high recurrence (up to 70%) after operative treatment, and

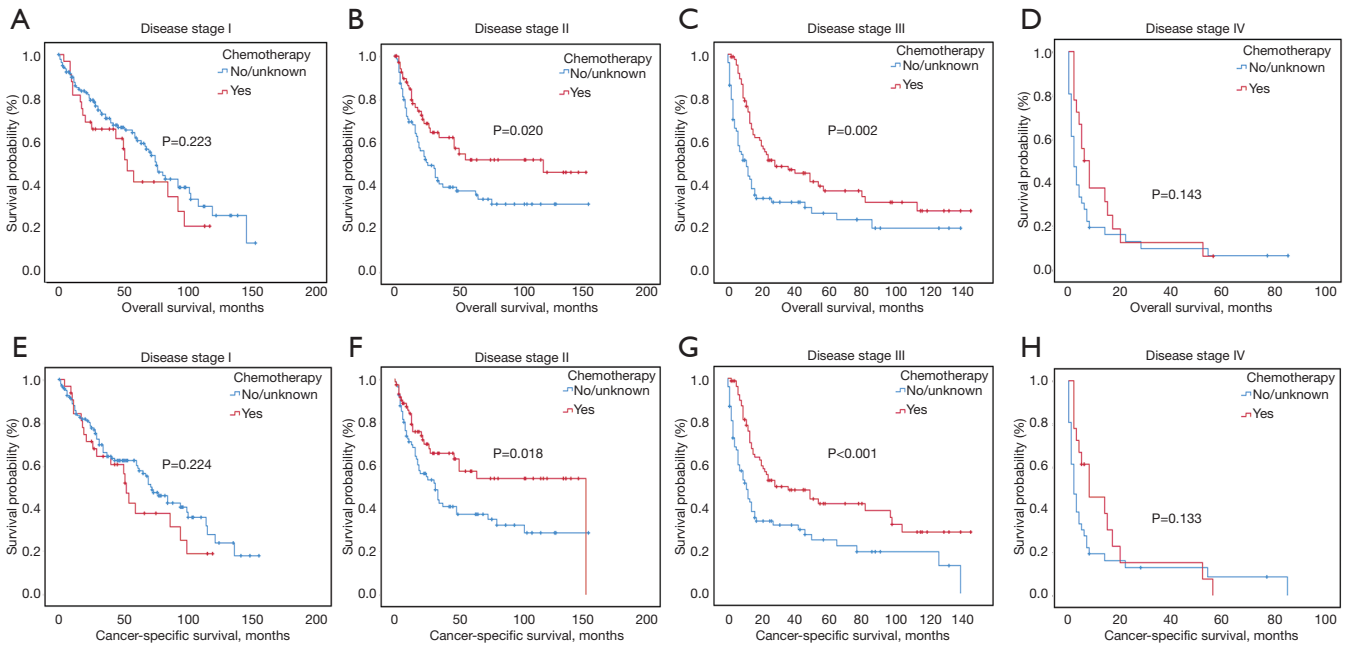

Figure 3 Univariate Kaplan-Meier analysis on overall survival and cancer-specific survival of PSC patients atin different stages:. Stage I (A,E); Stage II (B,F); Stage III (C,G); Stage IV (D,H). PSC, pulmonary sarcomatoid carcinoma.

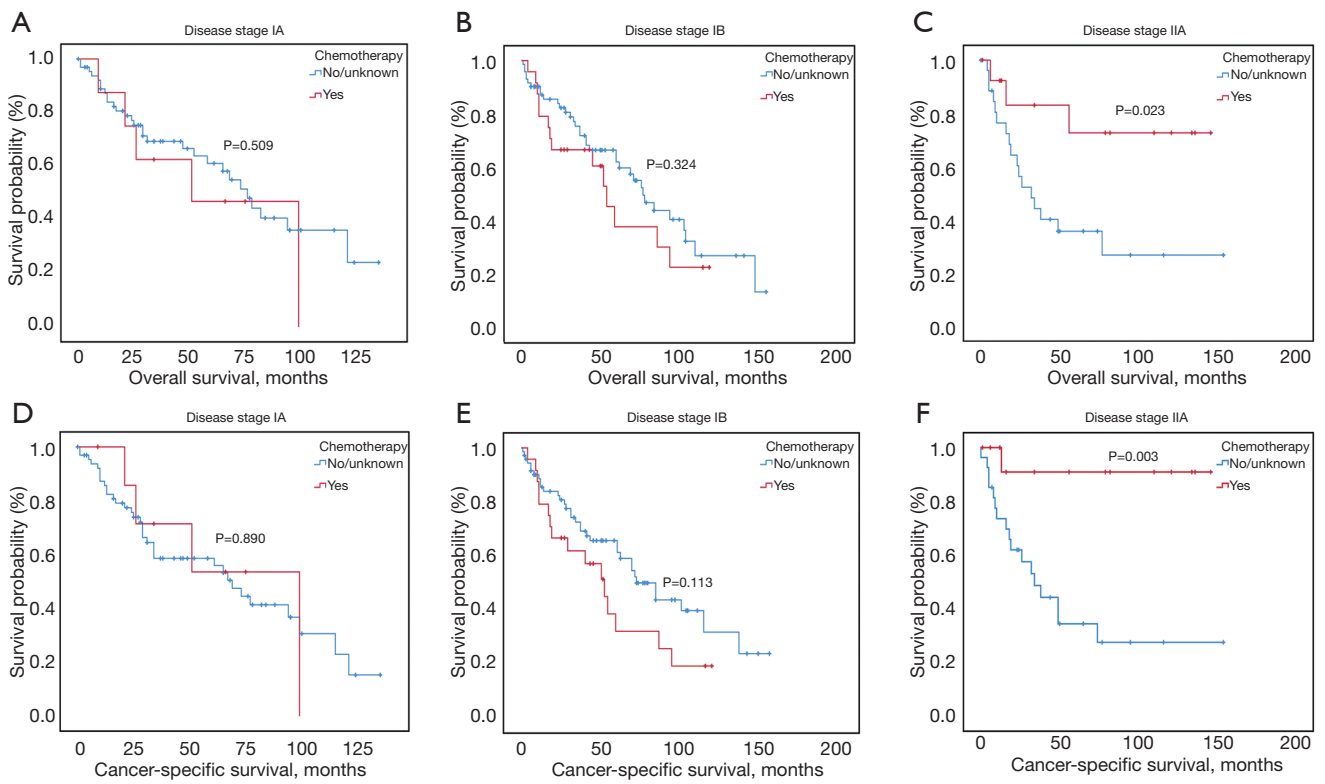

Figure 4 Subgroup Kaplan-Meier analysis on overall survival and cancer-specific survival of PSC patients inat different stages:. Stage IA (A,D); Stage IB (B,E); Stage IIA (C,F). PSC, pulmonary sarcomatoid carcinoma.

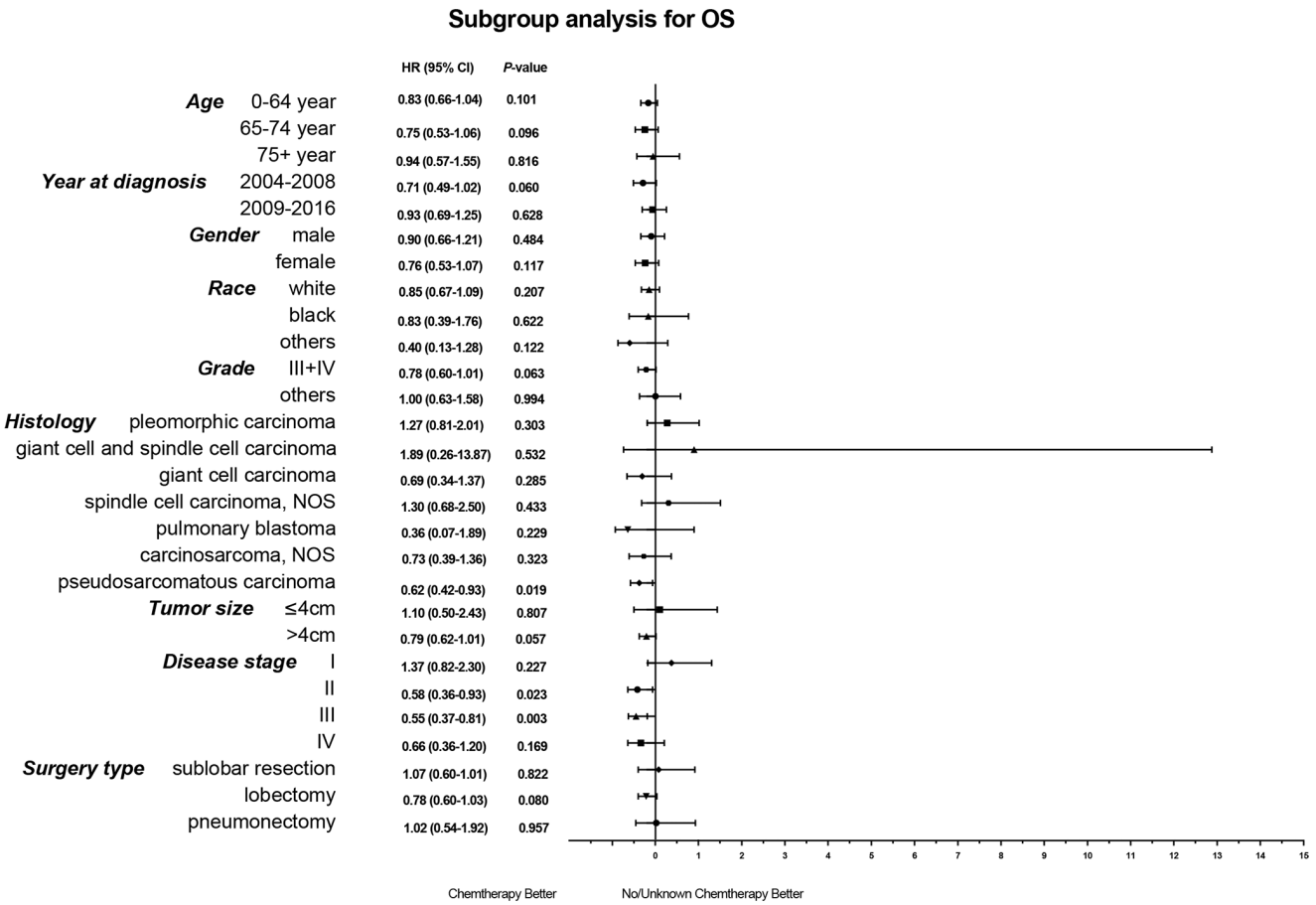

Figure 5 Subgroup Cox proportional hazard analysis on overall survival of PSC patients according to chemotherapy status. PSC, pulmonary sarcomatoid carcinoma; NOS, not otherwise specified.

distant metastasis was found more frequently than local metastasis (3,6,19). To improve PSC prognosis, combined therapy should be considered. In consideration of recurrence and metastasis, we conjectured that perioperative chemotherapy would have a better performance in efficacy than radiotherapy. However, it was still controversial whether additional chemotherapy was an independent factor for good prognosis in PSC patients or not (*Table 4*) (3,6,8,9,11-13,20). Our studies suggested the therapeutic values of perioperative chemotherapy for PSC patients.

In our study, most patients were male, in their 60s and classified as pleomorphic carcinoma. A total of 254 patients received chemotherapy, most of whom were younger, earlier diagnosed, with lower histology grade, larger tumor size, advance stage and had received lobectomy. Surprisingly, only 40% patients at stages II and III received chemotherapy, which might be associated with negative results of previous studies. We examined the temporal trends, excluding an overrepresentation from an earlier era. Our results suggested that chemotherapy improved the survival of PSC patients with surgery, supporting the results of previous small sample studies. We used both Cox proportional hazard model and PSM model to compare the OS and CSS between chemotherapy and no/unknown chemotherapy patients. In the PSM model, perioperative chemotherapy only showed an OS advantage with no statistical significance, perhaps due to the other uncontrolled confounding factors or limited sample sizes. To explore the proper patients, subgroup analysis was performed further. Our data suggested that patients at stage II and III with perioperative chemotherapy had a significant improvement in the OS and CSS. In a more detailed subgroup analysis, we observed a survival benefit in patients at stage IIA, but not at earlier stages (IA and IB).

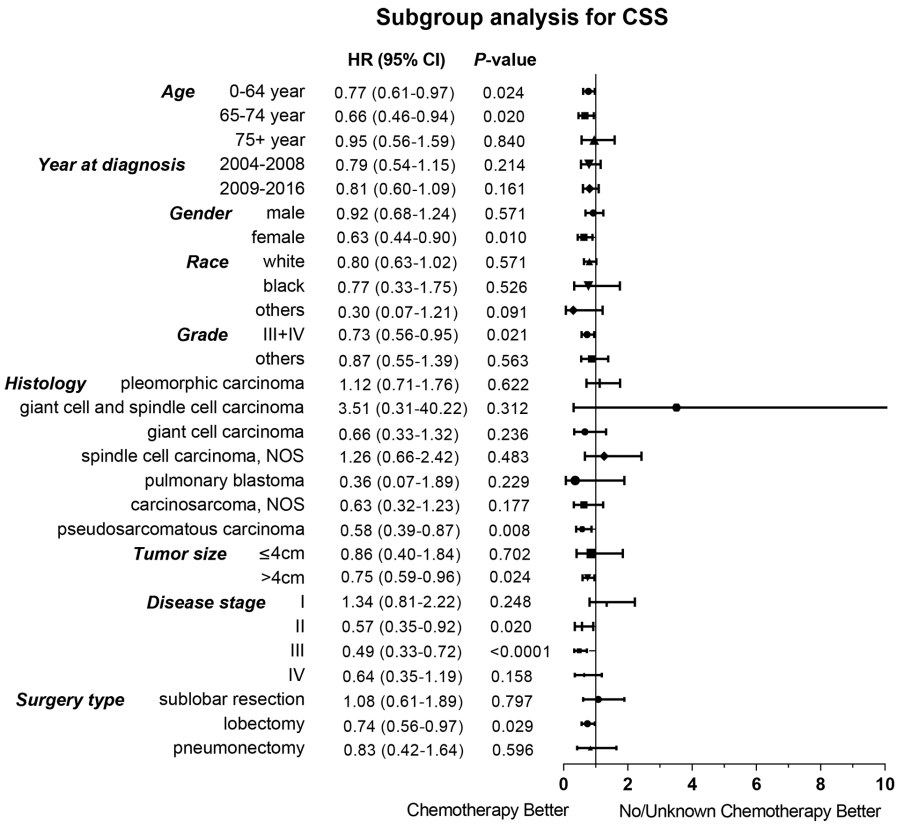

Figure 6 Subgroup Cox proportional hazard analysis on cancer-specific survival of PSC patients according to chemotherapy status. PSC, pulmonary sarcomatoid carcinoma; NOS, not otherwise specified.

It is interesting that patients at stage I, receiving sublobar resection and histological classified as "pleomorphic carcinoma", "giant cell and spindle cell carcinoma" and "spindle cell carcinoma, NOS" tend to have a worse prognosis after additional chemotherapy. The National Comprehensive Cancer Network (NCCN) clinical practice guideline in NSCLC recommended chemotherapy for NSCLC patients undergoing surgical resection and with stages IB, II and III diseases. Compared to conventional NSCLC, PSC seemed to be moderately sensitive to chemotherapy.

Our finding is contradictory with some of the literature. A published study by Karim *et al.* showed that patients with surgery alone had the best median OS of 713.5 days, longer than 457.6 days of the ones with additional chemotherapy (12). Another study reported that 99 patients received chemotherapy after surgery, but no obvious survival advantage was provided by adjuvant chemotherapy (3). The response to perioperative chemotherapy was poor in the Ung *et al.* study (6). All these previous studies were retrospective. Perioperative chemotherapy performed in patients who had higher clinical stages or other confounders were not balanced. Our research used the PSM model to balance baseline characteristics, and subgroup analysis were performed to control confounding factors.

Our study is one of retrospective studies with the largest patient population , and the first to use a PSM cohort to minimize confounding factors in PSC. However, we were aware of several limitations. First, as a retrospective study, it was unavoidable to have some biases on patient selection, although we used PSM to minimize confounding Second, the SEER database lacked general condition/performance status for true matching. Finally, our analysis was only based on the available data in one database. The number of cases in subgroup analysis was limited. Further clinical prospective trails are needed to confirm the findings of our

Table 4 Summary of additional chemotherapy effect on pulmonary sarcomatoid carcinoma patients undergoing surgery

Author	Year	Number	Time	Histology	Treatment	Outcome
Hendriksen *et al.*	2019	1408	2004–2015	Lung pleomorphic carcinoma	For stage I, 253 treated with surgery alone and 57 surgery with chemotherapy	Perioperative chemotherapy is associated with no survival advantage for stage I† pleomorphic carcinoma
Maneenil *et al.*	2018	127	1997–2015	Pulmonary sarcomatoid carcinoma	37 received surgery only. 3 received neo-adjuvant chemotherapy before surgery and 9 received adjuvant chemotherapy after surgery.	the median survival was prolonged with surgery plus neo-adjuvant/adjuvant chemotherapy, but have no statistically difference between with the patients treated with surgery alone and supportive care
Karim *et al.*	2018	25	2000–2014	Pulmonary sarcomatoid carcinoma	10 received surgery only. 3 underwent surgery and systemic chemotherapy	Adjuvant chemotherapy did not show a significant improvement in outcome than only surgical resection
Lococo *et al.*	2017	142	2003–2013	Pulmonary sarcomatoid carcinoma	All patients underwent curative resection. 99 patients received adjuvant chemotherapy after surgery.	Adjuvant chemotherapy did not show any survival advantage
Ung *et al.*	2016	93	2000–2012	Pulmonary sarcomatoid carcinoma	41 underwent surgery and 10 patients received adjuvant chemotherapy	Adjuvant chemotherapy have not significant influence on survival time
Lin *et al.*	2016	69	1991–2011	Pulmonary sarcomatoid carcinoma	61 received surgery, 4 received neo-adjuvant chemotherapy, 22 adjuvant chemotherapy, 5 received chemotherapy	Perioperative chemotherapy showed no overall survival benefit
Huang *et al.*	2013	51	2005–2012	Pulmonary sarcomatoid carcinoma	37 patients underwent surgery. After surgery, 19 cases received chemotherapy	postoperative adjuvant chemotherapy might result in better prognosis
Chaft *et al.*	2012	56	2000–2010	Pulmonary sarcomatoid carcinoma	All patients underwent R0 resection. Among these, 20 received perioperative chemotherapy (17 neoadjuvant, 5 adjuvant)	Perioperative chemotherapy should be considered in stage IIb†–IIIa† patients but not in stage Ia†–IIa† patients

†, according to AJCC 7th edition TNM staging system.

study.

Conclusions

Chemotherapy benefits stages II and III PSC patients undergoing surgical resection. Additional chemotherapy should be considered for PSC patients at stages II and III, especially for the patients with young age, female gender, poor differentiation or undifferentiated histology, large tumor size and lobectomy surgical resection.

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Footnote

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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. Since any information in the SEER database was anonymized data, no ethical approval requirements were needed in our study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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