

The prognosis of different types of pleural tags based on radiologic- pathologic comparison

Yao Meng

Capital Medical University

Jie Gao

Chinese PLA General Hospital

Chongchong Wu

Chinese PLA General Hospital

Mei Xie

Chinese PLA General Hospital

Xidong Ma

Chinese PLA General Hospital

Xuelel Zang

Chinese PLA General Hospital

Jialin Song

Weifang Medical University

Meng Zhou

Binzhou Medical University

Shikun Guo

Peking University Health Science Center

Yemei Huang

Capital Medical University

Hengyu Deng

Weifang Medical University

Hongli Li

Weifang Medical University

Bo Wei

Capital Medical University

Xinying Xue (✉ xuexinying2988@bjshjth.cn)

Capital Medical University

Research Article

Keywords: visceral pleural invasion, pleural tag, computed tomography, pathology, prognosis

Posted Date: May 13th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1553140/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Objectives: There are increasing numbers of studies of pleural tags (PTs). The purpose of this case series was to classify the PTs in patients with peripheral pulmonary adenocarcinoma based on radiologic-pathologic comparison and to study the prognosis.

Methods: The clinical, imaging, pathological and prognostic data of 161 patients with peripheral pulmonary adenocarcinoma in three hospitals were analyzed retrospectively. We classified PTs using computed tomography (CT) for pathologic comparison.

Results: The CT features were classified into non-interlobular PTs (type 1, one or more linear non-interlobular PT; type 2, one or more linear non-interlobular PT with soft tissue component at the pleural end; type 3, one soft tissue cord-like non-interlobular PT; type 4, directly abutting the non-interlobular pleura) and interlobular PTs (type 1, pulling the interlobular pleura to the homolateral side; type 2, one or more linear interlobular PT; and type 3, pushing the interlobular pleura to the contralateral side). In these PTs, the incidence of visceral pleural invasion (VPI) was high in type 2 (46.88%) and type 3 (56.41%) of non-interlobular PTs. Our prognostic analysis showed that micropapillary or solid histological subtype (HR = 5.766, 95% CI: 1.435-23.159, P = 0.014) and type 3 of non-interlobular PTs (HR = 11.058, 95% CI: 1.349-90.623, P = 0.025) were two independent risk factors for tumor progression.

Conclusions: PT is a risk factor for poor prognosis of patients, the presence of which on CT images can remind us to provide patients with a more reasonable treatment.

Introduction

Lung cancer is the primary cause of cancer-related mortality in most developed countries, with 5-year relative survival rates of 18% at present [1–3]. Currently, although surgical resection is the treatment of first choice for early stage non-small cell lung cancer (NSCLC), most patients have either locally advanced or metastatic disease, and only 20–30% of patients have potentially operable early stage disease [4]. The tumor node metastasis (TNM) staging influences the diagnosis, treatment plan and prognosis for this malignancy[1]. Visceral pleural invasion (VPI) is a significant stage descriptor in the eighth edition of the TNM staging system. Mayumi et al. [5] reported that the five-year survival rates decreased from 86% (for patients without VPI) to 62–70% (for patients with VPI). VPI is defined as the tumor that extends to the elastic layer of visceral pleura but not beyond the surface of visceral pleura [6, 7]. For parietal pleural invasion, extrapleural dissection with en-bloc resection were recommended [8], and lobectomy rather than segmentectomy was recommended in patients with VPI [9]. Therefore, accurate diagnosis of VPI is important preoperatively.

Computed tomography (CT) is currently the imaging method of first choice in the staging of lung cancer. The diagnosis of VPI on CT mainly depends on the contact of the tumor with the chest wall, mediastinum or interlobar fissure. However, simple contact of tumor and chest wall, mediastinum or interlobar fissure does not necessarily mean invasion. Pleural tags (PTs) refer to one or more linear strands extending from

the nodule surface to the pleural surface due to thickening of interlobular septa of the lung. PTs on CT images may help us improve the accuracy of early diagnosis of VPI [10]. The purpose of this case series was to classify the PTs in patients with peripheral pulmonary adenocarcinoma based on radiologic-pathologic comparison and to study the prognosis.

Materials And Methods

Patients

With approval from our institutional review board, our study was performed with exemption of informed consent. We retrospectively collected and analyzed the clinical, CT, and pathologic data in 161 patients with peripheral pulmonary adenocarcinoma. They were treated at one of three hospitals (the General Hospital of the People's Liberation Army, Affiliated Beijing Shijitan Hospital of Capital Medical University and Affiliated Hospital of Qingdao University) between 2013 and 2019. Imaging data were retrieved from the picture archiving and communication system (PACS). Tumors were characterized as peripheral pulmonary adenocarcinoma, and the diagnosis was confirmed by postoperative histopathologic examination. Sex, age, pleural invasion, the largest diameter of the tumor, pathological type, histological subtype and pathologic T stage (pT stage) of 161 patients were recorded. Tumor stage was determined according to the 2017 Union for International Cancer Control (UICC) TNM Staging (8th edition).

In addition to typical PTs on CT, only patients without other malignancies and without any postoperative adjuvant therapy were included in this study.

Ct Analysis

All patients included in this study received non-contrast CT of the chest performed by a GE LightSpeed 16-Slice CT scanner (GE Healthcare, Beijing, China) or a Siemens SOMATOM Sensation 64-Slice CT Scanner (Siemens, Forchheim, Germany). The CT parameters were as follows: routine section thickness, 1.0, 1.25, or 1.5 mm; section thickness after reconstruction, 0.625–1.25 mm; filtered back projection reconstruction method; 80–120 kV; 200–280 mAs; and a B70f kernel. We used the last CT studies in the lung just before histopathologic diagnosis as the CT observation.

A thoracic radiologist with 26 years of experience in cardiopulmonary imaging and a medical student with 2 years of experience in pulmonary imaging diagnosis consistently examined the CT images of each institution by using a PACS (AGFA Healthcare, Mortsels, Belgium) (lung window width, 1500 HU; level, -500 HU) and labeled the CT images including PTs. PTs were recorded as the radiological parameter for each patient.

Pathological Analysis

All existing histopathologic slides were reviewed by one senior pathologist with 12 years of experience with pathologic diagnosis of the lung and a Master of Pathology with 3 years of experience with pathologic diagnosis.

Statistical Analysis

We used telephone follow-up, but 29 patients were lost to follow-up immediately after surgery among all the 161 patients. Data were collected and entered by using Microsoft Excel and were analyzed using SPSS, version 26.0 (IBM Statistics, Armonk, NY). Age and the largest diameter of the tumor were expressed as means \pm standard deviations with ranges. Sex, diagnosis of VPI, pathologic type, histological subtype, pT stage and CT features are expressed as frequencies and percentages. Progression-free survival (PFS) was estimated using the Kaplan–Meier method, and differences in survival rates were determined by log-rank test. Variables with p value < 0.15 were included in the Cox-proportional hazards model for multivariable survival analysis to evaluate independent risk factors affecting the prognosis of patients. A p value < 0.05 was considered statistically significant.

Results

Clinical Characteristics

Figure 1 shows the patient inclusion flowchart. A total of 161 patients (mean age, 59.67 years \pm 10.44; age range, 27–84 years), with peripheral pulmonary adenocarcinoma were included (Table 1). Sixty-two (38.50%) of the 161 patients were men (mean age, 60.73 years \pm 10.00; age range, 33–84 years), and 99 (61.50%) were women (mean age, 59.01 years \pm 10.71; age range, 27–84 years). Seventy-five patients (46.58%) of the 161 patients were diagnosed with VPI and eighty-six patients (53.42%) were diagnosed without VPI. The largest diameter of the 161 patients' tumor was 2.32 cm \pm 1.33, and the diameter ranged from 0.5-11cm.

Table 1
Clinical Characteristics of Patients with peripheral pulmonary adenocarcinoma

Characteristic	No. of Patients	Datum
Age of all 161 patients (y)	161	59.67 ± 10.44(27–84)
Male		60.73 ± 10.00(33–84)
Female		59.01 ± 10.71(27–84)
Sex of all 161 patients		
Male	62	38.50%
Female	99	61.50%
VPI		
Yes	75	46.58%
No	86	53.42%
Largest diameter of 161 patients' tumor	161	2.32 ± 1.33(0.5–11)
Pathological type of 161 patients		
MIA	3	1.86%
INMA	153	95.03%
IMA	5	3.11%
Histological subtype of 161 Patients		
LPA	29	18.01%
APA	78	48.45%
MPA or SPA	14	8.70%
PPA	16	9.94%
Not available	24	14.90%
pT stage		
T1	76	47.21%
T2	81	50.31%
T3 ~ T4	4	2.48%

Characteristic	No. of Patients	Datum
<p>Note. – Data are means ± standard deviations or percentages. Data in parentheses are ranges. pT stage= pathologic T stage, IMA= invasive mucinous adenocarcinoma, MIA = minimally invasive adenocarcinoma, INMA= invasive non-mucinous adenocarcinoma, LPA = lepidic predominant adenocarcinoma, APA = acinar predominant adenocarcinoma, MPA = micropapillary predominant adenocarcinoma, PPA = papillary predominant adenocarcinoma, SPA = solid predominant adenocarcinoma, Not available=the histological subtype was not clearly defined</p>		

Three patients (1.86%) of the 161 patients were diagnosed with minimally invasive adenocarcinoma (MIA) in the pathology system, one hundred and fifty-three patients (95.03%) were diagnosed with invasive non-mucinous adenocarcinoma (INMA) and five patients (3.11%) were diagnosed with invasive mucinous adenocarcinoma (IMA). Twenty-nine patients (18.01%) of the 161 patients were diagnosed with lepidic predominant adenocarcinoma (LPA) in the histology system, seventy-eight patients (48.45%) were diagnosed with acinar predominant adenocarcinoma (APA), sixteen patients (9.94%) were diagnosed with papillary predominant adenocarcinoma (PPA), fourteen patients (8.70%) were diagnosed with micropapillary predominant adenocarcinoma (MPA) or solid predominant adenocarcinoma (SPA) and for twenty-four patients (14.90%) data were not available.

Seventy-six patients (47.21%) were diagnosed with pT1 in the pT stage system, eighty-one patients (50.31%) were diagnosed with pT2, and four patients (2.48%) were diagnosed with pT3 or pT4.

Ct Characteristics

Figure 2 shows the CT imaging features of the peripheral pulmonary adenocarcinoma determined in consensus. The CT features were classified into two forms (non-interlobular PTs and interlobular PTs). Non-interlobular PTs were classified into four types (type 1, one or more linear non-interlobular PT; type 2, one or more linear non-interlobular PT with soft tissue component at the pleural end; type 3, one soft tissue cord-like non-interlobular PT; type 4, directly abutting the non-interlobular pleura). Interlobular PTs were classified into three types (type 1, pulling the interlobular pleura to the homolateral side; type 2, one or more linear interlobular PT; and type 3, pushing the interlobular pleura to the contralateral side). In the non-interlobular PTs, nineteen patients (11.80%; eight patients [42.11%] with pleural invasion proved by pathologic analysis) of the 161 patients had type 1 of PTs; thirty-two patients (19.88%; fifteen patients [46.88%] with pleural invasion) had type 2 of PTs; thirty-nine patients (24.22%; twenty-two patients [56.41%] with pleural invasion) had type 3 of PTs and forty-five patients (27.95%; nineteen patients [42.22%] with pleural invasion) had type 4 of PTs. In the interlobular PTs, nineteen patients (11.80%; eight patients [42.11%] with pleural invasion proved by pathologic analysis) of the 161 patients had type 1 of PTs; five patients (3.11%; one patient [20.00%] with pleural invasion) had type 2 of PTs and two patients (1.24%) with pleural invasion had type 3 of PTs (Table 2).

Table 2
CT Characteristics in Patients with Peripheral Pulmonary Adenocarcinoma

CT Characteristics*	VPI n (%)	non-VPI n (%)	datum
Non-interlobular PTs			
Type1	8(42.11%)	11(57.89%)	11.80%
Type2	15(46.88%)	17(53.12%)	19.88%
Type3	22(56.41%)	17(43.59%)	24.22%
Type4	19(42.22%)	26(57.78%)	27.95%
Interlobular PTs			
Type1	8 (42.11%)	11(57.89%)	11.80%
Type1	1 (20.00%)	4(80.00%)	3.11%
Type2	2 (100.00%)	0(0.00%)	1.24%
Type3			
Note. – Data are the number of patients or percentages. Data in parentheses are percentages. PTs = pleural tags, * Based on evaluation of the last chest CT study performed before histopathologic diagnosis.			

Pathology

There were 161 patients with a definitive histopathologic diagnosis. Pathologic findings confirmed that 75 (46.58%) of the 161 patients were diagnosed with VPI, and 86 patients (53.42%) were diagnosed without VPI.

After surgery, we correlated the imaging findings with the pathologic findings. According to the characteristics of the CT images, under the ×20 magnification of hematoxylin-eosin staining, the linear pleural tags such as type 1 of non-interlobular PTs and type 2 of interlobular PTs were formed by the contraction of reactive proliferative fibrous tissue in the tumor. This was done by pulling the pleura to make it parallel, concave, and close to each other or the fibrous hyperplasia, and the thickening of the interlobular septae, along which carcinoma cells or inflammatory cells infiltrated. Type 2 of non-interlobular PTs included changes in linear PTs and terminal triangular pleural indentation. Type 3 of non-interlobular PTs were caused by the proliferative fibrous tissue in the tumor, which contracted and pulled pleura to form a V-shape shadow or caused compressive atelectasis to form a cord-like soft tissue shadow. Type 4 of non-interlobular PTs, types 1 and 3 of interlobular PTs showed tumor tissue attached to normal or thickened visceral pleura (Fig. 3).

In patients pathologically diagnosed with VPI, tumor cells were observed to penetrate the elastic fibrous boundary of the pleura and infiltrate into the pleura under the 20x microscopic scale of Elastica van

Gieson staining. In patients diagnosed without VPI, the tumor cells did not break through the elastic layer of the pleura (Fig. 3).

Prognosis

Patients in this study were followed up from 2 months to 77 months after surgery. Among the 132 patients included, 50 were males and 82 were females, aged 27–84 years, with a median age of 60 years. There were 32 patients with tumor progression (19 with new malignant nodules or distant metastasis, 13 died of lung cancer). Continuous variables, including age and tumor diameter, were transformed into categorical variables. Based on our prognosis data and pathological results, the type 1 of non-interlobular PTs and type 2 of interlobular PTs were combined into a group of type 1, the type 4 of non-interlobular PTs and type 1 and 3 of interlobular PTs were combined into a group of type 4, to increase the accuracy for PFS analysis.

The results of the univariate analysis affecting tumor progression are shown in Table 3. The univariate and multivariable survival analysis curves were shown in Fig. 4. Univariate analysis showed that tumor size, histological subtype and PTs (type) were significantly associated with prognosis. Cox-proportional hazards model was further used to analyze the prognostic factors. The variables with p value < 0.15, such as sex, tumor size, VPI, PTs and histological subtype, were included in the analysis to exclude the mutual influence of each factor on the prognosis in univariate analysis. The Cox regression survival curve showed that micropapillary or solid histological subtype (HR = 5.766, 95% CI: 1.435–23.159, P = 0.014) and type 3 of non-interlobular PTs (HR = 11.058, 95% CI: 1.349–90.623, P = 0.025) were two independent risk factors for tumor progression.

Table 3: The results of univariate analysis affecting tumor progression in 132 patients

Variables	Progression(n=32)	Progression-free(n=100)	P
Age(year)			0.308
≤60	14	56	
>60	18	44	
Sex			0.076
Male	18	32	
Female	14	68	
VPI			0.127
Yes	24	39	
No	8	61	
Largest diameter (cm)			0.019
≤3	24	92	
>3	8	8	
Pathological type			0.937
MIA	1	2	
INMA	30	94	
IMA	1	4	
Histological subtype			0.036
LPA	4	19	
APA	12	54	
MPA or SPA	5	6	
PPA	2	13	
Not available	9	8	
pT stage			0.222
T1	6	55	
T2	25	44	
T3~T4	1	1	
Type			0.016

1	1	16
2	5	19
3	16	19
4	10	46
Note. – Type: different type of pleural tags		

Discussion

In our study, PTs were classified into two forms and seven types (Fig. 5). Yang et al. categorized PTs into nine types and found that type 3 and type 4 of non-interlobular PTs and type 1 and type 3 of interlobular PTs may be indicators for VPI [11]. Our study found that the incidence of VPI was high in type 2 (46.88%) and type 3 (56.41%) of the non-interlobular PTs, while the ratio of VPI in type 3 of interlobular PTs was 2/2. According to our study, type 4 of non-interlobular PT often suggests that there is less possibility of VPI pathologically than type 2 and type 3. Excluding severe pleural adhesion due to inflammatory diseases, chest CT combined with artificial pneumothorax is useful for the evaluation of the extension of lung cancer into the chest wall [12]. This may help us diagnose VPI of type 4 of non-interlobular PTs.

VPI was a significant prognostic factor independently of tumor size, histology of tumor, lymph node status, age, sex, and smoking status [5]. In several previous reports, patients with tumors exhibiting pleural invasion had worse outcomes than those without pleural invasion [13–18]. Therefore, we included VPI ($P = 0.127$) into the multivariable analysis. Our prognostic results suggested that in addition to histological subtype which was an independent risk factor for poor prognosis, type 3 of non-interlobular PT was also an independent risk factor for tumor progression. This suggests to us that when this type of PT appears on CT, adjuvant therapy such as chemotherapy or targeted therapy should be used after surgery.

There were some limitations in our study. Although we chose patients from three hospitals, the sample size is relatively small, so patient selection bias is inevitable, and the follow-up time is short, which may affect our results. Larger sample studies and longer follow-up are needed to validate the value of PTs in the prognosis.

At present, artificial intelligence assisted diagnosis technology has appeared, which has certain advantages in diagnosing the benign or malignant pulmonary nodules on CT and even the occurrence of VPI. However, the prognosis of different types of PTs is different. In the future, artificial intelligence combined with our prognosis study will provide help in the formulation of a comprehensive treatment plan.

Conclusions

In conclusion, despite the limitations mentioned above, PT remains a risk factor for poor prognosis of patients. The presence of PTs on CT images can remind us to provide patients with a more complete surgical resection, pay attention to the postoperative pathological results and provide more reasonable treatments for the next steps.

Abbreviations

APA: acinar predominant adenocarcinoma

CT: computed tomography

IMA: invasive mucinous adenocarcinoma

INMA: invasive non-mucinous adenocarcinoma

LPA: lepidic predominant adenocarcinoma

MIA: minimally invasive adenocarcinoma

MPA: micropapillary predominant adenocarcinoma

NSCLC: non-small cell lung cancer

PPA: papillary predominant adenocarcinoma

PT: pleural tag

SPA: solid predominant adenocarcinoma

TNM: tumor node metastasis

UICC: Union for International Cancer Control

VPI: visceral pleural invasion

Declarations

Ethics approval and consent to participate

Approval was obtained from the ethics committee of Affiliated Beijing Shijitan Hospital of Capital Medical University (Ethics approval number: sjtkyll-ix-2022(035)), all methods were carried out in accordance with relevant guidelines and regulations. Due to the retrospective study design, the ethics committee of Affiliated Beijing Shijitan Hospital of Capital Medical University approved a waiver of written informed consent.

Consent for publication

Not applicable.

Data Availability Statement

To preserve patient confidentiality, the datasets generated for this study are not publicly available, but are available upon reasonable request.

Conflict of Interest

No conflicts of interest were declared. The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Funding

This work was supported by the

1. National Natural Science Fund Youth Project (81700007).
2. Research and innovation fund of the Ministry of Education (2018A03026).
3. Beijing Natural Science Foundation (2019A10).
4. "Qingmiao" plan of Beijing Municipal Hospital Administration (2018QM4).
5. Outstanding top talent(2019YXBJ1)
6. Capital health development scientific research unit matching fund(2020-2Z-2086)
7. Excellent talents in Beijing "Youth top team" (2019YXBJ2)

Author Contributions

YM collected data and wrote the main manuscript. YM, JG and CW conducted the data analysis and interpreted the results. BW and XX designed the research, supervised the data analysis, and critically revised the article. All authors contributed to the article and approved the submitted version.

Acknowledgments

We would like to thank Editage (www.editage.cn) for English language editing.

References

1. Kim H, Goo JM, Kim YT, Park CM: **CT-defined Visceral Pleural Invasion in T1 Lung Adenocarcinoma: Lack of Relationship to Disease-Free Survival.** *Radiology* 2019, **292**(3):741–749.
2. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ: **Cancer statistics, 2009.** *CA Cancer J Clin* 2009, **59**(4):225–249.
3. Onoda H, Higashi M, Murakami T, Tao H, Yokoyama S, Kunihiro Y, Kawano R, Tanabe M, Tanaka N, Matsumoto T: **Correlation between pleural tags on CT and visceral pleural invasion of peripheral lung cancer that does not appear touching the pleural surface.** *Eur Radiol* 2021.
4. Ellis PM, Vandermeer R: **Delays in the diagnosis of lung cancer.** *J Thorac Dis* 2011, **3**(3):183–188.
5. Oyama M, Miyagi Maeshima A, Tochigi N, Tsuta K, Kawachi R, Sakurai H, Watanabe S, Asamura H, Tsuda H: **Prognostic impact of pleural invasion in 1488 patients with surgically resected non-small cell lung carcinoma.** *Jpn J Clin Oncol* 2013, **43**(5):540–546.
6. Detterbeck FC, Boffa DJ, Kim AW, Tanoue LT: **The Eighth Edition Lung Cancer Stage Classification.** *Chest* 2017, **151**(1):193–203.
7. Zhao LL, Xie HK, Zhang LP, Zha JY, Zhou FY, Jiang GN, Chen C: **Visceral pleural invasion in lung adenocarcinoma ≤ 3 cm with ground-glass opacity: a clinical, pathological and radiological study.** *J Thorac Dis* 2016, **8**(7):1788–1797.
8. Santos HT, Lopes AJ, Higa C, Nunes RA, Saito EH: **Lung cancer with chest wall invasion: retrospective analysis comparing en-bloc resection and 'resection in bird cage'.** *J Cardiothorac Surg* 2014, **9**:57.
9. Jeon HW, Kim YD, Kim KS, Sung SW, Park HJ, Park JK: **Sublobar resection versus lobectomy in solid-type, clinical stage IA, non-small cell lung cancer.** *World J Surg Oncol* 2014, **12**:215.
10. Hsu JS, Han IT, Tsai TH, Lin SF, Jaw TS, Liu GC, Chou SH, Chong IW, Chen CY: **Pleural Tags on CT Scans to Predict Visceral Pleural Invasion of Non-Small Cell Lung Cancer That Does Not Abut the Pleura.** *Radiology* 2016, **279**(2):590–596.
11. Yang S, Yang L, Teng L, Zhang S, Cui Y, Cao Y, Shi H: **Visceral pleural invasion by pulmonary adenocarcinoma ≤ 3 cm: the pathological correlation with pleural signs on computed tomography.** *J Thorac Dis* 2018, **10**(7):3992–3999.
12. Watanabe A, Shimokata K, Saka H, Nomura F, Sakai S: **Chest CT combined with artificial pneumothorax: value in determining origin and extent of tumor.** *AJR Am J Roentgenol* 1991, **156**(4):707–710.
13. Shimizu K, Yoshida J, Nagai K, Nishimura M, Yokose T, Ishii G, Nishiwaki Y: **Visceral pleural invasion classification in non-small cell lung cancer: a proposal on the basis of outcome assessment.** *J Thorac Cardiovasc Surg* 2004, **127**(6):1574–1578.
14. Shimizu K, Yoshida J, Nagai K, Nishimura M, Ishii G, Morishita Y, Nishiwaki Y: **Visceral pleural invasion is an invasive and aggressive indicator of non-small cell lung cancer.** *J Thorac Cardiovasc Surg* 2005, **130**(1):160–165.
15. Manac'h D, Riquet M, Medioni J, Le Pimpec-Barthes F, Dujon A, Danel C: **Visceral pleura invasion by non-small cell lung cancer: an underrated bad prognostic factor.** *Ann Thorac Surg* 2001, **71**(4):1088–1093.

16. Osaki T, Nagashima A, Yoshimatsu T, Yamada S, Yasumoto K: **Visceral pleural involvement in nonsmall cell lung cancer: prognostic significance.** *Ann Thorac Surg* 2004, **77**(5):1769–1773; discussion 1773.
17. Kang J: **Prognostic value of visceral pleura invasion in non-small cell lung cancer.** *European Journal of Cardio-Thoracic Surgery* 2003, **23**(6):865–869.
18. Bunker ML, Raab SS, Landreneau RJ, Silverman JF: **The diagnosis and significance of visceral pleural invasion in lung carcinoma. Histologic predictors and the role of elastic stains.** *Am J Clin Pathol* 1999, **112**(6):777–783.

Figures

Figure 1

Patient inclusion flowchart shows the number of patients, evaluation of the imaging studies and pathologic analysis.

Figure 2

The CT features were classified into non-interlobular pleural tags (A, B, C, D) and interlobular pleural tags (E, F, G). The first image in each group had the pleural tag with VPI confirmed pathologically, and the second had not. There was only one image in group G (type 3 of interlobular pleural tags with VPI).

Figure 3

Pleural tags and corresponding hematoxylin-eosin-stained or elastica van Gieson stained histologic findings. (Original magnification, ×20.) At the arrow: (a1), (c1), (d1) tumor cells infiltrated the pleura; (a2), (c2) tumor cells were localized under the subpleural; (b1) tumor cells were observed to penetrate the elastic fibrous boundary of the pleura and infiltrate into the pleura; (b2) tumor cells did not break through the elastic layer of the pleura. (d2) Although the tumor was attached to the pleura on CT, it was pathologically confirmed to be pleural thickening and no tumor cell infiltration.

Figure 4

Kaplan-Meier (K-M) survival curves of variables with $P < 0.15$ and COX curves of multivariable analysis results.

Figure 5

Different types of pleural tags represented by pictograms (a-g, Fig.2 A-G). (a) type 1, one or more linear non-interlobular PT; (b) type 2, one or more linear non-interlobular PT with soft tissue component at the pleural end; (c1) type 3, one soft tissue cord-like non-interlobular PT; (c2) type 3, V-shape non-interlobular PT; (d) type 4, directly abutting the non-interlobular pleura; (e) type 1, pulling the interlobular pleura to the homolateral side; (f) type 2, one or more linear interlobular PT; (g) type 3, pushing the interlobular pleura to the contralateral side.