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Pulmonary carcinosarcoma: analysis from the Surveillance, Epidemiology and End Results database

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Key question

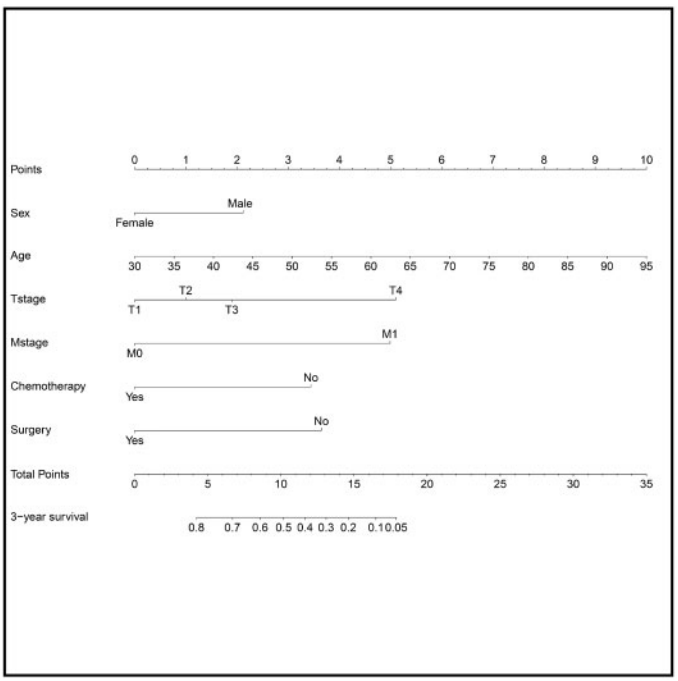
What were the prognostic factors and optimal treatment of pulmonary carcinosarcoma (PCS)?

Key finding(s)

Amongst elderly (aged ≥ 70 years) surgically treated patients, pneumonectomy (HR: 5.14; 95% CI: 1.64-16.07) was associated with poorer outcomes compared to lobectomy.

Take-home message

Men, age, T-stage, M-stage, surgery and chemotherapy were significantly associated with the overall survival of patients with PCS.



Abstract

OBJECTIVES: Pulmonary carcinosarcoma (PCS) is a rare neoplasm. This study explored the clinicopathological characteristics and survival outcomes of PCS.

METHODS: The Surveillance, Epidemiology and End Results (SEER) database (1988–2014) was queried for PCS. Overall survival (OS) was evaluated by multivariable Cox regression and nomograms were constructed to predict 3-year OS for PCS. Prognostic performance was evaluated using concordance index and area under the curve analysis. In M0 surgically treated patients, interaction assessments were

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performed using likelihood ratio tests. Subgroup analysis was performed according to patient age. The clinical features of PCSs were further compared to other non-small-cell lung cancers (NSCLCs).

RESULTS: Multivariable analysis identified age [hazard ratio (HR) 1.03, 95% confidence interval (CI) 1.01–1.04], surgery (HR 0.53, 95% CI 0.36–0.77) and chemotherapy (HR 0.51, 95% CI 0.36–0.73) as significantly associated with OS. The nomogram had a concordance index of 0.747 and an area under the curve of 0.803. The association between age and OS was stronger in those receiving pneumonectomy ($P = 0.04$ for interactions) compared to those that did not (HR 5.14, 95% CI 1.64–16.07), and was associated with a poorer outcome compared to lobectomy amongst the elderly (age ≥ 70 years). Patients with PCS were more likely to receive surgical treatment and had lower lymphatic metastasis compared to adenocarcinoma, squamous cell carcinoma and large cell carcinoma (all $P < 0.05$).

CONCLUSIONS: PCS had unique clinical features compared to common types of NSCLCs in terms of lymphatic invasion and surgical treatment. Pneumonectomy was associated with poorer survival in elderly patients.

Keywords: Pulmonary carcinosarcoma • Chemotherapy • Nomogram • Age • Surgical treatment

ABBREVIATIONS

AJCC	American Joint Committee on Cancer
CI	Confidence interval
HR	Hazard ratio
MVA	Multivariable analysis
NSCLC	Non-small-cell lung cancer
OS	Overall survival
PCS	Pulmonary carcinosarcoma
SEER	Surveillance, Epidemiology and End Results
TNM	Tumour, node and metastasis
WHO	World Health Organization

INTRODUCTION

Pulmonary carcinosarcoma (PCS) is a rare lung tumour characterized by a biphasic histopathological pattern consisting of both malignant epithelial and sarcomatous mesenchymal elements [1, 2] with a poor prognosis [3, 4]. The recent 2015 World Health Organization (WHO) classification defined PCS as a subtype of sarcomatoid carcinoma which was poorly differentiated [5]. The diagnosis of PCS is often complicated due to a lack of definitive and characteristic imaging findings; and the heterogeneity of PCS raises different diagnostic considerations. Small biopsies are generally unable to capture both the epithelial and sarcomatous components of the tumour [6]. Prompt and accurate diagnosis is essential as the tumour can progress from asymptomatic to life threatening over a short time period. Due to its rarity, the clinicopathological characteristics and survival outcomes of PCS are not fully understood. Previous studies have involved only a small case series which primarily focused on pathological descriptions [7–10]. Only a small number of retrospective studies have attempted to characterize this rare tumour [11, 12]. In this study, we reviewed a large database with the aim of improving our understanding of the clinicopathological characteristics of PCS to identify factors that affect survival outcomes with the intent to guide clinical practice.

MATERIALS AND METHODS

Ethical statement

We signed the Surveillance, Epidemiology and End Results (SEER) Research Data Agreement for access to the SEER data. The study was approved by the Ethics Committee and Institutional Review Board of Shanghai Pulmonary Hospital, Tongji University.

Study population

Patient data were obtained from the SEER database. Research data from 18 population-based cancer registries and the Hurricane Katrina impacted Louisiana cases from 1973 to 2014 that covers ∼27.8% of the population of the USA were obtained. Inclusion criteria were as follows: site recode ICD-O-3/WHO 2008 (International Classification of Diseases for Oncology, 3rd Edition) was restricted to 'Lung and Bronchus'; patients with single primary tumours; pathologically confirmed PCS [ICD-O-3 (8980/3)]; known age and survival data. Patients diagnosed before 1988 were excluded due to previous classification methods prior to 1988. Patients with incomplete tumour, node and metastasis (TNM) stage data were also excluded. Finally, 262 patients were included.

Covariates

Covariates included age, race, sex, grade, T stage, N stage, M stage, surgical status (non-surgery, sublobar resection, lobectomy or pneumonectomy), radiation, chemotherapy and survival data. For different criteria of the American Joint Committee on Cancer (AJCC) stage in the SEER database during the study period, the TNM stage was reclassified according to the AJCC 8th edition [13].

Statistical analysis

Continuous variables were presented as the mean ± standard deviation and were compared using the *t*-tests. Categorical variables were reported as numbers (frequency percentages) and compared using the χ^2 test. Cox proportional hazard ratios (HRs) were calculated to identify variables associated with both overall survival (OS) and cancer-specific survival. All clinically relevant variables were included in multivariable analysis (MVA). Based on the MVA of OS, significant variables ($P < 0.05$) were selected to construct the nomograms [14]. Three-year OS was estimated through the addition of points corresponding to the patient's characteristics. The *c*-index measures the ability of discrimination and ranges from 0.5 to 1.0. A larger *c*-index indicates greater accuracy for prognosis predictions [15]. Calibration plots were performed by regression analysis to compare predicted and OS [16, 17]. We further compared the clinicopathological

Table 1: Comparison between PCSs and other NSCLCs

Variables	PCS (*N* = 262)	Adenocarcinoma (*N* = 188 585)	Squamous cell carcinoma (*N* = 105 601)	Large cell carcinoma (*N* = 16 192)
Age (years), mean (SD)	66.73 (11.29)	66.39 (11.47)**	68.93 (9.88)*	66.07 (11.04)
Sex, *n* (%)				
Male	147 (56.1)	91 755 (48.7)*	68 381 (64.8)*	9638 (59.5)
Female	115 (43.9)	96 830 (51.3)	37 220 (35.2)	6554 (40.5)
Race, *n* (%)				
White	216 (82.4)	152 422 (80.8)*	87 126 (82.5)	13 186 (81.4)
Black/other	46 (17.6)	36 163 (19.2)	18 475 (17.5)	3006 (18.6)
Grade, *n* (%)				
Mild/moderately differentiated	99 (37.8)	112 786 (59.8)**	72 620 (68.8)**	4575 (28.3)**
Undifferentiated	163 (62.2)	75 799 (40.2)	32 981 (31.2)	11 617 (71.7)
T stage, *n* (%)				
T1	29 (11.1)	51 051 (27.1)**	18 830 (17.8)*	2323 (14.3)**
T2	69 (26.3)	49 166 (26.1)	26 924 (25.5)	2979 (18.4)
T3	44 (16.8)	17 330 (9.2)	15 525 (14.7)	1593 (9.8)
T4	120 (45.8)	71 038 (37.7)	44 322 (42.0)	9297 (57.4)
N stage, *n* (%)				
N negative	155 (59.2)	90 152 (47.8)**	48 265 (45.7)**	6306 (38.9)**
N positive	107 (40.8)	98 433 (52.2)	57 336 (54.3)	9886 (61.1)
M stage, *n* (%)				
M0	193 (73.7)	112 314 (59.6)**	75 877 (71.9)	9631 (59.5)**
M1	69 (26.3)	76 271 (40.4)	29 724 (28.1)	6561 (40.5)
Surgery status, *n* (%)				
No	88 (33.6)	113 846 (60.4)**	69 727 (66.0)**	11 575 (71.5)**
Yes	174 (66.4)	74 739 (39.6)	35 874 (34.0)	4617 (28.5)
Radiation, *n* (%)				
No	170 (64.9)	121 501 (64.4)	57 109 (54.1)**	8056 (49.8)**
Yes	92 (35.1)	67 084 (35.6)	48 492 (45.9)	8136 (50.2)
Chemotherapy, *n* (%)				
No	180 (68.7)	115 968 (61.5)*	67 650 (64.1)	10 278 (63.5)
Yes	82 (31.3)	72 617 (38.5)	37 951 (35.9)	5914 (36.5)

*P-value <0.05 and **P-value <0.001 when compared to pulmonary carcinosarcoma.
NSCLC: non-small-cell lung cancer; PCS: pulmonary cacinosarcoma; SD: standard deviation.

characteristics of 262 PCS patients with those of 188 585 patients with adenocarcinoma, 105 601 with squamous cell carcinoma and 10 222 with large cell carcinoma and met the PCS inclusion criteria. Interaction assessments were performed using likelihood ratio tests. Models were compared with and without cross product terms using age as a binary variable and other baseline variables. Statistical analysis was performed using R version 3.5.3 software (http://www.r-project.org/).

RESULTS

Demographics and clinicopathological data

A total of 262 PCS patients were identified, including 147 men and 115 women, with a mean age of 66 years (Table 1). The majority (82.4%) were Caucasian, with poorly differentiated tumours the most common (62.2%). Most were N negative (59.2%) and M0 (73.7%).

Subgroup analysis was performed on the year of PCS diagnosis, represented by 2 historical periods, early (1988–2003) versus late (2004–2014). The early time period had 125 (47.7%) patients and the late time period had 137 (52.3%) patients. More patients with PCS during the late period had M1 disease (34.1% vs 9.8%; $P < 0.001$) and received chemotherapy (42.1% vs 17.9%; $P < 0.001$).

Survival analysis in pulmonary carcinosarcoma

The median OS of the 262 PCS patients was 9 months [95% confidence interval (CI) 7–12], and 3- and 5-year survival rates were 27.1% and 21.0%, respectively. A total of 216 patients died during the follow-up, of which 176 deaths were cancer-specific and 40 were due to other causes including chronic obstructive pulmonary disease and heart disease. The predictors of OS in PCS according to MVA included age (HR 1.03, 95% CI 1.01–1.04), chemotherapy (HR 0.51, 95% CI 0.36–0.73) and surgery (HR 0.53, 95% CI 0.36–0.77) and were significantly associated with cancer-specific survival (Table 2).

The nomogram to predict 3-year OS was created based on significant prognostic variables (Fig. 1), resulting in a *c*-index of 0.747 and an area under the curve of 0.803 for 3-year OS, demonstrating good discriminative ability. The accuracy of the model was assessed by bootstrap validation after resampling in 200 individuals. The 60-sample bootstrapped calibration plots for the prediction of 3-year OS are shown in Fig. 2, showing a high consistency between predicted survival probability and actual survival proportions.

Due to the long study period, we examined the influence of time of PCS diagnosis on the treatment received and patient survival. The median OS in PCS patients during the early time period was 8 (95% CI 7–12) months, compared to 10 months (95% CI 7–14) during the late time period ($P = 0.08$). Patients receiving

Table 2: Univariable and multivariable Cox proportional hazards models for overall survival and cancer-specific survival for PCS

Variables	Univariable analysis		Multivariable analysis	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Overall survival				
Sex (male, *N* = 147)	1.33 (1.02–1.75)	0.04	1.51 (1.13–2.02)	0.005
Age (years)	1.03 (1.02–1.04)	<0.001	1.03 (1.01–1.04)	<0.001
Race (black/other, *N* = 46)	0.65 (0.45–0.95)	0.03	0.76 (0.52–1.13)	0.18
Grade (undifferentiated, *N* = 163)	1.19 (0.90–1.58)	0.214	1.00 (0.74–1.35)	0.98
T stage				
T1 (*N* = 29)	Reference		Reference	
T2 (*N* = 69)	1.13 (0.69–1.84)	0.64	1.24 (0.75–2.06)	0.41
T3 (*N* = 44)	1.05 (0.61–1.80)	0.87	1.34 (0.76–2.35)	0.31
T4 (*N* = 120)	2.43 (1.54–3.83)	<0.001	2.53 (1.55–4.13)	<0.001
N stage (positive, *N* = 107)	1.78 (1.36–2.35)	<0.001	1.17 (0.85–1.62)	0.32
M stage (M1, *N* = 69)	3.50 (2.58–4.74)	<0.001	2.43 (1.68–3.53)	<0.001
Chemotherapy (*N* = 82)	0.76 (0.56–1.02)	0.07	0.51 (0.36–0.73)	<0.001
Radiation (*N* = 92)	1.76 (1.33–2.34)	<0.001	1.09 (0.77–1.54)	0.62
Surgery (*N* = 174)	0.33 (0.25–0.45)	<0.001	0.53 (0.36–0.77)	0.001
Cancer-specific survival				
Sex (male, *N* = 147)	1.33 (0.98–1.79)	0.06	1.43 (1.04–1.96)	0.03
Age (years)	1.02 (1.01–1.04)	<0.001	1.02 (1.01–1.04)	<0.001
Race (black/other, *N* = 46)	0.68 (0.44–1.03)	0.07	0.76 (0.49–1.17)	0.22
Grade (undifferentiated, *N* = 163)	1.17 (0.86–1.59)	0.31	0.98 (0.71–1.37)	0.93
T stage				
T1 (*N* = 29)	Reference		Reference	
T2 (*N* = 69)	2.12 (1.10–4.09)	0.03	2.30 (1.17–4.51)	0.02
T3 (*N* = 44)	1.71 (0.83–3.51)	0.14	2.05 (0.98–4.28)	0.06
T4 (*N* = 120)	4.30 (2.29–8.04)	<0.001	4.07 (2.11–7.84)	<0.001
N stage (positive, *N* = 107)	2.21 (1.64–2.99)	<0.001	1.37 (0.97–1.94)	0.07
M stage (M1, *N* = 69)	3.88 (2.81–5.37)	<0.001	2.33 (1.56–3.46)	<0.001
Chemotherapy (*N* = 82)	0.86 (0.63–1.19)	0.36	0.53 (0.37–0.76)	<0.001
Radiation (*N* = 92)	2.08 (1.53–2.82)	<0.001	1.21 (0.84–1.75)	0.31
Surgery (*N* = 174)	0.29 (0.21–0.40)	<0.001	0.65 (0.35–0.79)	0.002

CI: confidence interval; HR: hazard ratio; PCS: pulmonary cacinosarcoma.

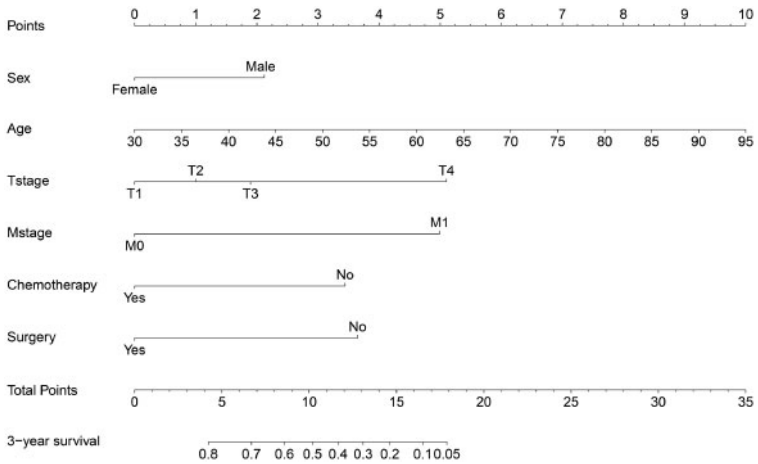

Figure 1: Nomogram to predict the 3-year overall survival rates of patients with pulmonary carcinosarcoma.

surgical treatment showed an improved prognosis compared to those assessed during early (HR 0.36, 95% CI 0.23–0.56) (Fig. 3A) and late time periods (HR 0.26, 95% CI 0.18–0.41; Fig. 3B).

Subgroup analysis of patient age

To elucidate the influence of age on the optimal management of PCS, we analysed the association of age and other potential baseline characteristics for OS in M0 surgically treated patients. The results showed that the association of age and OS were generally similar in subgroups when stratified by sex, race, grade, T stage, N stage, adjuvant chemotherapy and adjuvant radiation. Significant differences across different subgroups were observed for surgical treatment, and patients of a younger age and receiving pneumonectomy ($P = 0.04$ for interaction) acquired an improved OS compared to those receiving other surgical treatments (Fig. 4). In addition, pneumonectomy (HR 5.14, 95% CI 1.64–16.07; Table 3) was associated with poorer survival in elderly patients treated with surgery (age ≥ 70 years).

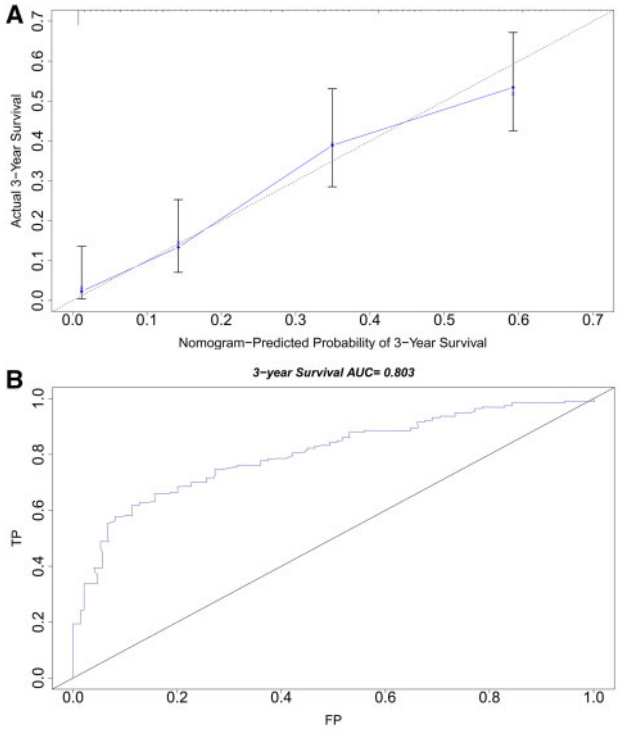

Figure 2: (**A**) Calibration plots of nomogram predictions of 3-year overall survival of PCS patients. Red line: equality of the observed and predicted probability; (**B**) AUC: 0.803 was calculated from the nomogram prognostic model. TP: true positive; FP: false positive.

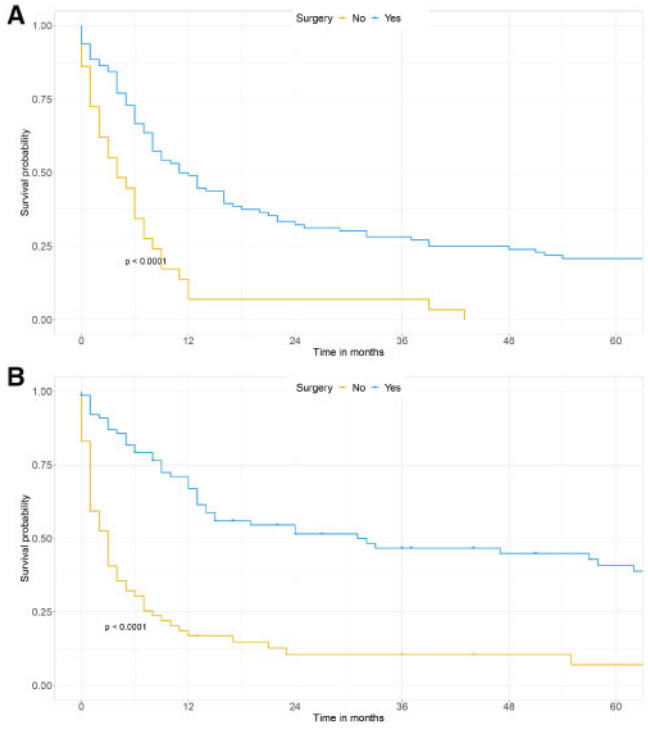

Figure 3: Kaplan–Meier curves of overall survival between surgical treatment and non-surgical treatment during the early time period (**A**) and late time period (**B**).

Comparison of adenocarcinoma, squamous cell carcinoma and large cell carcinoma

More than half (62.2%) of PCSs were poorly differentiated compared to adenocarcinoma (40.2%), squamous cell carcinoma (31.2%) and large cell carcinoma (71.7%, all $P < 0.001$; Table 1). Advanced T stages (T3–4) were more prevalent in PCSs (62.6%) than adenocarcinoma (46.9%) and squamous cell carcinomas (56.7%, both $P < 0.001$). A larger number of PCS patients had node-negative and M0 disease (both $P < 0.05$). In addition, PCS patients were more likely to receive surgical treatment.

DISCUSSION

In this study, we analysed 262 patients in the SEER database and found that males, age, T4 stage, M1 stage, surgery and chemotherapy were independently associated with survival. Nomograms could accurately predict the prognosis of PCS patients. A significant interaction between age and surgical treatment was reported and pneumonectomy was associated with a poorer prognosis in elderly surgically treated patients. PCSs tended to show lower levels of lymphatic metastasis and a higher percentage of surgical resections compared to adenocarcinoma, squamous cell carcinoma and large cell carcinoma.

According to Kakos *et al.* [18], the first reported case was attributed to Kika et al. in 1908 who defined PCS as a poorly differentiated non-small-cell lung cancer (NSCLC) containing a component of sarcoma or sarcoma-like features. The 2004 classification applied by the WHO classed pulmonary sarcomatoid carcinoma into 5 categories, namely pleomorphic carcinoma, spindle cell carcinoma, giant cell carcinoma, carcinosarcoma and pulmonary blastoma [19]. In this cohort, patients with PCS had a median age of 66 years, consistent with the average age of diagnosis of around 60 years reported in a previous study [1].

The 5-year survival rate of the SEER cohort was 21.0%, which is similar to that reported by Koss *et al.* [11] of 21.3%. In 1999, Koss *et al.* [11] retrospectively reviewed 66 PCS patients from the archives of the Armed Forces Institute of Pathology (AFIP) and found that only tumour size (≥6 cm) was related to poorer survival, which may result from the lack of surgical treatment, chemotherapy or radiation therapy during the study. Of note, Petrov *et al.* [12] emphasized the importance of complete surgical resection in PCS patients, showing a favourable cumulative survival rate of 49.38% in surgically treated PCS patients.

Sex, age, T stage, M stage, surgery and chemotherapy were significantly associated with OS in MVA, and nomograms were constructed to predict 3-year OS. Although many prognostic and predictive models had already been established in NSCLC [20] and small cell lung cancer [21], minimal attention was paid to this rare cancer. In this study, we developed a nomogram prognostic model with a *c*-index of 0.747 and an area under the curve of 0.803, indicating a strong predictive ability.

Lobectomy is often considered the standard surgery for the treatment of NSCLC [22]. The interaction between age and surgical treatment suggested that age may be a useful indicator for stratifying patients for the best possible treatment. Subgroup analyses showed that amongst elderly patients, pneumonectomy was associated with a poorer OS compared to lobectomy. Elderly patients showed an increased risk of postoperative death compared to younger patients [23]. Extended lung resection is associated with poorer survival outcomes in elderly patients with NSCLC [24]. Based on this study and previous findings, pneumonectomy is recommended with caution in elderly patients with

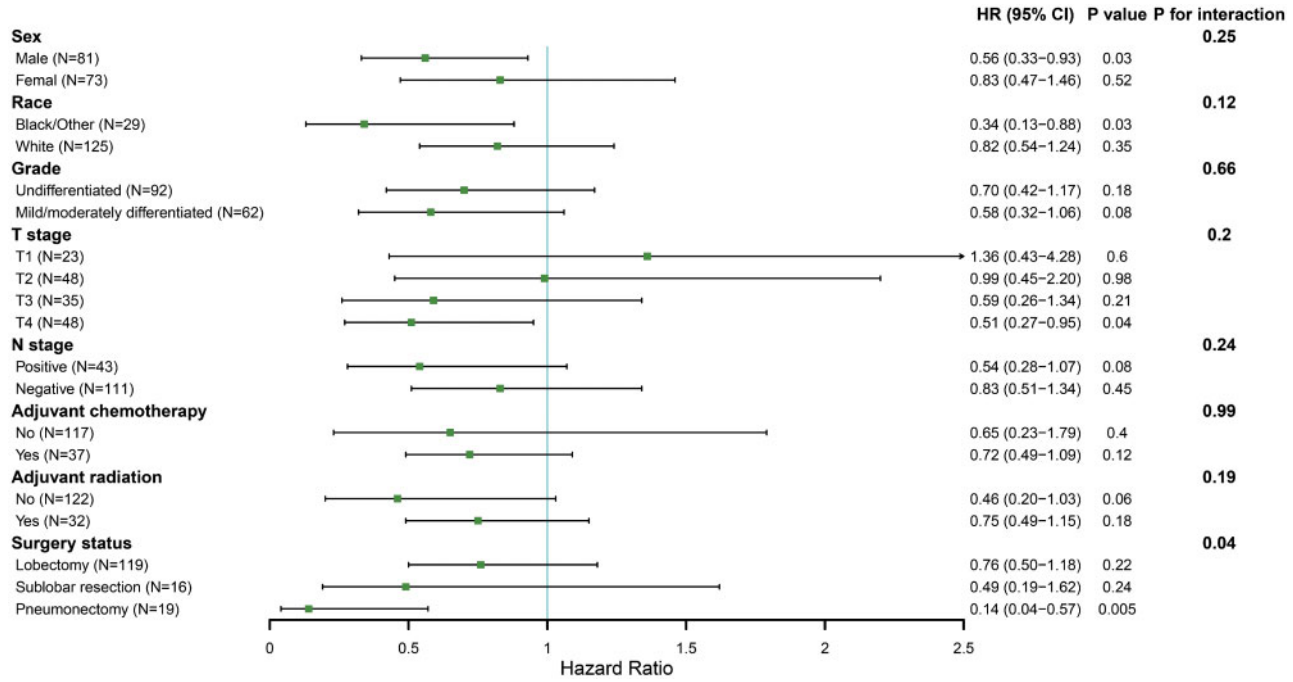

Figure 4: Subgroup analysis of the association between age and other potential baseline characters for overall survival in M0 surgically treated patients. Hazard ratios were calculated for comparison of younger and elderly patients.

Table 3: Univariable and multivariable Cox proportional hazards models for overall survival in subgroup analysis for surgically treated PCS

Variables	Univariable analysis		Multivariable analysis	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Younger patients (*N* = 97)				
Sex (male, *N* = 52)	1.12 (0.79–1.80)	0.64	1.14 (0.68–1.90)	0.63
Race (black/other, *N* = 22)	0.53 (0.29–0.98)	0.05	0.60 (0.31–1.18)	0.14
Grade (undifferentiated, *N* = 63)	1.28 (0.76–1.15)	0.36	1.11 (0.63–1.95)	0.73
T stage				
T1 (*N* = 15)	Reference		Reference	
T2 (*N* = 36)	0.84 (0.43–1.63)	0.60	1.01 (0.49–2.09)	0.97
T3 (*N* = 20)	0.70 (0.31–6.57)	0.39	0.70 (0.30–1.68)	0.43
T4 (*N* = 26)	1.43 (0.70–2.89)	0.32	1.94 (0.86–4.38)	0.11
N stage (positive, *N* = 23)	1.39 (0.80–2.41)	0.24	1.11 (0.63–1.95)	0.73
Adjuvant chemotherapy (*N* = 28)	0.65 (0.36–1.15)	0.14	0.44 (0.23–0.88)	0.02
Adjuvant radiation (*N* = 20)	1.50 (0.84–2.69)	0.17	1.66 (0.83–3.30)	0.15
Surgery status				
Lobectomy (*N* = 72)	Reference		Reference	
Sublobar resection (*N* = 11)	1.55 (0.78–3.05)	0.21	1.70 (0.83–3.45)	0.14
Pneumonectomy (*N* = 14)	1.04 (0.51–2.11)	0.92	0.69 (0.31–1.54)	0.37
Elderly patients (*N* = 57)				
Sex (male, *N* = 28)	1.78 (0.97–3.26)	0.06	1.01 (0.94–4.09)	0.07
Race (black/other, *N* = 7)	1.21 (0.54–2.74)	0.64	1.09 (0.39–3.11)	0.86
Grade (undifferentiated, *N* = 29)	1.13 (0.62–2.04)	0.70	1.60 (0.76–3.73)	0.22
T stage				
T1 (*N* = 8)	Reference		Reference	
T2 (*N* = 12)	1.41 (0.42–4.74)	0.58	1.57 (0.40–6.21)	0.52
T3 (*N* = 15)	2.12 (0.67–6.66)	0.20	2.49 (0.64–9.73)	0.19
T4 (*N* = 22)	4.05 (1.36–12.05)	0.01	5.43 (1.42–20.84)	0.02
N stage (positive, *N* = 20)	2.30 (1.20–4.40)	0.01	0.96 (0.33–2.81)	0.94
Adjuvant chemotherapy (*N* = 9)	0.60 (0.24–1.54)	0.30	0.39 (0.14–1.09)	0.07
Adjuvant radiation (*N* = 21)	2.57 (1.22–5.41)	0.01	2.77 (0.98–7.85)	0.06
Surgery status				
Lobectomy (*N* = 47)	Reference		Reference	
Sublobar resection (*N* = 5)	2.21 (0.84–5.84)	0.11	2.97 (0.97–9.04)	0.06
Pneumonectomy (*N* = 5)	5.41 (1.99–14.67)	<0.001	5.14 (1.64–16.07)	0.005

Younger patients: age <70 years; elderly patients: age ≥70 years.
CI: confidence interval; HR: hazard ratio; PCS: pulmonary cacinosarcoma.

PCS. We further analysed patients with lung sarcomatoid carcinoma in the Shanghai Pulmonary Hospital and found that the patients significantly benefited from chemotherapy. Compared to NSCLSs, PCSs tended to show reduced lymphatic metastasis, consistent with the classic statement that sarcomas of the lung rarely metastasized through the lymphatic system [25]. The most common carcinomatous component of PCS was squamous cell carcinoma (69%), followed by adenocarcinoma (20%) and large cell carcinoma (11%) [4]. Comparison of the survival data between PCS and other NSCLCs showed that PCS was associated with a poorer prognosis [26, 27]. The lower prognosis of PCS was determined by the malignant mesenchymal components of the tumour [4].

Limitations

This study had several limitations. Firstly, it was a retrospective analysis and selection bias cannot be excluded. Secondly, the SEER public dataset did not include detailed information on smoking history, computed tomography findings, specific chemotherapy agents and genetic mutations, which are important prognostic variables. Thirdly, although we restricted our cohort to patients diagnosed after 1988, the study period spanned 20 years, during which time improvements in surgery, chemotherapy and precision therapy have evolved. Finally, due to the rare nature of PCSs, the multivariable model was overly analysed, particularly during subgroup analysis.

CONCLUSION

In summary, we found that males, age, T4 stage, M1 stage, surgery and chemotherapy were significantly associated with the OS of PCS. Nomograms could accurately predict the 3-year OS. Amongst elderly patients with surgical resection, pneumonectomy was associated with a poorer OS compared to lobectomy. PCS patients had lower lymphatic metastasis and received more extensive surgical treatment than adenocarcinoma, squamous cell carcinoma and large cell carcinoma patients. These results enhance our understanding of PCS and highlight how cancer treatment strategies can be improved.

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REFERENCES

[1] Chuang TL, Lai CL, Chang SM, Wang YF. Pulmonary carcinosarcoma: 18F-FDG PET/CT imaging. Clin Nucl Med 2012;37:1105.
[2] Pelosi G, Sonzogni A, De PT, Galetta D, Veronesi G, Spaggiari L *et al*. Review article: pulmonary sarcomatoid carcinomas: a practical overview. Int J Surg Pathol 2010;18:103–20.
[3] Davis MP, Eagan RT, Weiland LH, Pairolero PC. Carcinosarcoma of the lung: mayo clinic experience and response to chemotherapy. Mayo Clin Proc 1984;59:598–603.
[4] Huwer H, Kalweit G, Straub U, Feindt P, Volkmer I, Gams E. Pulmonary carcinosarcoma: diagnostic problems and determinants of the prognosis. Eur J Cardiothorac Surg 1996;10:403–7.
[5] Travis WD, Brambilla E, Nicholson AG, Yatabe Y, Austin JH, Beasley MB *et al*. The 2015 World Health Organization classification of lung tumors: impact of genetic, clinical and radiologic advances since the 2004 classification. J Thorac Oncol 2015;10:1243–60.
[6] Fishback NF, Travis WD, Moran CA, Guinee DG, McCarthy WF, Koss MN. Pleomorphic (spindle/giant cell) carcinoma of the lung: a clinicopathologic correlation of 78 cases. Cancer 1994;73:2936–45.
[7] Braham E, Rejeb HB, Aouadi S, Kilani T, El Mezni F. Pulmonary carcinosarcoma with heterologous component: report of two cases with literature review. Ann Transl Med 2014;2:41.
[8] Tanimoto A, Takeuchi S, Kotani H, Yamashita K, Yamada T, Ohtsubo K *et al*. Pulmonary carcinosarcoma showing an obvious response to pazopanib: a case report. BMC Pulm Med 2018;18:193.
[9] Sanyal K, Sabanathan K. Lung carcinosarcoma as a rare biphasic sarcomatoid carcinoma: a case report. Cases J 2009;2:7968.
[10] Olobatoke AO, David D, Hafeez W, Van T, Saleh HA. Pulmonary carcinosarcoma initially presenting as invasive aspergillosis: a case report of previously unreported combination. Diagn Pathol 2010;5:11.
[11] Koss MN, Hochholzer L, Frommelt RA. Carcinosarcomas of the lung: a clinicopathologic study of 66 patients. Am J Surg Pathol 1999;23:1514–26.
[12] Petrov DB, Vlassov VI, Kalaydjiev GT, Plochev MA, Obretenov ED, Stanoev VI *et al*. Primary pulmonary sarcomas and carcinosarcomas—postoperative results and comparative survival analysis. Eur J Cardiothorac Surg 2003;23:461–6.
[13] Goldstraw P, Chansky K, Crowley J, Rami-Porta R, Asamura H, Eberhardt WE *et al*. The IASLC lung cancer staging project: proposals for revision of the TNM stage groupings in the forthcoming (eighth) edition of the TNM classification for lung cancer. J Thorac Oncol 2016;11:39–51.
[14] Frank EH Jr. RMS: Regression Modeling Strategies. 2015.
[15] Fidel-David HM, Marinela C, O'Reilly EM, Austin D, Bolorsukh G, Saltz LL *et al*. Advanced hepatocellular carcinoma: which staging systems best predict prognosis? J Clin Oncol 2010;28:2889–95.
[16] Wang S, Ma K, Wang Q, Sun F, Shi Y, Zhan C *et al*. The revised staging system for malignant pleural mesothelioma based on surveillance, epidemiology, and end results database. Int J Surg 2017;48:92.
[17] Heller G, Mo Q. Estimating the concordance probability in a survival analysis with a discrete number of risk groups. Lifetime Data Anal 2016;22:263–79.
[18] Kakos GS, Williams TE, Assor D, Vasko JS. Pulmonary carcinosarcoma: etiologic, therapeutic, and prognostic considerations. J Thorac Cardiovasc Surg 1971;61:777–83.
[19] Vohra A, Narula H. Imaging findings of pulmonary carcinosarcoma: a case report. Lung India 2014;31:164.
[20] Liang W, Zhang L, Jiang G, Wang Q, Liu L, Liu D *et al*. Development and validation of a nomogram for predicting survival in patients with resected non-small-cell lung cancer. J Clin Oncol 2015;33:861–9.
[21] Wang S, Yang L, Ci B, Maclean M, Gerber DE, Xiao G *et al*. Development and validation of a nomogram prognostic model for SCLC patients. J Thorac Oncol 2018;13:1338–48.
[22] Kates M, Perez X, Gribetz J, Swanson SJ, McGinn T, Wisnivesky JP. Validation of a model to predict perioperative mortality from lung cancer resection in the elderly. Am J Respir Crit Care Med 2009;179:390–5.
[23] Janssen-Heijnen ML, Smulders S, Lemmens V, Smeenk FW, Van Geffen H, Coebergh J. Effect of comorbidity on the treatment and prognosis of elderly patients with non-small cell lung cancer. Thorax 2004;59:602–7.
[24] Spaggiari L, Scanagatta P. Surgery of non-small cell lung cancer in the elderly. Curr Opin Oncol 2007;19:84–91.
[25] Janssen JP, Mulder JJ, Wagenaar SS, Elbers HR, van den Bosch JM. Primary sarcoma of the lung: a clinical study with long-term follow-up. Ann Thorac Surg 1994;58:1151–5.
[26] Martin LW, Correa AM, Ordonez NG, Roth JA, Swisher SG, Vaporciyan AA *et al*. Sarcomatoid carcinoma of the lung: a predictor of poor prognosis. Ann Thorac Surg 2007;84:973–80.
[27] Nalajima M. Sarcomatoid carcinoma of the lung. Cancer 1999;86:608–16.