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Cavity Formation is a Prognostic Indicator for Pathologic Stage I Invasive Lung Adenocarcinoma of ≥3 cm in Size

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Background: We investigated the correlation between cavity formation, prognosis, and tumor stage for pathologic stage I invasive lung adenocarcinomas (IADCs) ≤3 cm in size.

Material/Methods: 2106 candidates with pathologic stage I IADC were identified from Shanghai Chest Hospital between 2009 and 2014. There were 227 patients who were diagnosed as having cavity formation and another 1879 patients who were not (the non-cavitary lung cancer group). Kaplan-Meier analysis curves were conducted to compare the overall survival (OS) and relapse-free survival (RFS) between these 2 groups. Cox proportional hazards regression was performed to discover the independent risk factors of OS and RFS. Receiver operating characteristic (ROC) curve was done to determine the cutoff value of cavity size for predicting prognosis. Furthermore, subgroup analysis was stratified by the size of tumor and the 8th classification of T category.

Results: Compared with non-cavitary lung cancer group, patients with cavity formation were found to have a higher prevalence of male patients (P=0.015), older age patients (P=0.039), larger size tumors (P=0.004), and worse cancer relapse (P<0.001). Survival analysis found that patients with cavitary IADC had significantly shorter RFS than those with non-cavitary IADC (P=0.001). Further, subgroup analysis confirmed a significantly worse RFS in cavitary IADC group both in stage T1a (P=0.002) and T1b (P<0.001), but not for stage T1c (P=0.962) and T2a (P=0.364). Moreover, cavity formation was still less of a significant predictor of RFS in multivariable analysis (hazard ratio [HR] 1.810, 95% confidence level [CI] 1.229–2.665, P=0.003). The ROC curve showed that the best cutoff value of maximum diameter of the cavity for judging RFS was 5 mm (sensitivity: 0.500; specificity: 0.783). At the same time, multiple cavities were more likely to lead to recurrence (sensitivity: 0.605; specificity: 0.439).

Conclusions: Cavitary adenocarcinoma was a worse prognostic indicator compared with non-cavitary adenocarcinoma, especially for cavity >5 mm and multiple cavities. Thus, for stage T1a and T1b, cavitary and non-cavitary IADC should be considered separately.

MeSH Keywords: Adenocarcinoma • Prognosis • Thoracic Cavity

Abbreviations: **NSCLC** – non-small-cell lung cancers; **IADC** – invasive adenocarcinoma; **SCC** – squamous cell carcinoma; **RFS** – relapse-free survival; **OS** – overall survival; **LCSS** – lung cancer-specific; **CT** – computed tomography; **MRI** – magnetic resonance imaging; **IASLC** – International Association for the Study of Lung Cancer; **ATS** – American Thoracic Society; **ERS** – European Respiratory Society

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Background

Cavitation is a frequent phenomenon discovered among a variety of pulmonary diseases when computed tomography (CT) is conducted. The diagnosis related to this condition varies, including infection, tuberculosis, fungal infections, abscess, and malignant tumors [1–6]. According to previous studies, cavitation noted on plain chest radiographs has been reported to range from 2% to 25% for primary lung cancers, and 22% with chest CT scans [7–12]. Compared with the non-cavitary lung cancer group, male patients, a larger tumor size, and squamous cell histology were found to be more prevalent in the cavitary group, and had worse survival outcomes [8,9,10–13]. Squamous cell carcinoma was found to be the most diagnosed histological type among cavitary lung cancer patients [7,14]. In recent years, due to the increasing incidence in lung adenocarcinoma, more and more cavitary adenocarcinomas have been identified [15,16].

Previous reports of clinical and radiological characteristics have been largely based on squamous cell carcinomas. However, information on clinical and radiological characteristics and corresponding clinical prognosis of cavity formation among adenocarcinoma patients have been relatively rare. Therefore, we need to understand the significance of the cavity formation and its prognosis for early-stage adenocarcinoma patients.

In this study we analyzed the clinical records of 2106 patients with pathologic stage I IADC to investigate the prognosis and clinicopathological features of cavitary lung adenocarcinoma.

Material and Methods

Patients

The institutional review board from Shanghai Chest Hospital approved this study and provided informed consent for this operation [KS(Y)1668]. Totally, 3312 patients with pathologic stage I adenocarcinoma according to the 8th TNM staging system undergoing curative surgery between 2009 and 2014 in Shanghai Chest Hospital were identified. The inclusion and exclusion criteria in this research are listed in Figure 1. Finally, 2106 patients were eligible and enrolled in this research.

The patients underwent chest CT scan, abdominal color ultrasound, head magnetic resonance imaging (MRI), and bone scan before operation to rule out distant metastasis. Positron emission tomography (PET)-CT scan was performed if necessary.

Helical technique and additional continual thin section (collimation, 2.0 mm or 1.0 mm) scans were obtained in all 227 patients. Qiming Ni and Jing Jiao of the Radiology Department of Shanghai Chest Hospital examined the images according to high-resolution CT scans. The cavitary adenocarcinomas are shown in Figure 2.

The maximum diameter of cavitation, single or multiple, and the maximum cavitation diameter/maximum tumor diameter ratio were used as potential influencing factors to evaluate the effect on patient prognosis.

All the pathology reports were provided by the Department of Pathology in Shanghai Chest Hospital. All specimens were routinely stained with hematoxylin and eosin. Predominant

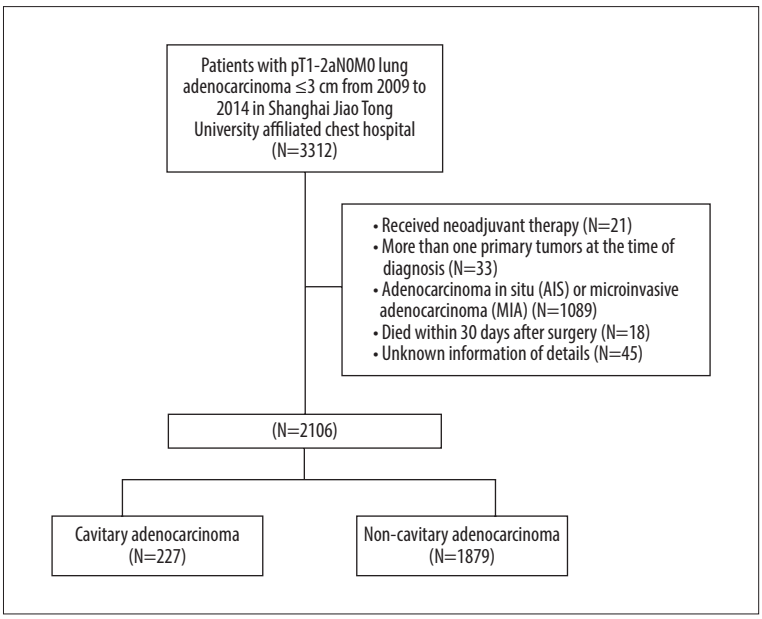

Figure 1. Flow diagram of patient selection.

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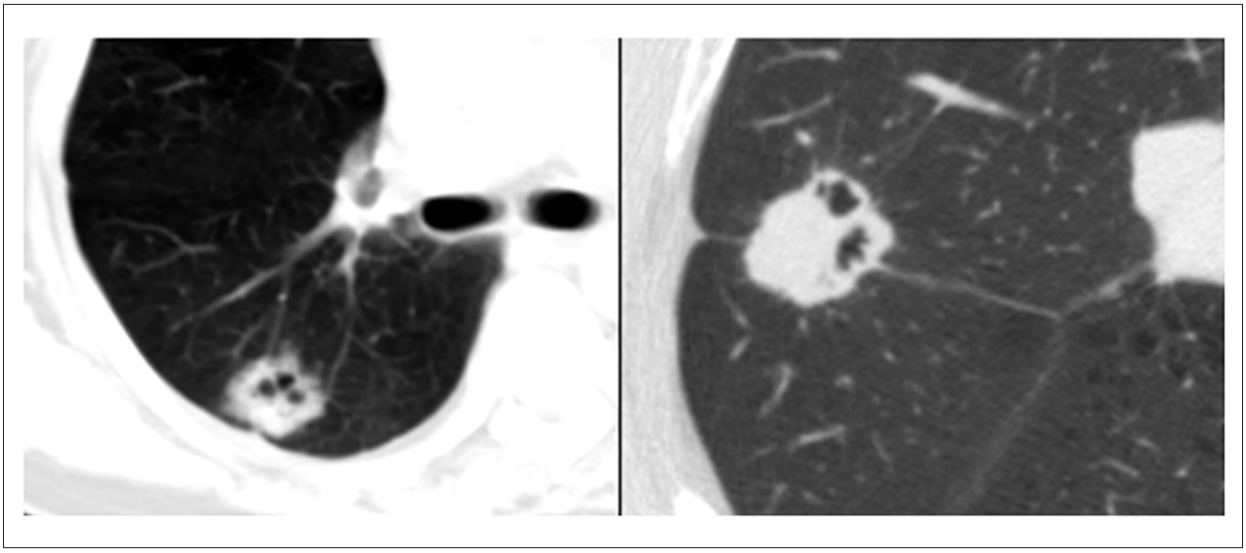

Figure 2. A case of a high-resolution computed tomography image of a cavitary tumor.

histology subtypes were divided into 4 groups according to the new classification categories published by the International Association for the Study of Lung Cancer (IASLC), American Thoracic Society (ATS), and European Respiratory Society (ERS) in 2011 [17]. In this novel proposal, they defined 5 distinctive subtypes of invasive lung adenocarcinoma in association with prognosis, stating lepidic as favorable, acinar and papillary as intermediate, and micropapillary and solid as poor. We also evaluated lymphatic vessel invasion (LVI), and visceral pleural invasion (VPI) based on Elastica van Gieson staining.

Statistical analyses

All the clinicopathologic data and distributions of survival were analyzed by SPSS 23.0 software package (SPSS Inc., Chicago, IL, USA) or Prism 5 (Graphpad Software Inc., La Jolla, CA, USA). The curves of RFS and OS, as well as their comparisons, were calculated by Kaplan-Meier method, testified by the log-rank test; *t* test was used in continuous variable analysis and χ^2 test was used in categorical variable analysis. Multivariable Cox proportional hazards regression model was applied to identify the independent predictors for survival. The receiver operating characteristic (ROC) cutoff point of the maximum diameter of the cavity and its relationship with the survival results were calculated. Two-sided $P<0.05$ was considered as statistical significance in this study.

Results

The patient characteristics are listed in Table 1. Of the 2106 patients included in this study, there were 844 males (40.1%) and 1262 females (59.9%), with an average age of 60.61 years (range from 24 to 85 years). The cavity adenocarcinoma group had more male patients ($P=0.015$), older age patients ($P=0.039$), much more common cancer recurrence ($P<0.001$), and larger tumor size ($P=0.004$) (Table 2). There were no significant differences in the T status and smoking history. Similarly, histologic findings showed that there were no significant differences in the LVI ($P=0.462$) and VPI ($P=0.754$) between the 2 groups. With respect to the predominant histologic subtypes, no significant differences were found between types with lepidic ($P=0.603$), papillary ($P=0.353$), acinar ($P=0.785$), solid ($P=0.516$), or micropapillary ($P=0.177$).

There were 176 patients who relapsed during follow-up; the 5-year RFS rate was 88.8%. Kaplan-Meier analysis shown a significantly shorter RFS in the cavitary adenocarcinoma group (Figure 3), $P=0.001$). In detail, adenocarcinoma patients with cavity formation showed 81.3% of 5-year RFS rate while 89.9% for patients without cavity formation.

Univariable analysis (Table 3) elucidated age, sex, cavity formation, tumor size, T status, predominant histology subtype, surgical resection, VPI, and LVI as potential predictors for RFS. The influence of cavity formation on the T stage found that the survival curve of cavitary adenocarcinoma was always between stage T1c and T2a ($P<0.001$) (Figure 4). Further, subgroup analysis was performed (Figure 5) and the survival outcome revealed that significantly shorter RFS was founded in cavitary adenocarcinoma patients with stage T1a ($P=0.002$) and T1b ($P<0.001$) but not stage T1c ($P=0.962$) and T2a ($P=0.364$). This suggests that patients with early-staged IADC with cavity formation should be considered separately, especially when stage T1a and T1b occurred. Subgroup analysis of OS in T status was also performed. Unfortunately, there was no significant difference among patients with or without cavity formation on neither stage T1a ($P=0.530$), T1b ($P=0.288$), T1c ($P=0.969$), or T2a ($P=0.591$).

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Table 1. Patient characteristics (n=2106).

Variable	Frequency	%
Age (years)	2106	
<65	1393	66.1
≥65	713	33.9
Sex		
Male	844	40.1
Female	1262	59.9
Cavity		
Yes	227	10.8
No	1879	89.2
Tumor size (cm)		
≤1	365	17.3
1–2	1108	52.6
2–3	633	30.1
p-T status		
1a	347	16.4
1b	930	44.2
1c	423	20.1
2a	406	19.3
Predominant histology subtype		
L	233	11.1
A+P	1645	78.1
M+S	127	6.0
Variant	101	4.8
Mediastinal lymph node assessed		
Yes	1824	86.6
No	282	13.4
Surgical resection		
Sublobectomy	307	14.6
Lobectomy	1799	85.4
Smoking history		
Former or current smoker	134	6.4
Never smoker	1972	93.6
Visceral pleural invasion		
Yes	406	19.3
No	1700	80.7
Lymphatic vessel invasion		
Yes	82	3.9
No	2024	96.1

Multivariate analysis revealed that cavity formation was an independent prognostic factor in pathologic stage I IADC (P=0.003; Table 4). There were 59 patients who died during the follow-up, whose causes included 49 patients with lung cancer-specific death (LCSS) (83.0%), 5 patients with non-cancer-related death (8.5%), and unknown causes in 5 patients (8.5%). Kaplan-Meier analysis demonstrated that there were no significant differences in the OS rate (Figure 6) or LCSS rate (Figure 7) between tumors with or without cavity formation (P=0.955 and P=0.628, respectively).

Moreover, sex, cavity formation, tumor size, predominant histology subtypes, surgical resection, VPI, and LVI were still significant predictors of RFS in multivariable analysis, while age, T status and mediastinal lymph node assessment were not (Table 4).

In order to further analyze the influence of cavity characteristics on prognosis, we carried out subgroup analysis of cavity lung adenocarcinoma. We measured the maximum diameter of the cavity, the maximum cavitation diameter/maximum tumor diameter ratio and recorded whether the cavity was multiple or not; the results are summarized in Table 5. We found that in the group with a maximum cavitation diameter/tumor diameter ratio of ≤15, the cavity was more likely to be in a multiple state (P<0.001), the ratio might not fully describe the actual situation of the cavity. Therefore, we conducted the ROC curve of the maximum diameter of the cavity, single or multiple, to judge the RFS (Figure 8). The results showed that the best cutoff value of maximum diameter of the cavity for judging RFS was 5 mm (sensitivity: 0.500; specificity: 0.783). At the same time, multiple cavities were more likely to lead to recurrence (sensitivity: 0.605; specificity: 0.439).

Discussion

In this study, we investigated the relationship between pathologic stage I IADC with and without cavity formation based on radiological and pathological features. Compared with non-cavitary IADC, we found that cavitation tumors tended to be larger and were significantly associated with worse prognosis. In our series, the incidence of cavitary IADC was 10.8%, which was in line with previous reports [8,15,18]. Squamous cell carcinoma was the major histological subtypes studied among cavity formation in the previous studies, however, we tried to focus on the other subtype of cavity cancer, invasive lung adenocarcinoma.

When compared with non-cavitary adenocarcinoma patients, male, older age, larger size of tumor, and patients with postoperative recurrence were more common among those patients

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Table 2. Patient characteristics in cavitary adenocarcinoma and noncavitary adenocarcinoma groups.

Variable	Cavity n (%)	Noncavity n (%)	P-value
Total (n=2106)	N=227	N=1879	
Age (years)			
Median	59	61	**0.039**
Range	24–82	24–85	
≥65	69 (30.3)	644 (34.3)	0.244
Sex			
Male	108 (47.6)	736 (39.2)	**0.015**
Female	119 (52.4)	1143 (60.8)	
Tumor size (cm)			
Median	2.0	1.7	**0.004**
Range	0.6–3.0	0.5–3.0	
>2 cm	82 (36.1)	551 (29.3)	**0.035**
p-T status			
1a	30 (13.2)	317 (16.9)	0.161
1b	100 (44.1)	830 (44.2)	0.973
1c	55 (24.2)	368 (19.5)	0.099
2a	42 (18.5)	364 (19.4)	0.754
Predominant histology subtype			
Lepidic	23 (10.1)	212 (11.3)	0.603
Papillary	83 (36.6)	626 (33.3)	0.353
Acinar	104 (45.8)	878 (46.7)	0.785
Solid	10 (4.4)	102 (5.4)	0.516
Micropapillary	0 (0)	15 (0.8)	0.177
Smoking history			
Former or current smoker	17 (7.5)	117 (6.2)	0.462
Never smoker	210 (92.5)	1762 (93.8)	
Postoperative recurrence	38 (16.7)	138 (7.3)	**<0.001**
Visceral pleural invasion	42	364	0.754
Lymphatic vessel invasion	11	71	0.462

with cavity formation. It was previously reported that cavitary squamous cell carcinoma tended to have a larger tumor size than its non-cavitary equivalent [19], and we have obtained similar findings with cavitary adenocarcinoma. Our results showed that cavitary adenocarcinoma were on average larger in size than non-cavitary adenocarcinoma, similar to previous studies. There was no significant difference with respect to the T stage and smoking history. Furthermore, there were no significant differences in VPI and LVI between tumors with and without cavity formation. Our results were in line with prior studies [8,9,11–13]. Whereas Watanabe et al. [18] found that cavity was more common in tumors located in the lower lobe with an advanced stage or with a predominantly papillary or solid histologic component. But their study included all lung adenocarcinoma patients from stage I to stage IV and the cavities they studied were all larger than 5 mm in diameter. This difference in patient tumors might partially explain the difference in results.

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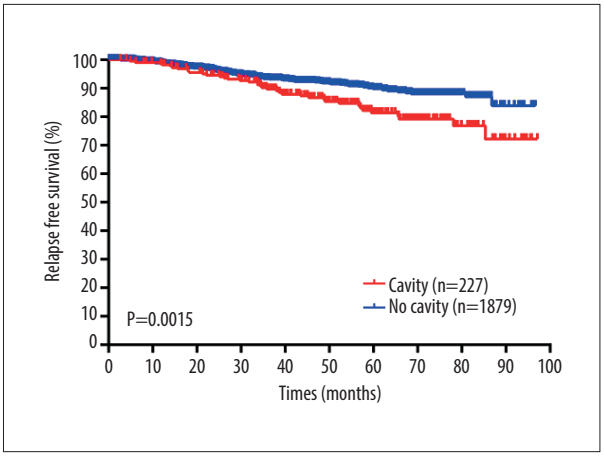

Figure 3. Kaplan-Meier curves of relapse-free survival for patients with and without cavitary lung adenocarcinoma.

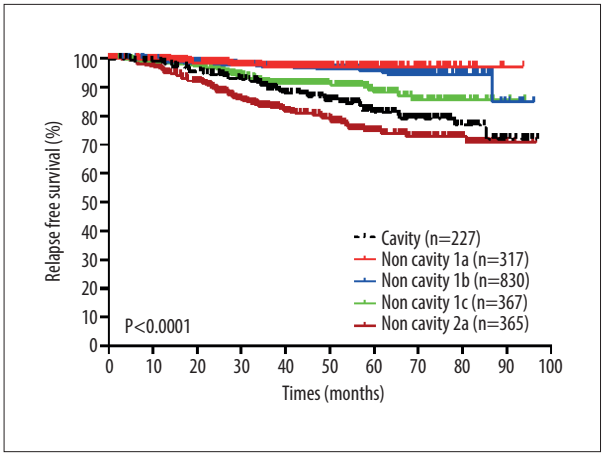

Figure 4. Kaplan-Meier analysis for T stage and cavitary adenocarcinoma.

Table 3. Univariable analyses for relapse-free survival (RFS) and overall survival (OS).

Variable	RFS	*P*-value	OS	*P*-value
	HR (95% CI)		HR (95% CI)	
Age (years)	1.026 (1.010–1.043)	**0.002**	2.244 (1.346–3.741)	**0.002**
Sex	1.601 (1.192–2.152)	**0.002**	2.125 (1.268–3.561)	**0.004**
Cavity (yes/no)	1.788 (1.246–2.567)	**0.002**	1.022 (0.484–2.158)	0.955
Tumor size (cm)	2.016 (1.584–2.566)	**<0.001**	2.210 (1.443–3.382)	**<0.001**
p-T status	2.223 (1.869–2.645)	**<0.001**	2.292 (1.693–3.102)	**<0.001**
Predominant histology subtype	1.602 (1.309–1.961)	**<0.001**	1.806 (1.300–2.508)	**<0.001**
Mediastinal lymph node assessed (yes/no)	0.486 (0.341–0.693)	**<0.001**	0.465 (0.255–0.850)	**0.013**
Surgical resection	0.403 (0.281–0.580)	**<0.001**	0.335 (0.185–0.605)	**<0.001**
Smoking history	1.172 (0.6662.063)	**0.581**	2.701 (1.327–5.498)	**0.006**
Visceral pleural invasion	3.837 (2.851–5.164)	**<0.001**	3.960 (2.373–6.608)	**<0.001**
Lymphatic vessel invasion	3.481 (2.195–5.521)	**<0.001**	2.139 (0.849–5.390)	**0.107**

The cause of the cavity has been often discussed. In the course of tumor progression, cancer cells gradually replaced normal alveolar tissue, and due to the inclusion of normal lung tissue, the density on CT image is often uneven. At lower densities, there is a small bright bubble shadow, called cavitation. Lung adenocarcinomas, moreover, often can cause internal fibrous tissue formation, scar tissue contraction, cause alveolar wall break merger, expand, and form a cavity. In addition, when necrotic tissue is excreted, dehydrated and reduced in volume to form a vacuum, or when lung tissue inside the tumor is replaced by cancer tissue, it is also called cavitation. In addition, Zhang et al. [20] reported that the number of tumor blood vessels decreased with increasing tumor size in non-small-cell lung cancers (NSCLC), and the possibility that NSCLC can thus outgrow its own blood supply has been previously stated [21], so inadequate vascularization might partly account for cavity formation in lung carcinoma.

With respect to the prognosis of cavity adenocarcinoma, we analyzed the stage-specific survival between the cavitary and the non-cavitary groups. Compared with non-cavitary adenocarcinoma, cavitary adenocarcinoma had a worse prognosis in RFS. Onn et al. study [9] revealed that cavitary lesions were significantly associated with shorter LCSS (P=0.010) and shorter OS (P<0.007), but it did not distinguish between the pathological types of adenocarcinoma and squamous cell carcinoma. Our findings provided the first evidence that pathologic stage I IADC with cavity formation was associated with a worse prognosis than without cavity.

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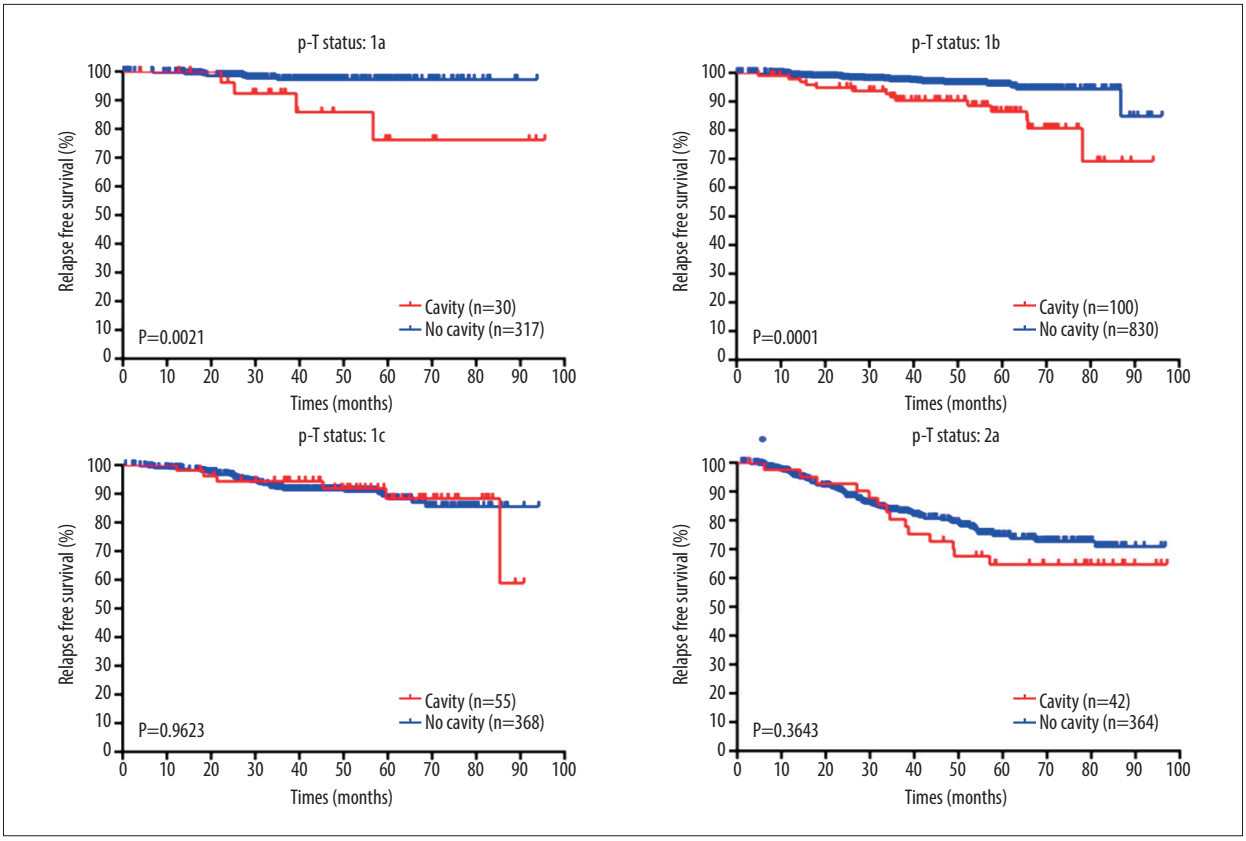

Figure 5. Kaplan-Meier analysis for subgroup of T stage with and without cavity formation.

Table 4. Multivariable analyses for relapse-free survival (RFS) and overall survival (OS).

Variable	RFS	*P*-value	OS	*P*-value
	HR (95% CI)		HR (95% CI)	
Age, (years)	1.011 (0.993–1.028)	0.243	1.050 (1.017–1.084)	**0.003**
Sex	1.405 (1.002–1.969)	**0.049**	1.964 (1.077–3.583)	**0.028**
Cavity (yes/no)	1.810 (1.229–2.665)	**0.003**	0.908 (0.403–2.046)	0.816
Tumor size (cm)	1.720 (1.200–2.466)	**0.003**	2.098 (1.097–4.012)	**0.025**
p-T status	1.093 (0.612–1.950)	**0.764**	0.863 (0.311–2.392)	0.776
Predominant histology subtype	1.356 (1.065–1.727)	**0.014**	1.485 (1.000–2.205)	**0.050**
Mediastinal lymph node assessed (yes/no)	0.698 (0.347–1.403)	0.312	0.728 (0.237–2.232)	0.579
Surgical resection	0.472 (0.260–0.857)	**0.014**	0.513 (0.191–1.373)	0.184
Smoking history	0.543 (0.260–1.134)	**0.104**	0.917 (0.346–2.426)	0.861
Visceral pleural invasion	2.505 (1.033–6.076)	**0.042**	3.225(0.691–15.042)	0.136
Lymphatic vessel invasion	1.979 (1.231–3.183)	**0.005**	1.106 (0.430–2.849)	0.834

The significance of cavity formation in the T stage of pathologic stage I IADC was unclear in our study. The subgroup analysis of T stage revealed that significantly shorter RFS was founded in cavitary adenocarcinoma patients with stage T1a and T1b but not stage T1c and T2a. This phenomenon was not found in stages 1c and 2a, which might be due to factors that determine the T stage, such as tumor size and LVI, which have a greater impact on staging than cavities. Therefore, upstaging of T stage when stage T1a and T1b IADC with cavity formation occurs is recommended. Unfortunately, our survival analysis

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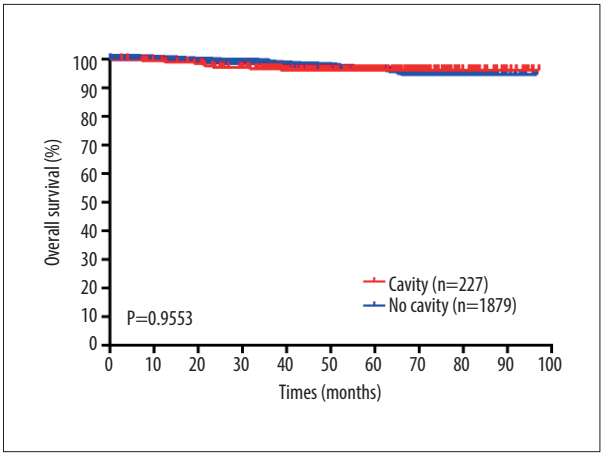

Figure 6. Kaplan-Meier curves of overall survival for patients with and without cavitary lung adenocarcinoma.

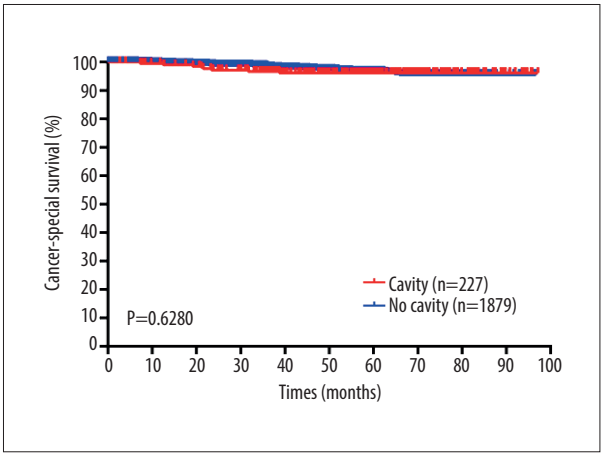

Figure 7. Kaplan-Meier curves of lung cancer specific survival for patients with and without cavitary lung adenocarcinoma.

demonstrated there was no significant differences in OS and LCSS rates between tumors with and without cavity formation.

Spread through air spaces (STAS) has been reported as a significant prognostic factor for NSCLC [22,23]. Tomizawa et al. [24] screened 59 patients with tumor cavitation from 602 patients with p-stage I–IIA primary lung cancer, and found STAS in 23 of 59 patients with tumor cavitation, 17 of 38 patients with adenocarcinoma (45%), and 3 of 17 with squamous cell carcinoma (18%). A higher proportion of STAS in cavitary lung cancer cases might be one of the reasons for poor prognosis, however, our study did not include STAS analysis.

There are some other limitations in this study. First, the number of patients was inadequate for some potential parameters such as size and cavity wall thickness, which limits clinical application. Second, data were retrospective in nature, and results should be confirmed in prospective trials. Nevertheless,

Table 5. Summary of the characteristics of cavitation.

Variable		
Total (n=227)	**n (%)**	
Maximum cavitation diameter, mm		
1–2	55	(24.2)
2–5	112	(49.3)
>5	60	(26.5)
Maximum cavitation diameter/tumor diameter ratio,%		
≤15	99	(43.6)
>15	128	(56.4)
Single or multiple		
Single	98	(43.2)
Multiple	129	(56.8)

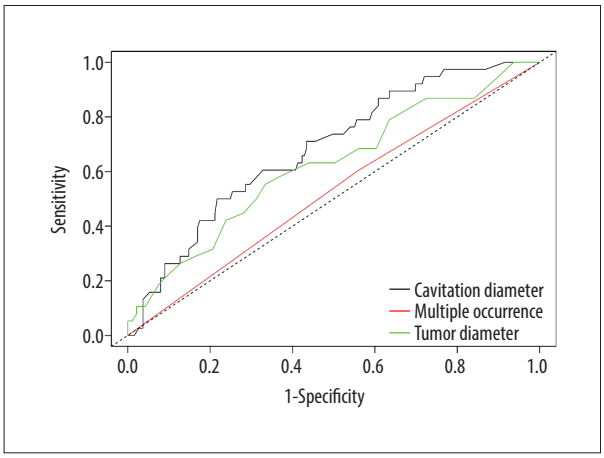

Figure 8. Receiver operating characteristic curve of the maximum diameter of the cavity and single or multiple of the cavity to judge the relapse-free survival.

our study provided important new findings on the clinical impact of the cavity formation in pathologic stage I IADC.

Conclusions

In summary, our findings indicated that cavitary adenocarcinoma has worse prognostic characteristics than non-cavitary adenocarcinoma, especially for cavities >5 mm and multiple cavities. For stage T1a and T1b, cavitary and non-cavitary IADC should be considered separately. Hence, we strongly recommended early stage IADC with cavity formation should be considered as an upstage situation, especially when stage T1a and T1b occurred.

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Conflict of interest

None.

References:

1. Miller WT, MacGregor RR: Tuberculosis: frequency of unusual radiographic findings. Am J Roentgenol, 1978; 130(5): 867–75
2. Van Dyck P, Vanhoenacker FM, Van den Brande P et al: Imaging of pulmonary tuberculosis. Eur Radiol, 2003; 13(8): 1771–85
3. Park Y, Kim TS, Yi CA et al: Pulmonary cavitary mass containing a mural nodule: Differential diagnosis between intracavitary aspergilloma and cavitating lung cancer on contrast-enhanced computed tomography. Clin Radiol, 2007; 62(3): 227–32
4. Cheon JE, Im JG, Kim MY et al: Thoracic actinomycosis: CT findings. Radiology, 1998; 209(1): 229–33
5. Kwong JS, Müller NL, Godwin JD et al: Thoracic actinomycosis: CT findings in eight patients. Radiology, 1992; 183(1): 189–92
6. Balikian JP, Herman PG: Non-Hodgkin lymphoma of the lungs. Radiology, 1979; 132(3): 569–76
7. Chaudhuri MR: Primary pulmonary cavitating carcinomas. Thorax, 1973; 28(3): 354–66
8. Mouroux J, Padovani B, Elkaïm D et al: Should cavitated bronchopulmonary cancers be considered a separate entity? Ann Thorac Surg, 1996; 61(2): 530–32
9. Onn A, Choe DH, Herbst RS et al: Tumor cavitation in stage I non-small cell lung cancer: Epidermal growth factor receptor expression and prediction of poor outcome. Radiology, 2005; 237(1): 342–47
10. Kolodziejski LS, Dyczek S, Duda K et al: Cavitated tumor as a clinical subentity in squamous cell lung cancer patients. Neoplasma, 2003; 50(1): 66–73
11. Gasinska A, Kolodziejski L, Niemiec J et al: Clinical significance of biological differences between cavitated and solid form of squamous cell lung cancer. Lung Cancer, 2005; 49(2): 171–79
12. Wang M, Zhao J, Pan Y et al: Do tumor cavitation and sex in resected stage I non-small-cell lung cancer correlate with prognosis? World J Surg, 2009; 33(3): 497–504
13. Coffey JP, Hill JC: 18F-fluoro-2-deoxy-D-glucose standardized uptake value in cavitating non-small-cell lung carcinoma. Nucl Med Commun, 2008; 29(12): 1040–45
14. Vourtsi A, Gouliamos A, Moulopoulos L et al: CT appearance of solitary and multiple cystic and cavitary lung lesions. Eur Radiol, 2001; 11(4): 612–22
15. Miura H, Taira O, Hiraguri S et al: Cavitating adenocarcinoma of the lung. Ann Thorac Cardiovasc Surg, 1998; 4(3): 154–58
16. Xue XY, Wang PL, Xue QL et al: Comparative study of solitary thin-walled cavity lung cancer with computed tomography and pathological findings. Lung Cancer, 2012; 78(1): 45–50
17. Travis WD, Brambilla E, Noguchi M et al: International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society International Multidisciplinary Classification of Lung Adenocarcinoma. J Thorac Oncol, 2011; 6(2): 244–85
18. Watanabe Y, Kusumoto M, Yoshida A et al: Surgically resected solitary cavitary lung adenocarcinoma: Association between clinical, pathologic, and radiologic findings and prognosis. Ann Thorac Surg, 2015; 99(3): 968–74
19. Usui S, Minami Y, Shiozawa T et al: Differences in the prognostic implications of vascular invasion between lung adenocarcinoma and squamous cell carcinoma. Lung Cancer, 2013; 82(3): 407–12
20. Zhang L, Yankelevitz DF, Henschke CI et al: Variation in vascular distribution in small lung cancers. Lung Cancer, 2010; 68(3): 389–93
21. Miles KA, Griffiths MR, Keith CJ: Blood flow-metabolic relationships are dependent on tumour size in non-small cell lung cancer: A study using quantitative contrast-enhanced computer tomography and positron emission tomography. Eur J Nucl Med Mol Imaging, 2006; 33(1): 22–28
22. Kadota K, Nitadori J, Sima CS et al: Tumor spread through air spaces is an important pattern of invasion and impacts the frequency and location of recurrences after limited resection for small stage I lung adenocarcinomas. J Thorac Oncol, 2015; 10(5): 806–14
23. Lu S, Tan KS, Kadota K et al: Spread through air spaces (STAS) is an independent predictor of recurrence and lung cancer – specific death in squamous cell carcinoma. J Thorac Oncol, 2017; 12(2): 223–34
24. Tomizawa K, Shimizu S, Ohara S et al: Clinical significance of tumor cavitation in surgically resected early-stage primary lung cancer. Lung Cancer, 2017; 112: 57–61

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