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ORIGINAL ARTICLE

Pulmonary Pleomorphic Carcinoma: Its Clinical Behavior, Prognostic Factor, and Keys to Treatment

Yoshinori Handa[1,2]; Takuhiro Ikeda[1]; Hideaki Hanaki[1]; Yoshihiro Miyata[2]; Kenichi Yoshimura[3]; Morihito Okada[2]; Hidenori Mukaida[1]

ABSTRACT —— ***Objective.*** Due to its rarity, the clinical behaviour of pulmonary pleomorphic carcinoma has not been elucidated. This study aimed to investigate the prognosis and prognostic factors of pulmonary pleomorphic carcinoma, especially factors associated with early recurrence and death. ***Methods.*** We retrospectively investigated 44 cases of pulmonary pleomorphic carcinoma. All patients underwent complete surgical resection. Factors affecting survival were assessed by the Kaplan-Meier method, and Cox regression and logistic regression analyses. ***Results.*** The prognosis of pleomorphic carcinoma was severe. In particular, there were high rates of early recurrence and death after surgery (the 1-year overall survival and recurrence-free survival rates were 52.6% and 45.8%). Although pleural invasion (P=0.95) and lymphatic invasion (P=0.39) did not affect the prognosis, patients with vascular invasion had a significantly worse prognosis than patients without vascular invasion (P=0.042). Similarly, tumors consisting mainly of sarcomatous elements showed a poorer prognosis than those consisting mainly of epithelial components (P=0.094). A multivariable Cox regression analysis revealed that vascular invasion was independently associated with a poor prognosis (hazard ratio, 3.11; 95% confidence interval, 1.04-13.3; P=0.026), and tumors consisting mainly of sarcomatous elements tended to have a poor prognosis (hazard ratio, 2.21; 95% confidence interval, 0.88-6.29; P=0.089). In addition, vascular invasion and tumors consisting mainly of sarcomatous elements were identified as risk factors for early recurrence and death after surgery by a multivariable logistic regression analysis. ***Conclusions.*** The prognosis of patients with pulmonary pleomorphic carcinoma is severe. Vascular invasion and tumors consisting mainly of sarcomatous elements are poor prognostic factors.

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KEY WORDS —— Pulmonary pleomorphic carcinoma, Prognosis, Vascular invasion

INTRODUCTION

Pleomorphic carcinoma is a rare malignant tumor.[1] It has been described in several human organs, including the lung parenchyma. The World Health Organization (WHO) classification identified pulmonary pleomorphic carcinoma as a specific type of lung cancer with pleomorphic, sarcomatoid, or sarcomatous elements,[2] namely, a group of non-small-cell lung carcinoma (NSCLC) that contains sarcomatous elements. Examples of pleomorphic carcinoma include NSCLC, adenocarcinoma, squamous cell carcinoma, large-cell carcinoma (containing spindle cells, giant cells, or both), and carcinoma consisting only of spindle cells and giant cells. Sarcomatous elements should comprise at least 10% of the neoplasm.

Since its diagnostic criteria were confirmed, pulmonary pleomorphic carcinoma has been diagnosed more frequently, however, few studies have been reported and its clinical and pathological characteristics are not well known. In particular, the grade of malignancy and clinical behavior remain to be defined. In the clinical set-

[1]Department of Surgery, Hiroshima City Asa Citizen Hospital, Japan; [2]Department of Surgical Oncology, [3]Department of Center for Integrated Medical Research, Hiroshima University, Japan.

Corresponding author: Yoshinori Handa.
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ting, we often experience patients with pulmonary pleomorphic carcinoma who "rush to death", where relapse occurs in multiple organs with the patient dying at a surprisingly early time after surgery (i.e., several weeks or several months), even though they are diagnosed with early-stage disease and receive complete resection. On the other hand, we also sometimes encounter pleomorphic carcinoma patients who survive for a long time without relapse. Furthermore, previous reports have presented conflicting results with regard to the prognosis. Some investigations reported pleomorphic carcinoma to have a more aggressive clinical course and significantly poorer survival in comparison to other variants of NSCLC, [3,4] while others failed to demonstrate that pleomorphic carcinomas were associated with a poorer prognosis. [5,6] Pulmonary pleomorphic carcinoma patients might be divided into two groups: one with markedly early recurrence and death and one that achieves long-term survival without relapse. The clinical behaviour of pulmonary pleomorphic carcinoma remains to be elucidated.

The purpose of this study was to investigate the prognosis and prognostic factors of pulmonary pleomorphic carcinoma, especially factors associated with early recurrence and death.

PATIENTS AND METHODS

Study population

We retrospectively analyzed 44 cases of pulmonary pleomorphic carcinoma that we experienced at two institutes (Hiroshima University Hospital, Hiroshima City Asa Citizen Hospital) between January 2006 and December 2013. The following data were collected: age, sex, smoking habit, serum carcinoembryonic antigen (CEA), tumor size, standard uptake value (SUV) max, clinical stage and surgical procedure. The preoperative evaluation included a physical examination, chest radiography, and measurement of tumor markers. Furthermore, computed tomography (CT) of the chest, abdomen, and positron emission tomography with 18-fluorodeoxyglucose (FDG-PET) were routinely performed. Staging was determined according to the TNM Classification of Malignant Tumors, 7th edition. [7] The Institutional Review Board of Hiroshima University Hospital and Hiroshima city Asa citizen Hospital approved this retrospective study (IRB number; E901, Approval date; September 4th, 2017).

Surgical procedure and postoperative therapy

The standard surgical technique was used and accompanied by routine systematic dissection or sampling of the hilar and mediastinal nodes. Intraoperative frozen examination was performed to determine the extent of resection and assess the nodal status. Segmentectomy was considered unless the tumor was >20 mm in size, located centrally, or patient consent was not obtained; the procedure was performed according to a previously described method. [8] Adjuvant chemotherapy was usually applied to pathological stage IA with tumors of >2 cm in size or cases with stage ≥IB disease.

Pathological diagnosis

Expert pathologists at the two institutions examined all of the pathologic material. The diagnosis was obtained based on the findings of light microscopy and completed with immunohistochemical examinations. Each case met the WHO criteria. The main histology was defined as the composition that occupied more than half of the tumor (i.e., sarcomatous elements or epithelial components). The histological composition was further subclassified, with sarcomatous elements classified into spindle cell carcinoma, giant-cell carcinoma and both and epithelial components classified into adenocarcinoma, squamous cell carcinoma, or large-cell carcinoma. Cases were classified as spindle cell carcinoma if at least 10% of the tumor was composed of fusiform malignant cells. Immunohistochemical procedures were performed and a positive reaction to 1 epithelial marker was useful for confirming epithelial differentiation in the sarcomatous elements when poor carcinomatous differentiation was observed by light microscopy.

Follow-up evaluation

All patients were followed up from the day of surgery. They were examined at three- to six-month intervals for five years, and at one-year intervals thereafter, until death or the date of the last follow-up. Evaluations included physical examinations, chest radiography or CT scan, and detection of tumor markers. When recurrence was suspected, FDG-PET, brain magnetic resonance imaging, or bone scintigraphy was performed. Recurrence was determined by radiographic features or histologic evidence. Tumor recurrence was classified into three subgroups: 1) distant, 2) locoregional, and 3) both. Locoregional recurrence was defined as recurrent tumor within the same side lobes and ipsilateral hilum or mediastinum lymph node metastasis. Recurrence at other lo-

cations was defined as distant recurrence.

Statistical analysis

We performed a survival analysis in December 2020. The summarized data are presented as the number or median (interquartile range). The duration of overall survival (OS) was defined as the interval between the day of the operation and the date of death from any cause or the date of the last follow-up examination. Recurrence-free survival (RFS) was defined as the interval between the day of the operation and the date on which recurrence or metastasis was identified. Survival data were calculated using the Kaplan-Meier method and were compared using the log-rank test. Univariate and multivariable Cox regression analyses were used to identify significant prognostic factors. In addition, we performed univariate and multivariable logistic regression analyses of factors associated with death, and recurrence or death within 1 year after surgery, to investigate the factors associated with early recurrence and death. *P*-values of <0.05 were considered to indicate statistical significance. Due to the rarity of the disease the study population was relatively small; thus, the inclusion of a large number of variables might have resulted in statistical inadequacy. Considering that pulmonary pleomorphic carcinoma is difficult to diagnose based on the examination of biopsy specimens, it is diagnosed postoperatively[3,4] in many cases. Accordingly, we only included postoperative factors in the Cox regression analysis and logistic regression analysis. Backward stepwise procedures were used to determine the combination of factors that were essential for predicting the prognosis.

All data were statistically analyzed using the JMP software program (SAS Institute Inc., Version 12.0, Cary, NC).

RESULTS

Patient characteristics

Patient characteristics are summarized in Table 1. The age at the diagnosis was 67.5 years (60-74 years) and the male:female ratio was 37:7, in addition, serum CEA and SUV values tended to be high, at 5.25 (1.5-20.0) ng/ml and 5.75 (2.0-12.5), respectively. The surgical procedures included lobectomy (n=33), segmentectomy (n=4), and wedge resection (n=7), Complete resection (R0) was achieved in all cases. The pathologic stages, main histology, subtypes of sarcomatous elements and epithelial components, and pathologic factors are shown in Table 1. Tumors consisting mainly of sarcomatous elements were found in 15 (34.1%) cases and tumors consisting mainly of epithelial components were found in 29 (65.9%). The nodal status was classified as pN0 in 24 (54.5%) patients, pN1 in 10 (22.7%) patients, and pN2 in 10 (22.7%) patients. Microscopic invasion into the visceral pleural and lymphatic vessels was found in 19 patients (43.2%) and 12 patients (27.3%), respectively. In addition, invasion into the vascular vessels was observed in 34 patients (77.3%). The in-hospital and 30-day mortality rates were 0%. There were no severe postoperative complications and no re-resection was performed for neoplastic involvement of the surgical margins.

Prognosis of pulmonary pleomorphic carcinoma

The prognosis of pulmonary pleomorphic carcinoma was severe, with 5 year-overall and recurrence-free survival rates of 41.3% and 38.1%, respectively (Figure 1). In addition, early recurrence and death, particularly within 1 year after surgery, were markedly high, with 1-year overall and recurrence-free survival rates of 52.6% and 45.8%, respectively. We performed a Kaplan-Meier analysis to identify prognostic factors and compared factors using a log-rank test. The prognosis tended to be poorer in patients with advanced disease (pathological stage II/III) than in those with pathological stage I disease, as we expected (5 year-OS: 33.8% vs. 66.7%, $P=0.083$); however, the prognosis of patients with and without pathological lymph node metastasis did not differ to a statistically significant extent (Figure 2). Invasion of the visceral pleural ($P=0.95$) and lymphatic vessels ($P=0.39$) did not affect the prognosis. In contrast, the overall survival of patients with vascular invasion were significantly worse than that of patients without vascular invasion (5 year-OS rates, 33.3% vs. 66.7%, $P=0.042$. Figure 3). As well as, tumors consisting mainly of sarcomatous elements were trend to be worse than consisting mainly of epithelial components (5 year-OS rates, 33.3% vs. 45.1%, $P=0.094$), although the subtype of the sarcomatous elements or epithelial components did not affect overall survival (Figure 4).

Univariate and multivariable Cox regression analyses for OS revealed that vascular invasion was an independent prognostic factor (multivariable analysis: hazard ratio, 3.11; 95% confidence interval, 1.04-13.3; $P=0.026$), and consisting mainly of sarcomatous elements tended to be associated with a poor prognosis (multivariable analysis:

Table 1. Clinical and Pathological Characteristics of Patients with Pulmonary Pleomorphic Carcinoma

Factor	
Age (median (IQR))	67.5 (60-74)
Sex (Male/Female)	37 (84.1%)/7 (15.9%)
Smoking status	
Smoker (Current&former) / Nonsmoker	32 (72.7%)/12 (27.3%)
CEA (ng/ml) (median (IQR))	5.25 (1.5-20.0)
Tumor size (mm) (median (IQR))	32.5 (10-62.5)
SUV max (median (IQR))	5.75 (2.0-12.5)
Clinical stage	
Ⅰ	26 (59.1%)
Ⅱ	12 (27.3%)
Ⅲ	6 (13.6%)
Ⅳ	none
Surgical procedure	
Pneumonectomy	none
Lobectomy	33 (75.0%)
Segmentectomy	4 (9.1%)
Wedge resection	7 (15.9%)
Pathological stage	
Ⅰ	19 (43.2%)
Ⅱ	13 (29.5%)
Ⅲ	12 (27.3%)
Ⅳ	none
Main histology	
Sarcomatous elements	15 (34.1%)
Epithelial components	29 (65.9%)
Sarcomatous elements	
Spindle	27 (61.4%)
Giant	12 (27.3%)
Both	5 (11.3%)
Epithelial components	
Adenocarcinoma	28 (63.6%)
Squamous cell carcinoma	16 (36.4%)
Large cell carcinoma	none
Pathological tumor size (mm) (median (IQR))	35.0 (12.5-65.0)
Pathological lymph node metastasis	20 (45.5%)
Pleural invasion	19 (43.2%)
Lymphatic invasion	12 (27.3%)
Vascular invasion	34 (77.3%)
Adjuvant therapy	22 (50.0%)

IQR, interquartile range; CEA, serum carcinoembryonic antigen.

hazard ratio, 2.21; 95% confidence interval, 0.88-6.29; P= 0.089). The analyses for RFS yielded similar results (Table 2). We added a logistic regression analysis for recurrence, and recurrence or death within 1 year after surgery, and obtained similar results: vascular invasion and consisting mainly of sarcomatous elements were identified as factors associated with early recurrence and death (Table 3).

Recurrence after surgery was frequently observed (26/44, 59.1%). Among 26 patients with recurrent disease, 18 (69.2%) initially had distant metastasis, 5 (19.3%) had locoregional relapse, and 3 (11.5%) had both (Table 4). The major sites of initial metastasis were bone (4/18 [22.2%]), the brain (4/18 [22.2%]) and the adrenal glands (4/18 [22.2%]). Surprisingly, when we limited the analysis to patients who died within 1 year after surgery, all cases had relapsed disease and almost all had distant metastasis (Table 4). Furthermore, the rate of overall

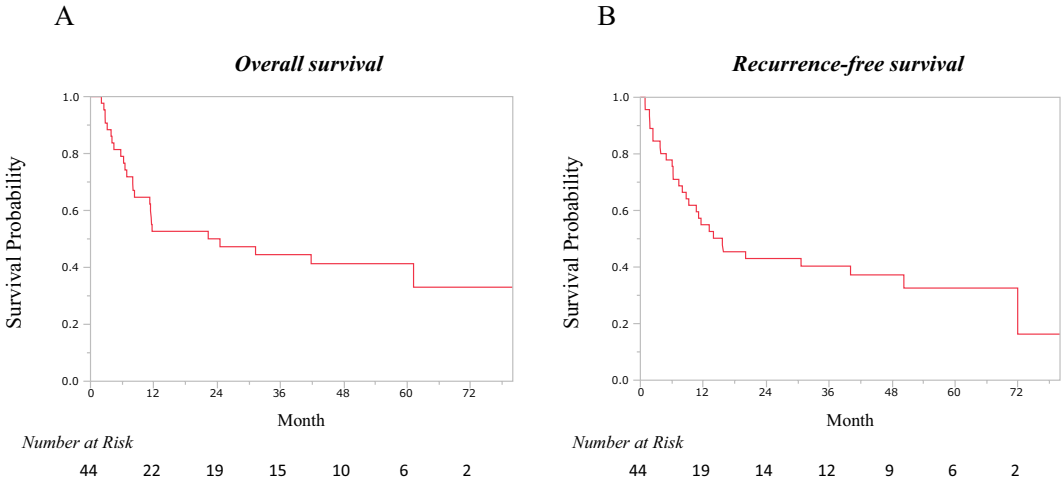

Figure 1. Overall survival **(A)** and Recurrence-free survival curves **(B)** for surgically resected pulmonary pleomorphic carcinoma.

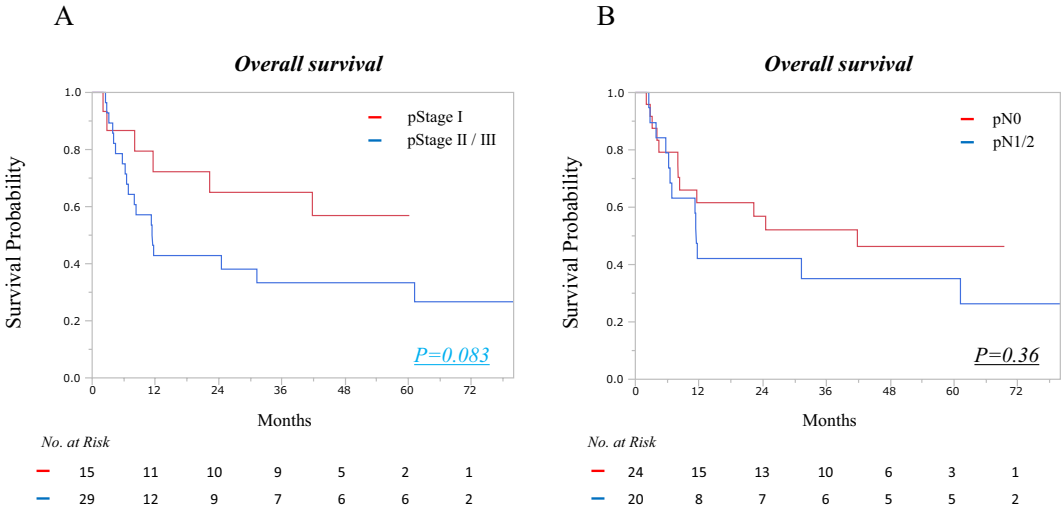

Figure 2. Kaplan-Meier survival curves for surgically resected pulmonary pleomorphic carcinoma according to the pathologic status. **A**, Pathologic stage. **B**, Pathological lymph node metastasis.

survival after confirmation of the initial relapse was 19.4% at 6 months, with a median survival time of 2.1 months. Among 26 patients with recurrent disease, 21 (80.7%) had vascular invasion.

COMMENT

In 1999 the WHO reclassified the pleomorphic carcinoma and set widely adopted criteria. Since then, pulmonary pleomorphic carcinoma has been diagnosed more frequently. [9] Several case reports have been published but very few studies have been published. Thus, we conducted the present study, which focused on the prognosis and prognostic factors.

Some studies reported that patients with pleomorphic carcinoma showed a worse prognosis in comparison to those with other variants of NSCLCs, [3,4] whereas Attanoos et al. [5] and Nakajima et al. [6] reported that the prognosis and clinical behavior of the 2 groups were similar. The important implication of the present study is the determination of the malignant grade of this entity. We found that the 5 year-overall survival rates of patients were 41.3%, and to our surprise, almost half of all patients (20/44, 45.5%) had died within 1 year after surgery although all patients had received complete re-

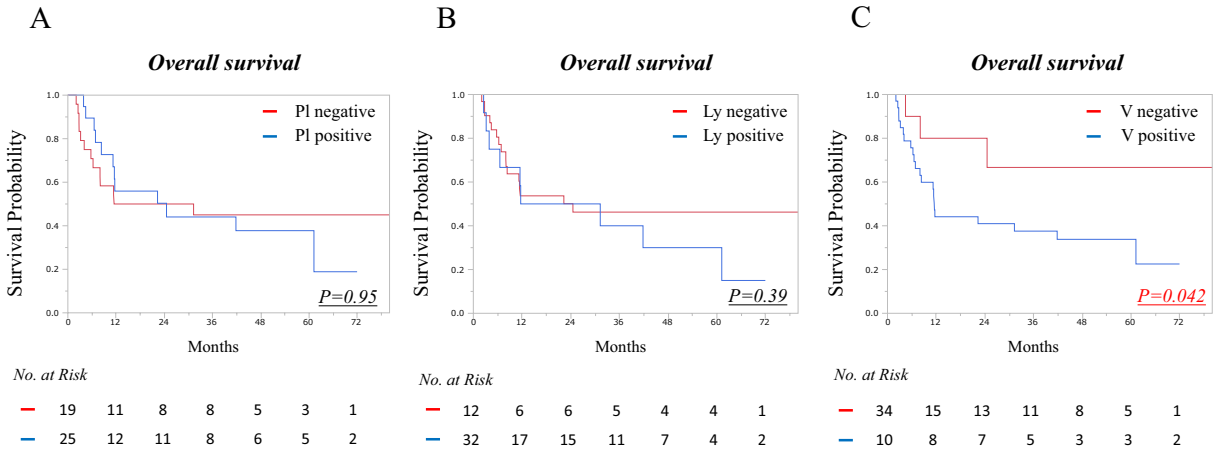

Figure 3. Kaplan-Meier survival curves for surgically resected pulmonary pleomorphic carcinoma according to pathological factors. **A**, Pleural invasion. **B**, Lymphatic invasion. **C**, Vascular invasion.

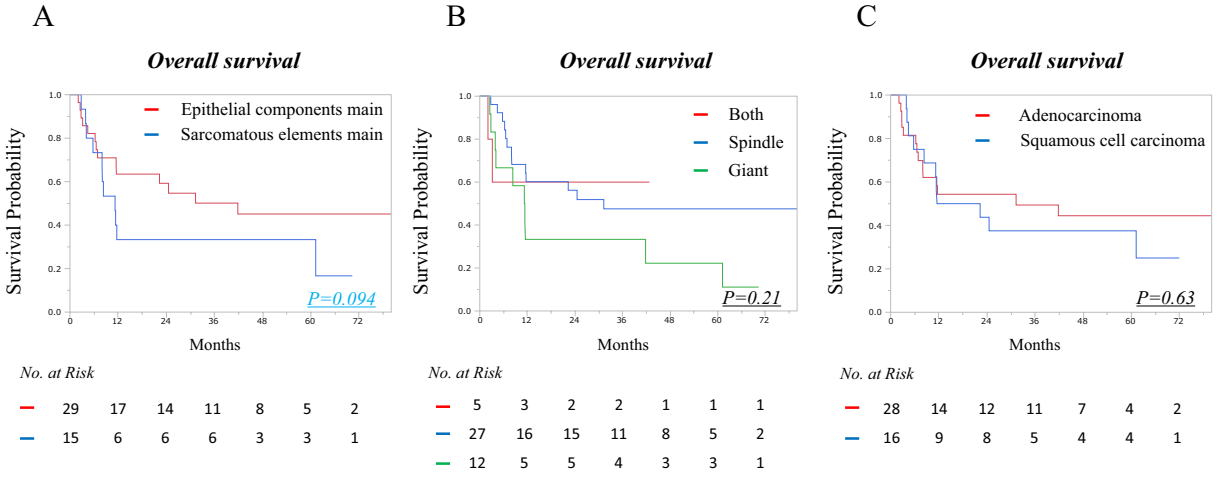

Figure 4. Kaplan-Meier survival curves for surgically resected pulmonary pleomorphic carcinoma according to the histology. **A**, Main histology. **B**, Sarcomatoid elements. **C**, Epithelial components.

section. In addition, recurrence after surgery was frequently observed (26/44, 59.1%), and among 26 patients with relapsed disease, 20 patients developed recurrent disease within 1 year after surgery. Distant metastasis was predominant pattern of recurrence. In addition, Ito et al. [9] reported that autopsies revealed that pulmonary pleomorphic carcinoma tended to expand into various lesions, including minor sites of metastasis such as the thyroid gland, peritoneum and abdominal lymph nodes that could not be found by clinical examination before death. Reflecting these characteristics, the 6-month survival rate after initial proof of postoperative recurrence was a only 19.4%, with a median survival time of 2.1 months. These results showed that pleomorphic carcinoma might be extremely aggressive, with more rapid progression in comparison to other NSCLCs.

Another important implication of the present study was the investigation of prognostic factors in pulmonary pleomorphic carcinoma. Many studies have been conducted to investigate predictive or prognostic factors for other variants of NSCLC; however, few have discussed the predictive or prognostic factors in pulmonary pleomorphic carcinoma. Previous reports have indicated that nodal involvement shortened patient survival. [10] In contrast, our data showed different results, namely, the survival rate was not strictly related to lymph node involvement with significant differences between N0 and N1/N2.

Table 2. Univariate and Multivariable Cox Regression Analyses of Overall Survival (OS) and Recurrence-free Survival (RFS)

Variables	Univariable			Multivariable[a]		
	Hazard ratio	95%CI	*P* value	Hazard ratio	95%CI	*P* value
Overall survival						
Stage: Ⅱ/Ⅲ (vs. Ⅰ)	2.06	0.85-5.72	0.11	1.71	0.64-4.45	0.27
Main histology: sarcomatous (vs. epithelial)	2.03	0.88-4.50	0.094	2.21	0.88-6.29	0.089
Sarcomatous elements: giant (vs. other)	1.67	0.72-3.63	0.18			
Epithelial components: adenocarcinoma (vs. Other)	0.82	0.37-1.86	0.63			
Tumor size: ≥3.0[b] (vs. <3.0)	0.82	0.32-1.98	0.79			
Lymph node metastasis: positive (vs. negative)	1.44	0.64-3.23	0.36			
Pleural invasion: positive (vs. negative)	1.02	0.46-2.25	0.95			
Lymphatic invasion: positive (vs. negative)	1.42	0.60-3.17	0.40			
Vascular invasion: positive (vs. negative)	3.01	1.04-12.7	0.040	3.11	1.04-13.3	0.026
Recurrence free survival						
Stage: Ⅱ/Ⅲ (vs. Ⅰ)	1.80	0.84-4.93	0.12	2.10	0.95-6.22	0.26
Main histology: sarcomatous (vs. epithelial)	2.44	1.06-5.34	0.036	2.68	0.90-8.24	0.074
Sarcomatous elements: giant (vs. other)	1.70	0.75-3.70	0.19			
Epithelial components: adenocarcinoma (vs. Other)	0.73	0.34-1.60	0.42			
Tumor size: ≥3.0[b] (vs. <3.0)	0.89	0.36-2.01	0.99			
Lymph node metastasis: positive (vs. negative)	1.54	0.70-3.37	0.26			
Pleural invasion: positive (vs. negative)	1.26	0.59-2.73	0.54			
Lymphatic invasion: positive (vs. negative)	1.67	0.73-3.62	0.20			
Vascular invasion: positive (vs. negative)	2.51	1.06-8.62	0.045	2.76	1.02-9.62	0.033

[a] Only factors with *P* values of <0.05 in the backward stepwise procedures were included.

[b] Continuous variables were dichotomized and converted to categorical variables using the mean values.

CI, confidence interval.

Pleural invasion, lymphatic invasion, and vascular invasion have been reported to be strong prognostic factors in other variants of NSCLCs.[11-14] We assessed these factors by a Kaplan-Meier analysis, a Cox regression analysis, and a logistic regression analyses. Vascular invasion was only detected as poor prognostic factor in pulmonary pleomorphic carcinoma. In the vascular invasion group, the hazard ratio for death and the odds ratio for death within 1 year after surgery were approximately 3 times higher in the multivariate Cox regression analysis and the logistic regression analysis. Vascular invasion is thought to reflect tumor aggressiveness, playing a crucial role in the first step of tumor metastasis in various human cancers, including NSCLCs.[15] Vascular invasion was identified as a poor prognostic factor in a multivariable Cox regression analysis by Suzuki et al.,[12] who analyzed 430 cases of pathologic Stage I NSCLC (hazard ratio, 3.79; 95% confidence interval, 2.07-6.80; $P<0.0001$). The prognosis was significantly different, and the 5-year survival rate of patients with vascular invasion was 69.3%, whereas that of patients without vascular invasion was 90.2%. In addition, Tsuchiya et al.[13] showed that vascular invasion was significantly correlated with recurrence in NSCLCs, and to our surprise, the frequency of distant metastasis in the vascular invasion group was 9 times higher than that in the non-vascular invasion group. Our results indicated that pulmonary pleomorphic carcinoma with vascular invasion is associated with a severe prognosis, similar to other NSCLCs with vascular invasion, and clos follow-up might be needed.

A tumor consisting mainly of sarcomatous elements was also identified as a poor prognostic factor. To our knowledge, no studies have directly compared tumors composed mainly of sarcomatous elements and those composed mainly of epithelial components in pulmonary pleomorphic carcinoma. However, sarcomatous tumor cells might be more aggressive and have higher malignant potential in comparison to epithelial tumor cells. In 2013, Spraker et al.[16] conducted the first large cohort study to examine pulmonary sarcoma and revealed that it was associated with a high rate of recurrence, and they considered the possibility that pulmonary sarcoma is associated with a poorer prognosis in comparison to

Table 3. Univariate and Multivariable Logistic Regression Analyses of Death/Recurrence or Death Within 1 Year After Surgery

Variables	Univariable			Multivariable[a]		
	Odds ratio	95%CI	*P* value	Odds ratio	95%CI	*P* value
Death within 1 year after surgery						
Stage: Ⅱ/Ⅲ (vs. Ⅰ)	2.04	0.83-5.00	0.11	1.24	0.43-3.51	0.68
Main histology: sarcomatous (vs. epithelial)	2.46	0.90-8.63	0.080	2.50	0.88-8.97	0.087
Sarcomatous elements: giant (vs. other)	2.04	0.79-4.95	0.13			
Epithelial components: adenocarcinoma (vs. Other)	0.82	0.37-1.86	0.62			
Tumor size: ≥3.0[b] (vs. <3.0)	0.85	0.30-2.01	0.89			
Lymph node metastasis: positive (vs. negative)	1.62	0.67-4.04	0.27			
Pleural invasion: positive (vs. negative)	0.72	0.28-1.74	0.47			
Lymphatic invasion: positive (vs. negative)	1.11	0.39-2.76	0.83			
Vascular invasion: positive (vs. negative)	3.55	1.02-22.3	0.045	3.49	1.00-22.4	0.034
Recurrence or death within 1 year after surgery						
Stage: Ⅱ/Ⅲ (vs. Ⅰ)	1.89	0.87-5.80	0.098	2.18	0.97-7.29	0.15
Main histology: sarcomatous (vs. epithelial)	2.66	1.14-5.99	0.024	2.69	0.89-8.49	0.077
Sarcomatous elements: giant (vs. other)	1.92	0.83-4.32	0.12			
Epithelial components: adenocarcinoma (vs. Other)	0.69	0.31-1.58	0.37			
Tumor size: ≥3.0[b] (vs. <3.0)	1.06	0.40-2.22	0.76			
Lymph node metastasis: positive (vs. negative)	1.53	0.67-3.45	0.29			
Pleural invasion: positive (vs. negative)	1.13	0.50-2.55	0.76			
Lymphatic invasion: positive (vs. negative)	1.44	0.58-3.27	0.40			
Vascular invasion: positive (vs. negative)	2.89	1.01-12.2	0.046	3.10	1.02-13.4	0.028

[a] Only factors with *P* values of <0.05 in the backward stepwise procedures were included.

[b] Continuous variables were dichotomized and converted to categorical variables using the mean values.

CI, confidence interval.

other NSCLCs (5 year-OS rates, 35.0%), as studies of small populations previously suggested.[17,18] This fact might explain our results that pleomorphic carcinoma consisting mainly of sarcomatous elements was associated with a poorer prognosis in comparison to pleomorphic carcinoma consisting mainly of epithelial components. We might also need to perform close follow-up for cases in which the tumor consists mainly of sarcomatous elements. Pulmonary pleomorphic carcinoma is known to be less susceptible to cytotoxic anticancer agents.[19,20] The median PFS is only 1.5 months and the median OS is 7.2 months in patients with pulmonary pleomorphic carcinoma treated with platinum-based chemotherapy.[20] Even in surgically-resected patients, the median OS is approximately 14.7 months.[21] Therefore, the development of new treatment strategies is urgently required.

The present study was associated with some limitations. The present study was retrospective in nature and the population was relatively small. However, multivariable Cox and logistic regression analyses were conducted to reduce potential confounding factors. Greater data accrual through multicenter studies may remedy this problem. Another limitation of this study is that the presented data were derived from only two institutions, in order to facilitate a detailed data analysis. In addition, we did not analyze the correlations between the surgical procedure, SUVmax, and adjuvant chemotherapy and the prognosis because most of the patients with pleomorphic carcinoma were treated by lobectomy, had a high SUVmax, and received adjuvant chemotherapy. We plan to conduct another large cohort study that includes these analyses

Pulmonary pleomorphic carcinoma is associated with a severe prognosis. In particular, vascular invasion and tumors consisting mainly of sarcomatous elements are risk factors for early (sometimes "rush") recurrence and death after surgery. Some important findings regarding this tumor have been described in this report, and further investigations are needed to elucidate more definitive clinical features and establish appropriate treatment strategies for pulmonary pleomorphic carcinoma.

本論文内容に関連する著者の利益相反：なし

Table 4. Recurrence Pattern of Patients with Surgically Resected Pulmonary Pleomorphic Carcinoma

Analysis for all patients	
Recurrence pattern (n = 26)	
[a] Distant (n = 18)	
Bone	4 (22.2%)
Brain	4 (22.2%)
Lung	2 (11.1%)
Liver	2 (11.1%)
Adrenal gland	4 (22.2%)
Small intestine	1 (5.6%)
Dissemination	1 (5.6%)
Locoregional (n = 5)	
Mediastinal lymph node	5 (100.0%)
Both (n = 3)	
Analysis for patients who died within 1 year after surgery	
Recurrence pattern (n = 20)	
[a] Distant (n = 16)	
Bone	3 (18.7%)
Brain	3 (18.7%)
Lung	2 (12.5%)
Liver	2 (12.5%)
Adrenal gland	4 (25.0%)
Small intestine	1 (6.3%)
Dissemination	1 (6.3%)
Locoregional (n = 1)	
Mediastinal lymph node	1 (100.0%)
Both (n = 3)	

[a] When several sites of distant metastasis were identified, only the site with largest recurrent tumor was described.

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