cytokine receptor interaction, toll-like receptor signaling pathway, chemokine signaling pathway, primary immunodeficiency and natural killer cell mediated cytotoxicity were also altered (Tables II and III). These results suggest that the possibility of metastasis of early-stage lung adenocarcinoma was closely related to the CAM pathway. Interestingly, considering the relationship between group A or group B and histological differentiation as poor or well/moderate, respectively, the metastatic possibility of poorly differentiated early adenocarcinoma appeared to be correlated with tumor development factors, such as the cell cycle, whereas that of well/moderately differentiated early-stage adenocarcinoma appeared to be correlated with host immunological factors, such as the T cell receptor signaling pathway, cytokine-cytokine receptor interaction, the toll-like receptor signaling pathway, the chemokine signaling pathway, primary immunodeficiency and natural killer cell mediated cytotoxicity.

Our results suggest that the particular genes that define the clusters and molecular pathways, or that are associated with early recurrence, likely reflect the characteristics of the particular tumors included in the analysis. Current therapy for patients with early-stage disease usually consists of surgical resection without adjuvant treatment. Clearly, the identification of a high-risk group among early-stage patients would lead to consideration of additional therapeutic interventions, possibly leading to improved survival of these patients.

To our knowledge, this is the first study utilizing cDNA microarray techniques, followed by molecular functional pathway analysis, concerning the early recurrence of early-stage adenocarcinoma of the lung. However, there were some limitations to this study. Firstly, this was a small data set analysis at a single institute. A large cohort sample of patients from multiple institutions is needed. Secondly, the potential interactions of the many specific individual genes and their clusters in lung tumor biology and clinical outcome exist. This may be due to the different platforms used (different genes analyzed) and the different algorithms for selecting functional categories. Thirdly, hierarchical clustering methods and functional analysis offer a powerful approach to class discovery, but provide no means of determining validity for the classes discovered. This is still a putative functional analysis. It is important to state that several *in vitro* and *in vivo* studies are still needed to demonstrate whether these mechanisms are effective in reality.

In conclusion, in the present study, we present a comprehensive gene expression analysis and functional pathway analysis of early-stage lung adenocarcinomas, wherein we identified a distinct molecular pathway category, the CAMs, which correlated with the early relapse of early-stage lung adenocarcinoma subclasses. Further *in vitro* and *in vivo* studies, which can demonstrate these mechanisms, are warranted.

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Case Report

Intracaval and intracardiac extension of invasive thymoma complicated by superior and inferior vena cava syndrome

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We present a case of an aged male with invasive thymoma that extended into the right atrium and led to superior and inferior vena cava syndrome. The patient initially presented with edema of the face and bilateral lower extremities. Echocardiography revealed a mass within the right atrium. Imaging studies demonstrated an anterior mediastinal tumor that continuously occupied the bilateral brachiocephalic veins, superior vena cava, and right atrium. Pathological diagnosis of the tumor biopsy was highly suspicious of thymoma. Due to the high risk of wide spread of the tumor, treatments including resection of the tumor were impossible. Several days later he died, and an autopsy was performed. The tumor was type B2 thymoma invading bilateral brachiocephalic veins, superior vena cava and right atrium. Multiple tumor emboli within the pulmonary arteries were identified. Direct cause of death was deemed to be tumor strangulation at the tricuspid orifice. In addition to the superior vena cava syndrome, inferior vena cava syndrome including ectasia of the intrahepatic vessels was confirmed along with pericarditis. To our knowledge, this is the first English report of an autopsy case of intracardiac thymoma extension, and a detailed literature review of similar cases is also presented.

Key words: intracaval, IVC syndrome, right atrial invasion, SVC syndrome, thymoma.

Thymoma is one of the most common tumors in the mediastinum and accounts for 45% of anterior mediastinal tumors in adults, mainly affecting people aged 40–60 years.[1] Thymomas are classified as invasive or noninvasive, depending on the presence or absence of tumor capsular invasion and/or anatomic extension.[1,2] Invasive thymomas, accounting for approximately 30% of thymomas, may invade mediastinal organs such as pleura and pericardium, but they rarely invade the superior vena cava (SVC).[2] Indeed, although SVC syndrome may be associated in 4% of thymomas, the most common cause is extrinsic compression rather than intracaval growth.[3] Furthermore, intracaval growth with extension into the right atrium, called 'transvenous' cardiac metastasis, is extremely rare.[2] We herein report an autopsy case of this rare manifestation of thymoma, and identified complication by inferior vena cava (IVC) syndrome and peculiar pericarditis.

CLINICAL SUMMARY

The case of a 74-year-old Japanese male with SVC syndrome is presented here. His past history includes colon cancer at the age of 65 and cerebral infarction with hypertension at the age of 72. Edema appeared in the face and bilateral lower extremities in mid-December, 2010. Right pleural effusion was pointed out, and a diuretic was prescribed by a local doctor late in December, 2010. A mass within the right atrium was discovered by echocardiography in mid-January, 2011, thus, he was subsequently transferred and admitted to our hospital.

Computerized tomography (CT) of the chest revealed an anterior mediastinal tumor invading the left brachiocephalic vein and SVC (Fig. 1a). Coronal view of a chest magnetic resonance imaging (MRI) scan showed a mediastinal mass occupying the SVC, which extended into the right brachiocephalic vein and right atrium (Fig. 1b). Angiography demonstrated occlusion of the SVC and bilateral brachiocephalic veins as well as meandering dilated thoracoepigastric veins (collaterals), which connect subclavian veins with superficial epigastric veins that inflow into the inferior vena cava (Fig 1c), signs that were compatible with obstruction of the SVC proximal to the inflow portion of the azygos vein.

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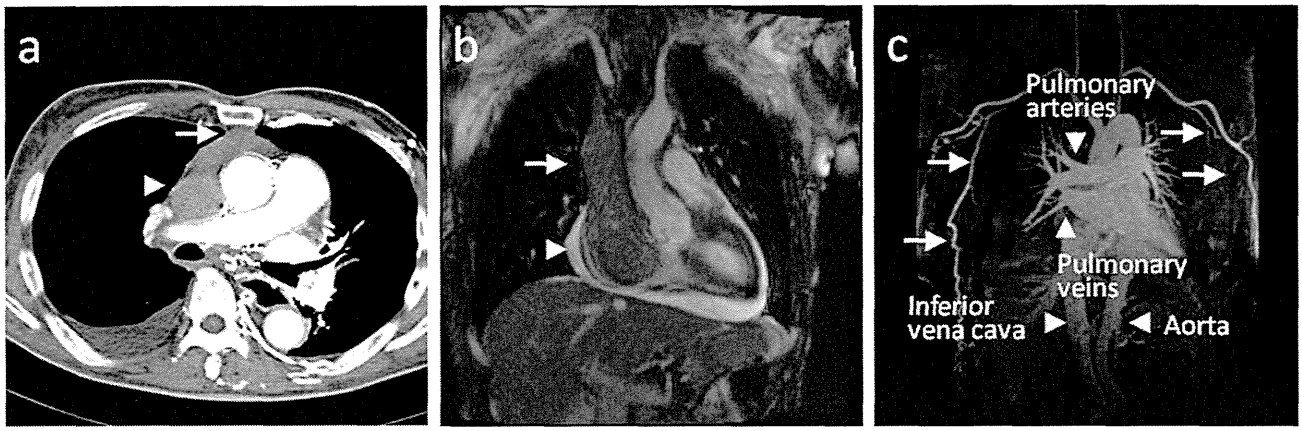

Figure 1 Imaging studies. (a) Chest computerized tomography showing an anterior mediastinal tumor (arrow) that consecutively extends into the left brachiocephalic vein and superior vena cava (arrowhead). (b) Coronal view of a chest magnetic resonance imaging scan showing a mediastinal mass within the superior vena cava (arrow) that consecutively extends into the right atrium (arrowhead). (c) Angiography of large vessels including the pulmonary arteries and veins, aorta, and inferior vena cava. The superior vena cava is not observed. Instead, meandering dilated thoracoepigastric veins are delineated (arrows).

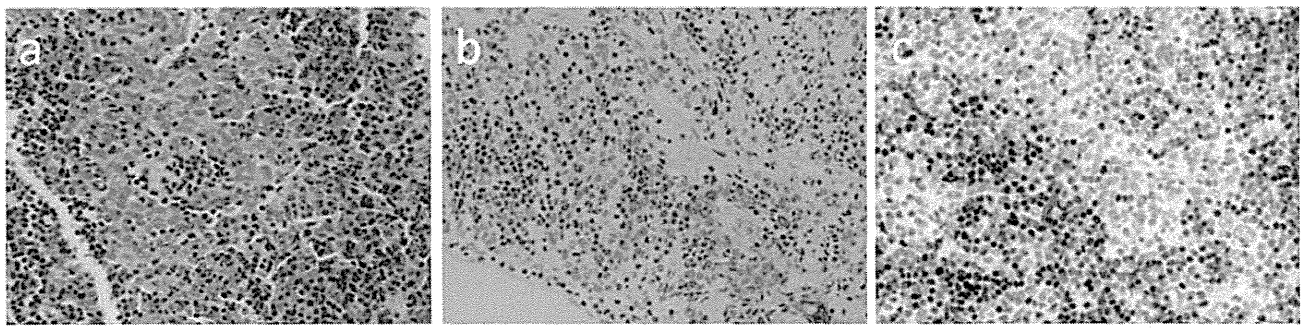

Figure 2 Microscopical features of the tumor. (a) HE staining showing polygonal or rounded epithelial components with an admixture of lymphocytes. (b) Immunohistochemistry of cytokeratin showing focal positive staining for the epithelial cells. (c) Immunohistochemistry of TdT showing diffuse positive staining for the tumor-infiltrating lymphocytes.

Table 1 Antibodies used in immunohistochemistry

Antibody to	Clone	Source	Dilution	Antigen retrieval	Pretreatment
Cytokeratin	AE1/AE3	Dako, Glostrup, Denmark	x400	pH 6CB	Autoclave
CD5	CD5/54/F6	Dako	x50	pH 9EDTA	Autoclave
TdT	SEN28	Nichirei, Tokyo, Japan	x1	pH 6CB	Autoclave
CD99	12E7	Dako	x100	pH 6CB	Autoclave
Fascin	55K-2	Dako	x200	pH 6CB	Autoclave
MMP-2	C-19	Santa Cruz Biotechnology, Santa Cruz, CA	x200	pH 9EDTA	Autoclave
VEGF	A-20	Santa Cruz	x200	pH 9EDTA	Autoclave

MMP, matrix metalloproteinase; pH 6CB, pH 6 Citrate Buffer Solution; pH 9EDTA, pH 9 EDTA buffer; VEGF, vascular endothelial growth factor.

Tumor biopsy using a right heart catheter was performed late in January. The biopsy material was highly cellular and consisted of polygonal or rounded epithelial cells with an admixture of lymphocytes (Fig. 2a). Immunohistochemistry was performed, using avidin-biotin-peroxidase complex according to standard methods. Table 1 lists all of the antibodies used along with the clone and dilution, the antigenic retrieval method used, and pretreatment methods. Immunohistochemically, cytokeratin was focally positive (Fig. 2b) but CD5 was negative in the epithelial cells, and CD5 and immature lymphocytic markers TdT were diffusely positive for the lymphocytes (Fig. 2c). Therefore, although the quantity of the material was insufficient, the histopathological diagnosis of 'highly suggestive of thymic tumor, in favor of type B1 or B2 thymoma' was made.

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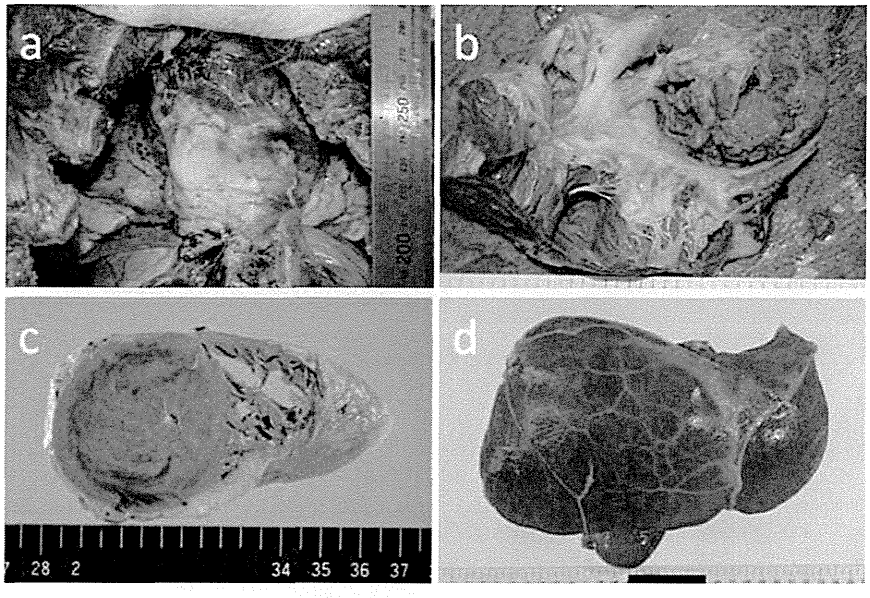

Figure 3 Macroscopical features at autopsy. (a) Poorly demarcated yellowish white anterior mediastinal tumor, 6 × 4 × 1 cm in size, at thoracotomy. (b) Intra-atrial tumor forming a ball-like structure, 6 × 5.5 × 3.5 cm in size. (c) The cut surface of the heart showing hemorrhage in the mid to outer zone of the anterior, lateral, and posterior walls. (d) The liver with dilated lymph vessels.

Considering the patient's age and the wide extension of the tumor, resection of the tumor using cardiopulmonary bypass was deemed too high risk and was thus not performed. Chemotherapy or radiotherapy was also considered impossible based on the results of a clinical conference among thoracic surgeons, cardiovascular surgeons and medical oncologists. He was found fallen and unconscious in a hospital ward early in February, 2011, and without recovering consciousness, he subsequently died.

PATHOLOGICAL FINDINGS

An autopsy was performed 1 hour and 41 minutes after death. The cadaver (61.5 kg, 160 cm) showed edema around the neck. Initial thoracotomy disclosed a poorly demarcated anterior mediastinal tumor, 6 × 4 × 1 cm in size (Fig. 3a), with invasion of the right parietal pleura. Left pleural effusion was yellowish and small (60 ml), while right pleural effusion was bloody and massive (1300 ml). The pericardial effusion was yellowish and increased (300 ml), while the ascites was yellowish and small (100 ml). The tumor extended through the bilateral brachiocephalic veins and SVC into the right atrium (heart: 405 g), forming a ball-like structure, 6 × 5.5 × 3.5 cm in size, with partial adhesion to the endocardium (Fig. 3b). The cut surface of the heart revealed almost whole circumferential hemorrhage in the mid to outer zone of the myocardium (Fig. 3c). The liver (1030 g) showed dilated lymph vessels (Fig. 3d). The lungs (lt. 290; rt. 305 g) showed mild congestion.

Histologically, the tumor formed multiple nodules in a fibrous background (Fig. 4a). Similar to the biopsy material, the tumor nodules consisted of a large number of polygonal or rounded epithelial cells with admixture of lymphocytes; therefore, the tumor was diagnosed as type B2 thymoma. Although the tumor occasionally invaded small veins, direct invasion of the brachiocephalic vein or SVC was not identified. The mass within the right atrium showed the same histology as the primary tumor except for superimposed fibrinous exudates. Multiple tumor emboli were also confirmed in bilateral pulmonary arteries (Fig. 4b). Immunohistochemistry for CD5, CD99, fascin, matrix metalloproteinase (MMP)-2, and vascular endothelial growth factor (VEGF) was performed on the primary and intra-atrial tumors (Table 1). The results were identical between these two tumors; CD5 and CD99 were positive for infiltrating lymphocytes but negative for the tumor epithelium, fascin was weakly positive for the tumor epithelium with an intermix of fascin$^+$ dendritic cells, MMP-2 was negative for the tumor epithelium, and VEGF was diffusely positive for the tumor epithelium (Fig. 4c). Dilatation of subcapsular lymph vessels was confirmed in the liver as well as occasional dilatation of hepatic and portal veins. The hemorrhagic parts of the myocardium showed thinning, disarray and eosinophic change. The external zone of the hemorrhagic parts occasionally showed myocardial necrosis with lymphocytic infiltration beneath the epicardium (Fig. 4d). Detailed investigation of the coronary arteries was performed, and stenosis in up to 90% of the left anterior discending, 40% of the circumflex, and 40% of the right coronary artery was observed along with atherosclerosis, but occlusion was not detected.

DISCUSSION

This aged male patient presented with type B2 thymoma in the anterior mediastinum that extended through the

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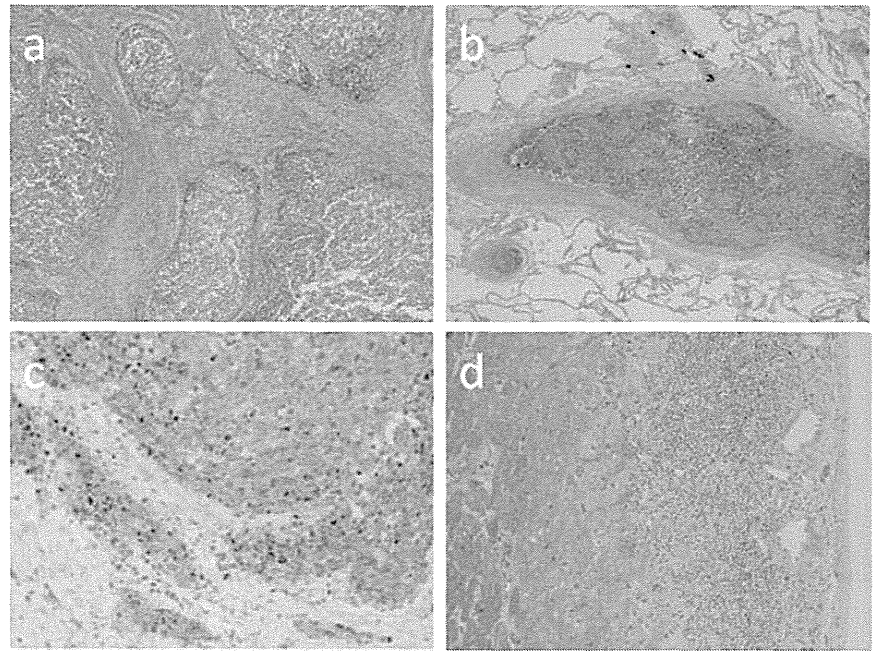

Figure 4 Microscopical features at autopsy. (a) The primary tumor showing multiple nodules with fibrous stroma. (b) Multiple tumor emboli in the pulmonary arteries. (c) The tumor epithelium diffusely immunostained by VEGF (d) Myocardial necrosis with lymphocytic infiltration beneath the epicardium.

brachiocephalic veins and SVC into the right atrium, forming a ball-like structure. Although multiple tumor emboli were discovered in the bilateral pulmonary arteries, and pericarditis was a complication, their extents were not sufficiently indicative of pulmonary and cardiac insufficiencies. Therefore, death of the patient appeared to have been due to tumor strangulation at the tricuspid orifice.

Intracaval growth of invasive thymoma with extension into the right atrium as shown in the present case is extremely rare,[2] and to our knowledge, only 27 cases have been reported in the English literature or in Japanese literature with English abstract (Table 2). As shown in Table 2, this manifestation of thymoma may occur in any age of adults (25–80 y.o.; mean: 55.1 ± 15.1 y.o.) and in both sexes (M:F = 16:12). In virtually all reported cases, SVC syndrome such as swelling of the face and/or upper extremities was also present. Myasthenia gravis was not an accompaniment in any of the cases, which can be found in 30–50% of patients with thymoma.[1] This may be associated with the advanced extension of thymoma in these reported cases, since complication of myasthenia gravis usually facilitates earlier discovery of thymoma.[10] Histological subtypes may not be contributory to the highly aggressive nature, since those with favorable prognosis such as type A and type AB (mixed-type) thymomas are included in Table 2 as well.[28] Although tumor invasion of mediastinal organs such as the pericardium, pleura, and lungs have been reported, a case with tumor emboli in the pulmonary arteries has never been reported to the best of our knowledge, partly because the present case is a rare autopsy report. Indeed, only two autopsy reports in this category have been published in Japanese,[23,26] but the present case is the first English autopsy report.

In most reported cases with intracardiac extension of thymoma in which tumor resection were performed, cardiopulmonary bypass was required. Cardiopulmonary bypass is an invasive technique with increased mortality and complications such as postoperative bleeding associated with full heparinization are known.[24,27] Cases in which tumor resection was performed without cardiopulmonary bypass included partial resection of the lesion,[4,9] a tumor that only protruded into the right atrium without adhesion,[13] a tumor that was reduced by preoperative radiotherapy,[21] and performance of a transient cava-pulmonary shunt.[2,27] More than half of the cases (17 cases) were alive after follow-up of at least 6 months. Therefore, favorable prognosis is likely to be obtained after successful resection in combination with chemoradiotherapy.

With regard to the pathway of entry into the SVC, the tumor invaded small veins, but direct invasion of the brachiocephalic vein or SVC was not identified in the present case. As pointed out by other authors,[16] although tumors may directly invade the wall of the brachiocephalic vein or SVC, it is more likely for tumors to spread into the brachiocephalic vein through a small vein such as the thymic vein, and then grow along the venous stream into the SVC down to the right atrium in a polyp-like fashion.

As mentioned earlier, histological subtypes do not appear to contribute to the highly aggressive nature of this type of tumor. In order to further investigate the cause for aggressiveness, immunohistochemistry was performed. Although CD5 immunopositivity has been reported to be observed

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Table 2 Literature review of thymic tumors with right atrial invasion

No.	Year	First Author	Age	Sex	SVC syn.	Histology	Other organ invasion	Therapy	Follow up	Out come
1	1985	Fujio[4]	53	M	(+)	Mixed-type thymoma	(–)	Resection, radiation, chemotherapy	4 y	Alive
2	1989	Korobkin[5]	80	F	(+)	Malignant thymoma	(–)	Radiation	n.r.	n.r.
3	1990	Airan[6]	38	M	(+)	Thymoma	Right ventricle	Resection (CPB), radiation	n.r.	n.r.
4	1992	Missault[7]	65	F	(+)	Thymoma	(–)	Resection, radiation	1 y	Alive
5	1992	Yokoi[8]	72	M	(+)	Thymoma	Pericardium, lungs	Chemotherapy, resection (CPB), radiation	2 y	Alive
6	1993	Futami[9]	56	M	(+)	Mixed-type thymoma	(–)	Resection, radiation	n.r.	n.r.
7	1994	Okereke[10]	25	M	(+)	Mixed-type thymoma	Pericardium, pleura	Resection (CPB)	1 y	Dead
8	1995	Kohiyama[11]	45	F	(+)	Mixed-type thymoma	Pericardium, lung	Chemotherapy, radiation, resection (CPB)	1 y	Alive
9	1996	Sato[12]	43	F	(+)	Predominantly epithelial thymoma	(–)	Resection (CPB), chemotherapy	3 y	Alive
10	1997	Gleeson[13]	50	F	(+)	Invasive cortical thymoma	Pericardium, lung	Resection	1 y	Alive
11	1997	Filippone[14]	52	F	(+)	Type II malignant thymoma	(–)	Resection (CPB), chemotherapy	1 y	Alive
12	1998	Tsuji[15]	59	M	(+)	Invasive thymoma	(–)	Resection (CPB), radiation, chemotherapy	4 y	Alive
13	1999	Minato[16]	44	M	(+)	Mixed-type thymoma	Pericardium, lungs, pleura	Resection (CPB), chemotherapy	29 mo	Alive
14	2000	Hayashi[17]	72	M	(+)	Mixed-type thymoma	Right ventricle	Resection (CPB), radiation	4 y	Alive
15	2002	Ozer[18]	40	M	(+)	Malignant thymoma (s/o anaplastic carcinoma)	Pericardium	Radiation, chemotherapy	n.r.	n.r.
16	2002	Yamazaki[19]	72	F	(+)	Thymic carcinoma	(–)	Resection (CPB)	10 mo	Alive
17	2003	Funakoshi[20]	77	M	(+)	Type A thymoma	Right ventricle	Resection (CPB), radiation	21 mo	Alive
18	2003	Funakoshi[20]	27	F	(–)?	Consistent with thymoma	(–)	Chemotherapy, radiation, resection (CPB)	<1 mo	Dead
19	2006	Ichimura[21]	56	F	(+)	Type AB thymoma	Lung	Chemotherapy, radiation, resection	23 mo	Alive
20	2007	Shudo[22]	48	M	(+)	Type AB thymoma	Pericardium, lung	Resection (CPB), radiation	6 mo	Alive
21	2007	Noguchi[23]	74	M	(+)	Type B3 thymoma	Pericardium, lung	Warfarin, diuretic	4 y	Dead
22	2008	Dursun[2]	50	F	(+)	Invasive thymoma	(–)	Chemothrapy, resection	2 mo	Dead
23	2008	Pastorino[24]	50	F	(+)	Type B3 thymoma	Pericardium, pleura	Chemotherapy, radiation, resection (CPB)	8.5 y	Alive
24	2009	Amirghofran[25]	53	M	(+)	Type AB thymoma	Pericardium, lung	Resection (CPB), radiation, chemotherapy	5 y	Alive
25	2010	Li[3]	40	M	(+)	Type B3 thymoma	Lung	Resection (CPB), radiation	10 mo	Alive
26	2011	Maekura[26]	76	M	(+)	Thymic carcinoma	Inferior vena cava, pleura, pericardium	Radiation, chemotherapy	7 mo	Dead
27	2012	Toker[27]	53	F	(+)	Invasive thymoma	(–)	Resection, radiation, chemotherapy	n.r.	n.r.
28		Present case	74	M	(+)	Type B2 thymoma	Pleura, pulmonary arteries	(–)	<1 mo	Dead

CPB, cardiopulmonary bypass; n.r., not reported.

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frequently (~60%) in the epithelium of thymic carcinomas but not in that of thymomas,[28] the tumor epithelium in the present case was negative for CD5. Although we have recently reported that a lack of fascin immunopositivity in the tumor epithelium and less fascin$^+$ dendritic cells are associated with invasiveness of the thymic neoplasms,[29] the present case demonstrated a typical fascin expression pattern for benign thymoma showing fascin$^+$ tumor epithelium with abundant fascin$^+$ dendritic cells. Although MMP-2 has been reported to be a key enzyme for invasiveness of thymic neoplasms,[30] the tumor in the present case was negative for MMP-2. However, the positivity for VEGF in the present tumor is interesting, since VEGF has been reported to be associated with invasiveness of thymic neoplasms through increased microvessel density.[31] Although more than half of invasive thymomas were reported to be immunopositive for VEGF,[31] VEGF may be associated with intracaval extension.

With regard to the cause for dilatation of the intrahepatic vessels, IVC syndrome associated with obstruction of the right atrium may be concerned. To the best of our knowledge, this is the second case of IVC syndrome associated with thymic neoplasms extending into the right atrium. The first case was a 76-year-old Japanese man with thymic carcinoma that invaded the region surrounding the IVC through the diaphragm, compressing the IVC.[26] Furthermore, myocardial necrosis with lymphocytic infiltration beneath the epicardium was observed in the present case. Pericarditis associated with myocardial infarction may be reminiscent of post-acute myocardial infarction syndrome, also known as Dressler syndrome.[32] However, the occurrence of Dressler syndrome has greatly diminished in the modern era due to advancements in therapy.[33] Further, subacute or chronic myocardial infarction that is associated with Dressler syndrome was not observed in the present case. Although coronary arterial stenosis of up to 90% was observed, no arterial occlusion was detected. Usually, myocardial infarction occurs from the inner myocardium since the blood supply starts from the outer myocardium. Interestingly, it has been reported from canine experiments that myocardial infarction induced by coronary venous or coronary sinus thrombosis is localized on the epicardial side.[34,35] Therefore, we postulate that obstruction of the right atrium may have brought about venous infarction of the myocardium through obstruction of the coronary sinus in the present case.

In conclusion, we report a rare case with invasive thymoma extending into the right atrium. To our knowledge, this is the first documentation of tumor emboli in the pulmonary arteries and the first English report of an autopsy case and a case with IVC syndrome in this category.

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REVIEW ARTICLE

Recent advances in video-assisted thoracoscopic surgery for lung cancer

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Keywords
Lung cancer surgery; minimal invasive surgery; video-assisted thoracoscopic surgery (VATS)

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Abstract

As a result of increased use of CT in both screening and daily practice, the number of early lung cancers has increased enormously. Surgeons pursue both curativity and reduced invasiveness in treating patients with early stage lung cancer; therefore, minimally invasive operations, such as video-assisted thoracoscopic surgery (VATS) lobectomy are now being routinely performed. Most previous reports have shown that there is no difference in mortality and local recurrence between open surgery and VATS in stage I patients. However, surgeons' improved technical experience and patients' demands could soon make VATS lobectomy the operative method of choice for early stage lung cancer. Moreover, the indications for VATS are expanding to encompass complex procedures such as segmentectomy or sleeve resection. Training and dissemination of the technique and the monitoring of outcomes are necessary.

Introduction

Since CT has become commonly used in routine practice, we have been able to detect early stage lung cancers more easily. Furthermore, minimally invasive surgery has become widely performed, mainly for early stage lung cancers. In Japan, more than half of lung cancer operations are performed with video-assisted thoracoscopic surgery (VATS) (1). For some lesions, such as adenocarcinoma *in situ* or minimally invasive adenocarcinomas of a relatively non-aggressive biological nature (2), conventional operations may be overtreatment. This means that minimally invasive operations, such as VATS lobectomy or segmentectomy, are increasingly being demanded by society. In addition to meeting patient demands, minimally invasive surgery would help address issues related to the increased number of octogenarian patients. It also could be used when surgical treatment for second primary lung cancer is indicated.

Recent systematic reviews and large case studies have demonstrated that VATS lobectomy for lung cancer is associated with reduced chest tube placement duration, shorter length of hospital stay and lower rates of postoperative complications (3,4). However, the definition of VATS can vary according to individual surgeons, and we lack prospective scientific data demonstrating the superiority of VATS over thoracotomy. At present, VATS is a routine surgical procedure used mainly for early stage lung cancer. However, efforts should be made to establish a consensus regarding the indications and limitations of VATS through the collection of scientific data.

What is VATS lobectomy?

It seems that there are two kinds of VATS lobectomy, hybrid VATS and complete VATS (5), though these terms have not been standardized In hybrid VATS, the surgeon makes a small thoracotomy (8–10 cm) with rib spreading and employs both direct vision inside the chest and video monitor imaging. A thoracoscope is also used for the purpose of illumination. In contrast, when performing complete VATS, the surgeon makes three or four small incisions with no rib spreading and looks only at the video monitor during the operation. Thoracic surgeons are still debating the correct definition of VATS lobectomy. In the Cancer and Leukemia Group B 39802 prospective, multi-institutional study, Swanson *et al.* defined

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VATS lobectomy as anatomic lobectomy with individual ligation of lobar vessels and bronchi as well as hilar lymph node dissection or sampling with the video monitor used for guidance, two or three ports, and no retractor use or rib spreading (6). The Swanson *et al.* study aimed to evaluate the feasibility of performing VATS lobectomy in a standardized manner for patients with peripheral lung cancers less than 3 cm in size.

Given that there is no generally accepted definition of "VATS lobectomy," we believe that the classifications referenced above, complete VATS and hybrid VATS, should become the standard. Otherwise, varying terminology among thoracic surgeons could hinder the collection of accurate perioperative data on lung cancer.

Evidence in VATS lobectomy

Outcome

There have only been two small randomized studies concerning VATS lobectomy. Kirby *et al.* randomized 61 stage I lung cancer patients into two groups: VATS lobectomy or open surgery. This study showed reduction of postoperative complications in the VATS group (6% vs 16%), but no significant decrease in the duration of chest tube drainage, length of hospital stay or postoperative pain (7).

Sugi *et al.* randomized 100 stage IA lung cancer patients into VATS lobectomy or thoracotomy groups. After an average of 5 years of follow-up, there were no statistically significant differences in recurrence and survival rates. The 5-year survival in the VATS and open thoracotomy groups were 90% and 85%, respectively (8). There have been two large-scale systematic reviews to compare the performance of VATS and open surgery. Whitson *et al.* collected and analyzed 39 studies (1 randomized, 38 non-randomized) and showed that VATS lobectomy was associated with shorter chest tube drainage duration, reduced hospital stay and improved survival (at 4 years postoperative) (3). Yan *et al.* analyzed 21 eligible comparative studies (2 randomized, 19 non-randomized) and found no significant statistical differences between VATS and open thoracotomy lobectomy in terms of postoperative complications such as prolonged air leakage ($P = 0.71$), arrhythmia ($P = 0.86$), and pneumonia ($P = 0.09$). Additionally, there were no differences in mortality ($P = 0.49$) and locoregional recurrence ($P = 0.24$), but the data suggested a reduced systemic recurrence rate in VATS patients ($P = 0.03$) (4). These systematic reviews suggest that VATS lobectomy, when compared with open surgery, is an appropriate procedure for selected patients with early stage lung cancer. Gopaldas *et al.* analyzed a total of 13 619 discharge records of lung cancer patients who had been surgically treated (thoracotomy 12 860, VATS 759). The two groups had similar mortality rates (3.1% vs 3.4%, $P = 0.67$), hospital stays (9.3 vs 9.2 days, $P = 0.84$), pulmonary complications (32.2% vs 31.2%, $P = 0.55$). However, the VATS group had more complications during operation (odds ratio: 1.6, 95% confidence interval: 1.0–2.4, $P = 0.04$) (9).

Table 1 shows representative reports of VATS lobectomy from multiple studies. VATS seems to be associated with shorter chest drainage tube duration and hospital stay, which suggests that VATS lobectomy may actually be a safe operation in appropriately selected patients (3,4,9–11).

Lymph node dissection

Mediastinal lymph node dissection is a critical issue that needs to be solved in order to expand the indications of VATS in patients with lung cancer. D'Amico *et al.* evaluated patients who underwent lobectomy (VATS 199, open thoracotomy 189) and suggested that the mean number of N2 lymph node stations was similar in VATS ($n = 3.15$) and thoracotomy ($n = 2.91$). Furthermore, the difference in the total number of N1 and N2 nodes resected in each group was not statistically significant (12). Boffa *et al.* analyzed 11 531 clinical stage I lung cancer operations (7137 thoracotomy, 4394 VATS). Nodal upstaging was seen in 14.3% in the thoracotomy group and 11.6% in VATS group ($P < 0.001$). Among these, hilar or peribronchial nodal metastases were identified more often by thoracotomy than by VATS (54% vs 42%, $P = 0.002$), but upstaging from cN1 to pN2 was similar (15.6% in thoracotomy vs 15.3% in VATS). The importance of complete hilar and peribronchial dissection must be emphasized in the VATS approach (13). Denlinger *et al.* evaluated clinical stage I patients treated by VATS lobectomy ($n = 79$) and open lobectomy ($n = 464$) (14). Fewer lymph nodes (7.4 vs 8.9, $P = 0.029$) and fewer mediastinal lymph nodes (2.5 vs 3.7, $P = 0.004$) were dissected with VATS than with thoracotomy. Subset analysis revealed that there was no difference in lymph node 4R, 5 and 6, but lymph node 7 was dissected more extensively by thoracotomy (14). This fact might suggest the difficulty of subcarinal nodes, which many surgeons might encounter. Systemic lymph node dissection has not been proven to improve the prognosis of lung cancer, but it might be helpful in accurate staging (15). Standardization of the technique and expertise of VATS lymph node dissection is necessary to resolve this issue.

VATS segmentectomy

Lobectomy has been a standard operative procedure for lung cancer. However, given the tremendous increase in

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Table 1 Representative reports on VATS lobectomy

Author (reference)	Scott *et al.* (10)	Paul *et al.* (11)	Gopaldas *et al.* (9)	Whitson *et al.* (3)	Yan *et al.* (4)
Database	ACSOG Z0030	STS database		Meta-analysis	Meta-analysis
Number of cases					
VATS	66	1281	759	3114	1391
Thoracotomy	686	1281	12860	3256	1250
Length of stay (day)					
VATS	5	4	9.2	8.3	12
Thoracotomy	7	6	9.3	13.3	12.2
	$P < 0.001$	$P < 0.0001$	$P = 0.84$	$P = 0.016$	NA
Complication rate					
VATS	27.3%	26.2%	43.1%	16.4%	NA
Thoracotomy	47.8%	34.7%	44.1%	31.2%	NA
	$P = 0.005$	$P < 0.0001$	$P = 0.592$	$P = 0.018$	NA
Duration of chest tube drainage (day)					
VATS	1.5% > 7	3	4.2	NA	4.6
Thoracotomy	10.8% >7	4	5.7	NA	5.3
	$P = 0.029$	$P < 0.0001$	$P = 0.025$	NA	NA
Duration of air leak (day)					
VATS	1.5% > 7	7.6% > 5	NA	5%	NA
Thoracotomy	7.3% > 7	8.7% > 5	NA	8.8%	NA
	$P = 0.155$	$P = 0.35$	NA	$P = 0.27$	$P = 0.75$

ACSOG Z0030, American College of Surgeons Oncology Group Z0030; STS, Society of Thoracic Surgeons; VATS, video-assisted thoracoscopic surgery.

the number of peripheral early stage lung cancers, segmentectomy is more frequently performed for selected early stage lung cancer to pursue both curability and reduced invasiveness (16,17). There has been a debate about the indications and outcome of segmentectomy for lung cancer, and the results of an ongoing prospective randomized trial (lobectomy vs segmentectomy) should clarify the role of this procedure (18). Thoracoscopic segmentectomy is more controversial because of the procedure's complexity and the need to ensure the safety margin without palpation of the tumor. Theoretically, VATS segmentectomy can preserve the pulmonary volume and decrease the chest wall damage, and thus, it is attracting great interest with advances in VATS. VATS segmentectomy has been performed in some leading facilities, and preliminary results have shown equivalent rates of morbidity, recurrence and survival for early lung cancers less than 2 cm in diameter (19–21).

Simulation of VATS

Anatomic variations of pulmonary vessels make lung resection more difficult, especially when the separation of the interlobular fissure is incomplete. Thus, preoperative knowledge of each patient's surgical anatomy would contribute greatly to the safety of operations. The development of multi-detector CT has made it feasible to obtain 3-D images of the lung structures. These 3-D displays of anatomic structures have enabled improved decision-making on surgical methods and preoperative planning. There are several reports demonstrating the usefulness of 3-D CT for preoperative simulation and navigation during surgery (22–24).

Fukuhara *et al.* performed preoperative 3-D CT for stage I lung cancers that were scheduled for VATS lobectomy. A total of 49 patients were studied and all cases successfully underwent VATS, with 95% of pulmonary artery branches depicted on 3-D CT identified during operation (23). Oizumi *et al.* used this technique to support VATS segmentectomy in 52 patients; 3-D imaging was useful in identifying the intersegmental vein, which was the key structure in identifying the intersegmental plane (resection line) (24).

Using new generation software, we can automatically calculate the distance between the tumor and surgical margin after 3-D reconstruction of the tumor, pulmonary artery and vein, bronchial tree, and lung parenchyma. This function is useful in planning segmentectomy, engaging in preoperative virtual simulation, ensuring an accurate safety margin and gaining intraoperative guidance regarding surgical anatomy (25).

Discussion

VATS lobectomy for lung cancer has evolved over the past 20 years. There are many reports suggesting the superiority of VATS lobectomy over open thoracotomy, mainly in terms of perioperative outcome. However, most of these reports involve retrospective data obtained

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from single institutions (26). Also, analysis should differentiate between two procedures, complete VATS and hybrid VATS, rather than simply using "VATS procedure."

As this minimally invasive approach becomes more widely available, we should investigate the present status of VATS lobectomy in terms of safety and survival advantages. Robotic surgery has recently been employed in the field of thoracic surgery (27–29), and it may play a more important role in the near future. However, expanding the indications for VATS, as well as for complex procedures such as segmentectomy or sleeve resection, is currently a more pressing issue for treating advanced lung cancer. Training surgical staff, teaching the technique widely, and keeping robust databases and monitoring outcomes are essential in applying VATS to a wider range of procedures.

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Lung cancer with scattered consolidation: detection of new independent radiological category of peripheral lung cancer on thin-section computed tomography

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Abstract

OBJECTIVES: Ground glass opacity (GGO) on thin-section computed tomography (CT) has been reported to be a favourable prognostic marker in lung cancer, and the size or area of GGO is commonly used for preoperative evaluation. However, it can sometimes be difficult to evaluate the status of GGO.

METHODS: A retrospective study was conducted on 572 consecutive patients with resected lung cancer of clinical stage IA between 2004 and 2011. All patients underwent preoperative CT and their radiological findings were reviewed. The areas of consolidation and GGO were evaluated for all lung cancers. Lung cancers were divided into three categories on the basis of the status of GGO: GGO, part solid and pure solid. Lung cancers in which it was difficult to measure GGO were selected and their clinicopathological features were investigated.

RESULTS: Seventy-one (12.4%) patients had lung cancer in whom it was difficult to measure GGO. In all these cases, consolidation and GGO were not easily measured because of their scattered distribution. In this cohort, nodal metastases were not observed at all. The frequency of other pathological factors, such as lymphatic and/or vascular invasion, was significantly lower ($P < 0.0001$).

CONCLUSIONS: This new category of lung cancer with scattered consolidation on thin-section CT scan tended to be pathologically less invasive. When lung cancer has GGO and is difficult to measure because of a scattered distribution, its prognosis could be favourable regardless of the area of GGO. This new category could be useful for the preoperative evaluation of lung cancer.

Keywords: Lung cancer • Thoracic surgery • Diagnosis • Lymph node • Ground glass opacity

INTRODUCTION

Small-sized lung cancer tends to be found in screening with computed tomography (CT). CT can detect not only small tumours but also tumours that are faint on chest roentgenogram, such as tumours with ground glass opacity (GGO). GGO on thin-section CT is one of the most favourable prognostic factors in lung cancer. In most previous reports, the size of GGO has been evaluated in one dimension for predicting the prognosis [1–10]. These authors have claimed that the proportion of GGO and consolidation was important for predicting the prognosis, and their findings were confirmed by a prospective multi-institutional trial (JCOG0201) [4]. On the other hand, it is often difficult to measure the dimension of GGO or consolidation. In this study, we investigated the clinicopathological features of lung cancer with a GGO appearance that was difficult to measure on thin-section CT scan to aid in determining the optimal management.

MATERIALS AND METHODS

Study population

A retrospective study was conducted on 1179 patients with primary lung cancer, which was resected between January 2004 and April 2011 at our institute. Among them, 637 patients had clinical stage IA lung cancer, and thin-section CT was available for 572. Clinical stage IA was defined as follows: (1) primary tumor was 3 cm or less in greatest dimension, (2) there was no regional lymph node metastasis and distant metastasis, according to the 7th edition of the Union International Contre le Cancer TNM staging system. Thin-section CT was performed to evaluate the entire lung with collimation of 1–2 mm. The lung was photographed with a window level of −500 to −700 Hounsfield units (HU) and a window width of 1500–2000 HU as a lung window.

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Definition of lung cancer with scattered consolidation (LCSC)

All thin-section CT scans were reviewed by 3 of the authors (T.M., K.S. and K.T.), and the following radiological factors were investigated: maximum tumour dimension, maximum dimension of consolidation, distribution of GGO and pleural tail. The ratio of consolidation to tumour size was evaluated. We defined LCSC as follows:

(1) lung cancer with consolidation that is difficult to be measured on thin-section CT scan (Fig. 1),
(2) lung cancer with GGO whose distribution is scattered. In all these cases, consolidation and GGO were not easily measured because of discontinuous consolidation of tumour. So these tumours have more than two parts of consolidation with >1 mm.
(3) We exclude tumours with emphysematous lung because some of these areas of consolidation seem to be discontinuous. We investigated the clinicopathological features of LCSC and compared them with those of other types of lung cancer. We also determined the category to which LCSC had originally belonged. Our classification of GGO consisted of three types: GGO, part solid and pure solid. Conventional classification is based on the findings on thin-section CT scan, i.e. the consolidation/tumour ratio (CTR). The GGO, part solid and pure solid groups were defined as tumour having a CTR of ≤0.5, >0.5 and 1.0, respectively. Finally, we divided all the lung cancers into four categories, i.e. the three conventional categories and the new category of LCSC.

Statistical analysis

To compare two factors, the χ^2 test or Fisher's exact test was used. Multivariate analyses were performed by logistic regression analysis. A P-value of <0.05 was considered to be statistically significant. All statistical calculations were performed using SPSS.

RESULTS

Characteristics of lung cancer with scattered consolidation

LCSC was observed in 71 (12%) of 572 patients. The clinicopathological features of these patients were compared according to radiological findings (Table 1). There were 29 men and 42 women who ranged in age from 24 to 86 years (median 66 years). Compared with other tumours, the LCSCs were significantly bigger in the maximum tumour dimension. Women tended to have LCSC, and the CTR was ≥0.5 in more than half of the patients with LCSC, but this difference was not statistically significant. All the LCSCs were histologically adenocarcinomas and showed pathological invasiveness, such as nodal metastasis, or lymphatic or vascular invasion, and these differences were statistically significant ($P < 0.0001$).

Relationship between conventional ground glass opacity status and lung cancer with scattered consolidation

The relationships between the three conventional categories and LCSC are shown in Table 2. None of the patients in the pure solid group was categorized as LCSC. LCSC was found in the part solid and GGO groups, significantly more often than in the pure solid group. With regard to pathological invasiveness, the conventional GGO, part solid and pure solid groups showed 0, 5.9 and 25.0% nodal metastasis, respectively (Table 3). For other forms of invasiveness, such as lymphatic or vascular invasion, there were significant relationships between these pathological factors and conventional GGO status.

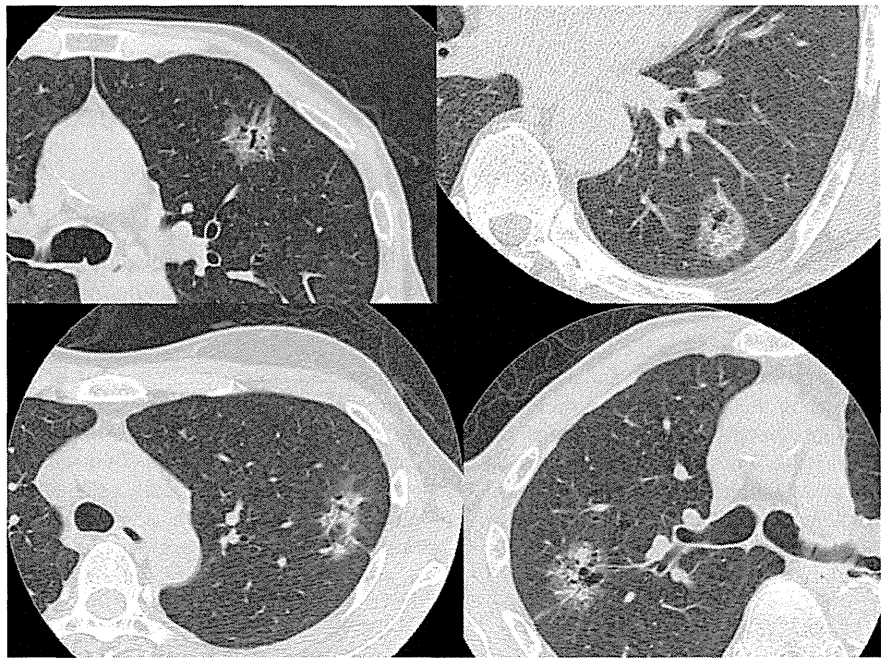

Figure 1: The proportions of consolidation and ground glass opacity were not easily measured because of their scattered distribution such as in these cases.

Table 1: Clinicopathological features by radiological findings

Clinicopathological factors	LCSC	Others	*P*-value[a]
Gender			
Men	29 (40.8%)	247 (49.3%)	0.1820
Women	42 (59.2%)	254 (50.7%)	
Age			
Years (median)	66 (24–86)	66 (26–89)	0.4508
Smoking states (pack-year)			
≥40	11 (11.3%)	113 (23.5%)	0.2142
<40	55 (88.7%)	368 (76.5%)	
CEA (ng/ml)			
≥5.0	7 (10.4%)	89 (18.1%)	0.1657
<5.0	60 (89.6%)	402 (81.9%)	
Tumour size (mm)			
20	38 (53.5%)	329 (65.7%)	0.0458
<20	33 (42.5%)	172 (34.3%)	
Visual CTR			
<0.5	25 (35.2%)	126 (25.1%)	0.0719
≥0.5	46 (64.8%)	375 (74.9%)	
Histology			
Adenocarcinoma	71 (100%)	430 (85.8%)	<0.0001
Others	0 (0%)	71 (14.2%)	
Pathological N status			
N0	71 (100%)	424 (84.8%)	<0.0001
N1 or 2	0 (0%)	76 (15.2)	
Lymphatic invasion			
Positive	12 (16.9%)	235 (46.9%)	<0.0001
Negative	59 (83.1%)	266 (53.1%)	
Vascular invasion			
Positive	5 (7.0%)	213 (42.5%)	<0.0001
Negative	66 (93.0%)	288 (57.5%)	

[a]χ^2-test or Fisher's exact test.
LCSC: lung cancer with scattered consolidation; CEA: carcinoembryonic antigens; CTR: consolidation tumour ratio.

Table 2: The relationship between ground glass appearance and lung cancer with scattered consolidation

Conventional category	LCSC	non-LCSC	*P*-value[a]
GGO group (CTR ≤ 0.5)	25 (35.2%)	126 (25.1%)	<0.0001
Part solid group (0.5 < CTR < 1.0)	46 (64.8%)	106 (21.2%)	
Pure solid group (CTR = 1)	0 (0%)	269 (53.7%)	

[a]Fisher's exact test.
GGO: ground glass opacity; CTR: consolidation tumour ratio.

Predictors of pathological invasiveness

In a multivariate analysis for predictors of lymphatic and vascular invasion, the new category LCSC was an independent predictor along with gender, the preoperative serum CEA titer, maximum tumour dimension and CTR (Table 4). LCSC showed pathological invasiveness more often than GGO, but less often than part solid lung cancer. LCSC did not show lymph node metastasis (Table 5).

Table 3: The relationship between conventional categories and p-N status

Conventional category	p-N1 or 2	p-N0	*P*-value[a]
GGO group (CTR ≤ 0.5)	0 (0%)	151 (100%)	<0.0001
Part solid group (0.5 < CTR < 1)	9 (5.9%)	143 (94.1%)	
Pure solid group (CTR = 1)	67 (25.0%)	201 (75.0%)	

[a]Fisher's exact test.
GGO: ground glass opacity; CTR: consolidation tumour ratio.

Table 4: Results of multivariate analysis for predictors of lymphatic invasion

Variables	Hazard ratio	95% CI	*P*-value[a]
LCSC (vs non-LCSC)	0.208	0.100–0.433	<0.0001
Gender (male)	1.584	1.055–2.378	0.0264
CEA (≥5 ng/ml)	3.033	1.744–5.274	<0.0001
Tumour size (>20 mm)	2.520	1.647–3.855	<0.0001
Visual CTR (≥0.5)	16.414	7.724–34.883	<0.0001

[a]*P*-value in logistic regression analysis.
CI: confidence interval; LCSC: lung cancer with scattered consolidation; CEA: carcinoembryonic antigens; CTR: consolidation tumour ratio.

Table 5: Incidence of nodal metastasis and lymphatic invasion according to a new radiological grouping

New category	pN	Ly	*P*-value[a]
GGO group (CTR ≤ 0.5)	0/126 (0%)	7/126 (5.5%)	<0.0001
LCSC group	0/71 (0%)	12/71 (16.9%)	
Part solid group (0.5 < CTR < 1)	9/106 (8.5%)	41/106 (38.7%)	
Pure solid group (CTR = 1)	67/268 (25.0%)	187/268 (69.5%)	

[a]Fisher's exact test.
pN: pathological nodal metastasis; Ly: lymphatic invasion; GGO: ground glass opacity; CTR: consolidation tumour ratio; LCSC: lung cancer with scattered consolidation.

DISCUSSION

As CT is used more widely, we increasingly have opportunities to detect small or faint lung nodules that could be diagnosed as lung cancer. Although lobectomy is now a standard operation based on the results of LCSG [11], limited resection such as wide wedge resection or segmentectomy has been studied in many institutions [12–15]. Many surgeons think that limited resection could be equivalent to lobectomy for appropriately selected patients.

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Table 6: Meta-analysis on ground glass opacity (GGO) as a prognostic factor for lung cancer

Authors/year	No.	Cases	Methods	Good prognosis	Study design
Jang/1996 [9]	14	-	-	Focal area of GGO	Retrospective
Suzuki/2000 [7]	69	Ad, cIA	CTR	GGO > 0.5	Retrospective
Aoki/2001 [1]	127	3 cm	CTR	GGO > 0.5	Retrospective
Takamochi/2001 [8]	269	Ad	TDR	TDR and CEA	Retrospective
Kim/2001 [10]	224	Ad, cIA	Visual	GGO extent	Retrospective
Okada/2003 [3]	167	Ad, 3 cm	TDR	TDR > 0.5	Retrospective
Ohde/2003 [2]	98	Ad, 2 cm	CTR	GGO > 0.5	Retrospective
Suzuki/2006 [6]	349	Ad, 2 cm	CTR	CTR and CEA	Retrospective
Suzuki/2011 [4]	811	Ad, 3 cm	CTR	CTR < 0.25	Prospective

CTR: consolidation tumour ratio; Ad: adenocarcinoma; TDR: tumour shadow disappearance rate.

Preoperative GGO on thin-section CT has been reported to be a favourable prognostic factor (Table 6) [1–10, 16–18]. The preoperative GGO status is important for selecting patients who are suitable for limited surgical resection [19–22]. While most authors have evaluated GGO in terms of the maximum tumour size and consolidation in one dimension, there is still some controversy regarding the optimal methods for the evaluation of ground glass. It is not uncommon for lung cancers to show GGO that is difficult to measure. Thus, we identified the clinicopathological characteristics of this type of lung cancer.

None of the patients with LCSC was in the pure GGO or pure solid group. There were more women than men in the LCSC group, but this difference was not statistically significant. Generally, men are more likely to have lung cancer, and the observed predominance of women could mean that this type of lung cancer is not related to smoking status or that carcinogenesis could be associated with gender. Tumours in LCSC were significantly larger than those in the other groups ($P = 0.0458$). LCSC shows atypical radiological findings on thin-section CT, and thus, a preoperative diagnosis could be difficult. This is one of the reasons for the larger size of LCSC. LCSC tends to grow slowly, which makes diagnosis difficult. All the LCSCs were histologically adenocarcinoma, and this is a distinct characteristic of LCSC.

LCSC did not show nodal metastases. LCSC tends to be less invasive pathologically, such as with regard to lymphatic or vascular invasion. One of the most potent prognostic factors is the size or nature of a central fibrosis of adenocarcinoma of the lung [7, 12, 23, 24]. Active fibroblasts in the central fibrosis have been reported to be associated with a poor prognosis [23]. Active fibroblasts are a sign of destruction of the basement membrane by cancer cells, which leads to mesenchymal destruction of the lung. This destruction results in the exclusion of air in the lung. This is a phase of consolidation on CT scan. If the invasion or destruction of the mesenchyme of the lung is minimal, air in the lung remains within the lung cancer, resulting in a ground glass appearance on thin-section CT. Thus, consolidation on thin-section CT could be strongly associated with the invasiveness of lung cancer [4]. According to the above considerations, LCSC has no pure consolidation and its pathological invasiveness should be minimal. When LCSC grows, it should show pure consolidation and could metastasize to nodes and distant organs. So an early diagnosis is necessary.

LCSC is a new radiological entity for lung cancer. This category is included mainly in the part-solid group. It is difficult to measure the size of consolidation for LCSC, which makes classification of this tumour vague. Similar radiological findings for lung cancer have been reported as part-solid groups [6]. However, this is the first report to focus on this category of lung cancer. JCOG0201 defined peripheral early lung cancer to be lung cancer of ≤2.0 cm in size in which consolidation is less than one fourth of the maximum tumour dimension [4]. Most of these lesions could be cured with limited surgical resection [13–15, 25]. LCSC should also be curable by limited surgical resection, although a clinical trial is needed to support this supposition. This study was limited in that it was a retrospective study in a single institute and the sample size was small. Thus, we are planning to perform a prospective multicentre trial in the near future to collect more patients with lung cancer having scattered consolidation.

In conclusion, the new category lung cancer with scattered consolidation has been proposed, and recognition of this category could resolve the problem of misclassification of lung cancer with difficult-to-measure consolidation on thin-section CT. Limited surgical resection may be the preferred option for lung cancers in this category in the near future.

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Conflict of interest: none declared.

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ORIGINAL ARTICLE

The size of consolidation on thin-section computed tomography is a better predictor of survival than the maximum tumour dimension in resectable lung cancer

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Abstract

OBJECTIVES: Ground-glass opacity (GGO) is a preoperative prognostic factor in resectable lung cancer. However, the impact of GGO on the T factor in the TNM staging system remains unclear and the maximum tumour dimension is also an uncertain measurement for assessing the prognosis of early lung cancer with a mixture of consolidation and GGO. Thus, we sought to determine which the better prognostic factor was, the size of the consolidation on computed tomography scan or the conventional maximum tumour dimension.

METHODS: Between January 2004 and January 2011, 398 consecutive clinical stage IA lung cancer patients underwent surgical resection at our hospital. Univariate and multivariate analyses were performed by the logistic regression procedure to determine the relationship between pathological lymph node metastasis-positive status and clinical or radiological findings such as the maximum dimensions of consolidation and the tumour, the presence of air bronchogram, pleural indentation and the preoperative serum carcinoembryonic antigen (CEA) level.

RESULTS: Of the 398 patients, 59 (14.8%) had pathological lymph node metastasis. Univariate analysis revealed four significant predictors of pathological nodal involvement: the presence of air bronchogram, the size of consolidation, the maximum tumour dimension and the preoperative CEA level ($P < 0.01$, respectively). In a multivariate analysis, the size of consolidation and the presence of air a bronchogram were significant predictors of nodal metastasis ($P < 0.01$, respectively).

CONCLUSIONS: The maximum dimension of the consolidation was an independent unfavourable prognostic factor, regardless of the maximum tumour dimension. This could lead to the more accurate prediction of pathological lymph node metastasis with both GGO and consolidation.

Keywords: Consolidation • Lung cancer • Computed tomography

THORACIC

INTRODUCTION

Ground-glass opacity (GGO) on thin-section computed tomography (CT) has been reported to be one of the most important prognostic factors in resected lung cancers [1–4]. Our recent prospective study on clinical stage IA adenocarcinoma of the lung led to a new definition of radiological non-invasive adenocarcinoma of the lung based on the findings of a CT scan [5]. These data demonstrated that lung cancer that shows GGO on thin-section CT scan has a very good prognosis and a minimally invasive nature on pathological examination.

In contrast, in the current TNM classification, T1 tumours, i.e. primary lung cancers smaller than 30 mm in diameter, are divided into two groups: those smaller than 20 mm are considered T1a, and those 20–30 mm are T1b. Thus, only the maximum tumour dimension has been considered when defining the T factor. However, even T1a lung cancer can show pathological nodal involvement by tumour cells, and this leads to the dogma that major lung resection, such as lobectomy or pneumonectomy, should be performed even for small-sized lung cancer [6]. T2 tumour which is predominated by GGO on thin-section CT scan could have a better prognosis than T1 tumour with no GGO on thin-section CT scan, which would mean that T2 tumour is associated with better survival than T1 tumour. This is paradoxical. Thus, we intended to determine which is a better prognostic factor in resected lung cancer patients, just the solid part on thin-section CT scan or the conventional maximum tumour dimension on CT scan.

MATERIALS AND METHODS

Between January 2004 and January 2011, a total of 749 patients underwent surgery for lung cancer at Juntendo Hospital. Among them, 398 consecutive patients with lung cancers with the following criteria were enrolled in this study: (i) complete resection,

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