Original Article

Clinical analysis of progressive destroyed lung after lung cancer surgery

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Background: "Progressive destroyed lung (PDL)" refers to a state in which the normal structure and function of the lung are permanently disrupted owing to repeated inflammation. After lung cancer surgery, the remaining lung tissue can experience progressive destruction; however, the exact cause remains unclear. In this study, we retrospectively analyzed cases in which the remaining lung deteriorated after lung cancer surgery and investigated the associated risk factors.

Methods: A case-control study was conducted on 31 cases of PDL and 247 cases of non-PDL among 1,234 patients who underwent surgery for primary lung cancer from 2006 to 2021. The following factors were analyzed: age, sex, medical history, smoking status, surgical procedure, lung cancer histology, surgical approach, postoperative complications, chemotherapy, radiation therapy, and lung cancer recurrence. Patients were matched 1:1 based on preoperative factors, and postoperative risk factors were evaluated using multivariate logistic regression analysis.

Results: A higher proportion of men and higher prevalence of chronic lung diseases, smokers, squamous cell carcinoma (SCC), postoperative acute pneumonia, chronic pneumonia, air leak, and history of radiation therapy were noted in the PDL group than in the non-PDL group. In the analysis following propensity score matching, chronic pneumonia [odds ratio (OR): 10.1, 95% confidence interval (CI): 2.9 to 35.8] was identified as an independent risk factor for PDL.

Conclusions: In this study, PDL after lung cancer surgery was associated with postoperative chronic pneumonia, including *Aspergillus* infection and aspiration pneumonia.

Keywords: Postoperative lung cancer; destroyed lung; chronic pneumonia; risk factors; pleuroparenchymal fibroelastosis (PPFE)

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Introduction

Background

Destroyed lung is a condition wherein the normal structure and function of the lungs are permanently destroyed by chronic or recurrent lung infections, with radiological findings characterized by diffuse lung shadows and large cavities (1). Destroyed lung is commonly observed in developing countries with a high prevalence of inflammatory lung diseases, such as tuberculosis or bronchiectasis (2). According to previous reports, the most common cause of lung destruction is tuberculosis, with other causes including

bronchiectasis, chronic interstitial pneumonia, lung abscess, necrotizing pneumonia, fungal infections, bronchial stenosis, and congenital lung diseases (3,4). Halezeroglu *et al.* (5) and Sayir *et al.* (1) reported that bronchiectasis (44.1%) was the most frequent cause of destroyed lung in retrospective analyses of patients who underwent lung resection, followed by tuberculosis (36.4%). Bronchiectasis, primarily caused by airflow obstruction, can lead to the buildup of airway secretions due to lymph node enlargement and luminal thickening. This exacerbates bronchiectasis associated with pneumonia and lung destruction, potentially leading to total bronchiectasis (1,6,7).

In previous studies, highly invasive surgeries such as pneumonectomies were performed for destroyed lung; this reduced mortality rates and potentially improved the quality of life (5,8-10). Li *et al.* outlined the following surgical indications for pneumonectomy in cases of destroyed lung: (I) unilateral destroyed lung with recurrent pulmonary infections and hemoptysis; (II) no or few lesions in the contralateral lung; (III) lung function tolerable for lung resection; and (IV) absence of other severe organic diseases (11). Surgery for destroyed lung is highly invasive and should be avoided whenever possible. Previous cohort studies have suggested a correlation between the severity of chronic lung diseases, as indicated by decreased spirometry values, and increased hospitalization rates and higher mortality rates (12-14). With progressive destruction of the remaining lung, patients may experience a further decline in respiratory function as well as adverse events after lung resection, which in turn will reduce their quality of life.

Highlight box

Key findings

- Progressive lung destruction following lung cancer surgery has been suggested to involve various factors, particularly postoperative complications, such as chronic infections occurring after 3 months postoperatively, postoperative acute pneumonia, air leaks, and radiation exposure, with a tendency for progressive destruction to occur in the apical part of the remaining lung lobes.

What is known and what is new?

- Respiratory infections such as tuberculosis and bronchiectasis are known causes of destroyed lung tissue. While remaining lung tissue after lung cancer surgery may also undergo progressive destruction, the exact underlying cause remains unclear.
- In this study, we found that progressive destruction of the remaining lung after lung cancer surgery was primarily associated with postoperative chronic pneumonia, *Aspergillus* infection, and aspiration pneumonia. Destruction tended to develop in the upper lobe on the right side and the lower lobe on the left side in the remaining lung. Pleuroparenchymal fibroelastosis and postoperative progressive destroyed lung following lung cancer surgery are clinically similar and may partially overlap.

What is the implication, and what should change now?

- Interventions and preventive measures for complications such as chronic pneumonia, which influence the progression of destruction of the remaining lung after lung resection, can improve patient outcomes.

Rationale and knowledge gap

As mentioned earlier, destroyed lung is often associated with inflammatory lung diseases, and in some cases, imaging modalities may continue to reveal progressive lung destruction following pulmonary resection, even in the absence of a clear medical history. Little research has been conducted on the medium-to-long-term effects of and risk factors for destroyed lung in the presence or absence of a history of pulmonary resection. Moreover, there are no clear diagnostic criteria, definitions, or guidelines for the diagnosis and management of destroyed lung.

Meghji *et al.* conducted a cohort study on post-tuberculosis lung damage (PTLD) in Malawi, establishing a novel protocol for image scoring and PTLD analysis based on the protocol (15). Specifically, the authors defined "destroyed lung" as lung lobes in which ≥90% of the tissue has been replaced by banding, atelectasis, or cavities/cystic air spaces. However, this evaluation requires radiological expertise, which complicates the scoring process. In clinical practice, diagnosing destroyed lung based on image interpretation alone is challenging for physicians, and diagnosing and managing destroyed lung is often based on experience. In this study, we collected cases of lung cancer surgery in which inflammatory lung diseases and infections were not directly related, focusing on general lung resections. High-resolution computed tomography (CT) images were used to define "progressive destroyed lung (PDL)" with a relatively simple set of criteria tailored to the clinical setting.

Objective

This study aimed to identify predictive factors for progressive destruction of the remaining lung after pulmonary resection for the most common indication, lung cancer. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-452/rc).

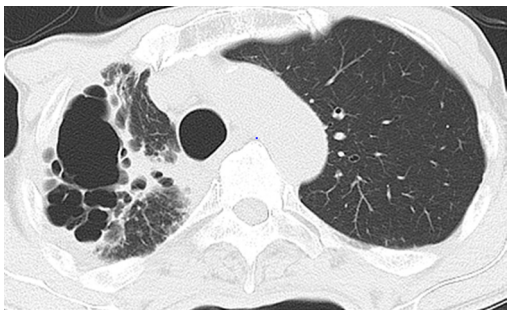

Figure 1 Typical computed tomography findings of a progressive destroyed lung.

Methods

PDL

Patients with gradually progressive, distinctive, irreversible shadows in the remaining lung lobes after lung cancer surgery were identified as having "PDL". We extracted a cohort including not only cases of fully developed destroyed lung, but also cases of what appeared to be relatively early-stage destroyed lung, termed "PDL". Specifically, patients were selected if at least 1 year had passed since lung cancer surgery and had CT images showing that more than 30% of the lung lobe had been partially replaced by banding, atelectasis, or cavities/cystic airspaces, resulting in irreversible structural distortion and destruction. Patients found to have reversible shadows on radiological imaging, such as those with heart failure, or with clinical diagnoses of recurrent tumor lesions due to lung cancer or acute exacerbation of interstitial pneumonia, were excluded. Additionally, cases were selected in which the attending respiratory physician recognized the presence of chronically progressing irreversible shadows in the clinical course. Two certified thoracic surgeons (T.I. and T.F.) independently selected cases based on the abovementioned criteria. In case of a disagreement, the selection was performed after a discussion. *Figure 1* illustrates a representative case of PDL.

Study population and cohort

The case selection diagram is shown in *Figure 2*. We focused on 1,234 patients with primary lung cancer who underwent surgery at our hospital between January 2006 and December 2021. Among these, 172 patients exhibited progressive, distinctive shadows in their lung fields postoperatively. However, we excluded patients with reversible shadows, such as those caused by heart failure as well as those resulting from recurrent lung cancer tumors, acute exacerbation of interstitial pneumonia, and other reversible conditions. Thus, 46 patients with irreversible progressive distinctive shadows in the remaining lung lobes remained. We further excluded fifteen patients with acute progression due to postoperative complications, such as acute pneumonia. The remaining 31 patients with a chronic progressive course were considered cases of PDL and included in the study. During a specific period when extracting cases of PDL, it was challenging to identify patients without distinctive shadows as control cases owing to significant data gaps, since they were not adequately tracked. Therefore, we established a control group comprising 247 patients who underwent lung cancer resection between January 2014 and December 2016, in whom no distinctive shadows were observed in the postoperative lung fields. The following clinical data were collected: age, sex, smoking history, presence of emphysema or interstitial lung disease in the background lung, history of tuberculosis or non-tuberculous mycobacterial infections, presence of diabetes, pathological type of lung cancer, stage of lung cancer, laterality of lung cancer, surgical procedure, surgical approach [thoracotomy/video-assisted thoracoscopic surgery (VATS)], acute pneumonia developing within one month postoperatively, presence of chronic pneumonia including *Aspergillus* infection and aspiration pneumonia occurring after three months postoperatively, presence of postoperative air leak (prolonged air leak and late-onset air leak), presence of lung cancer recurrence and its detail, history of chemotherapy after lung cancer resection and its detail, and history of radiation therapy in the thoracic region after lung cancer surgery and its detail. For cases of PDL, the localization of the destroyed lung was documented.

Matching cohort

Given the potential heterogeneity within the PDL cases across preoperative, perioperative, and postoperative patient backgrounds, adjusting for preoperative factors was deemed useful for analyzing the perioperative and postoperative effects. Therefore, covariate adjustment was performed for preoperative factors with P values <0.10 in the two groups, namely, the 31 PDL cases and 247 control cases. Using a 1:1 propensity score matching method (*Figure 2*), we obtained matching pairs of 31 cases of PDL and 31 cases of non-PDL.

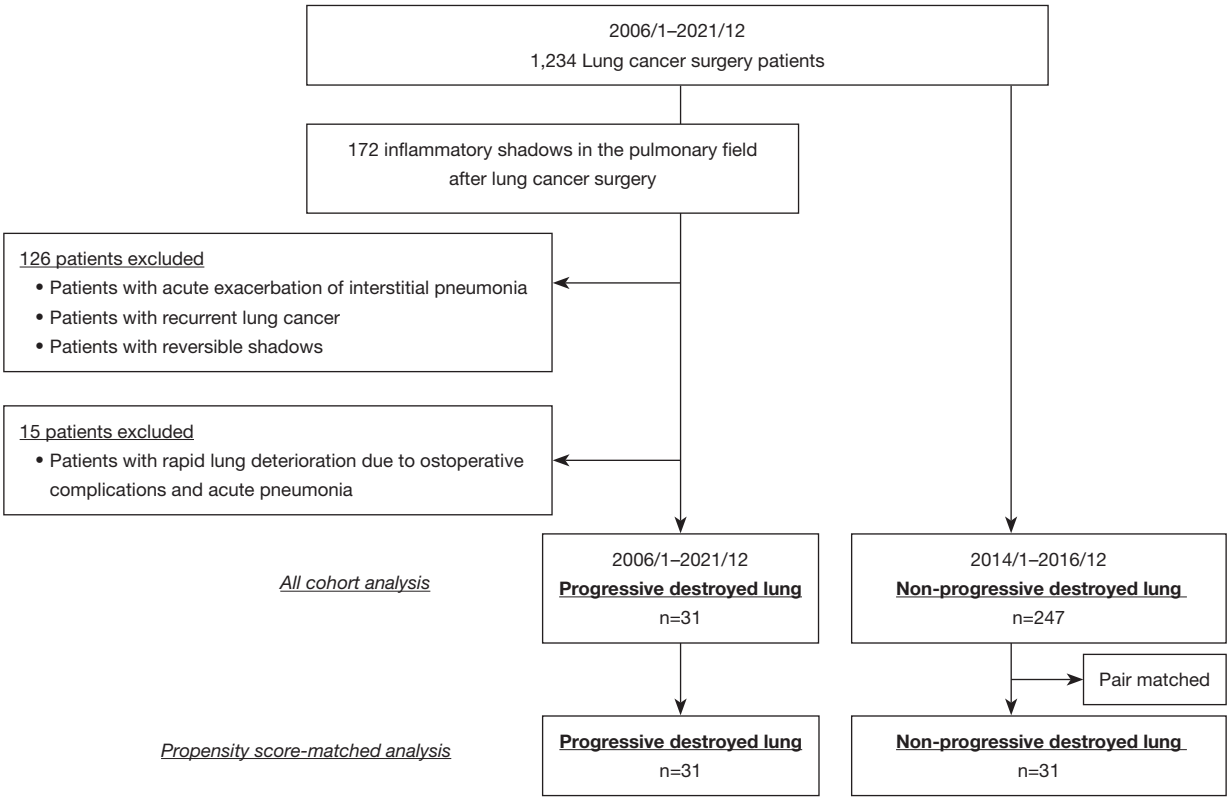

Figure 2 Flow chart of the study population.

Two different case-control studies

First, to assess the impact of risk factors on PDL, we compared patients with PDL with those with non-PDL. Next, to evaluate the effects of postoperative factors on PDL, patients with PDL matched 1:1 with those with non-PDL were compared.

Statistical analysis

Risk factors for PDL were evaluated using univariate and multivariate logistic regression analyses, and the results were expressed as odds ratios (ORs) and 95% confidence intervals (CIs). Ordinal variables were presented as median and interquartile range (IQR) and were analyzed using the Wilcoxon test. Categorical variables were analyzed using Fisher's exact test. Statistical significance was set at $P<0.05$. The comparison of the two cohorts after propensity score matching was conducted using the standardized mean difference (SMD). Factors with $P<0.05$ were included in the multivariate logistic regression model, with consideration of multicollinearity during variable selection. Firth's bias adjustment was used to address issues related to small sample sizes and rare events in the logistic regression. JMP (version 16.0; SAS Institute Inc., Cary, NC, USA) was used for statistical analysis.

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of the National Hospital Organization Tokyo National Hospital (No. 220036) and the requirement for individual consent for this retrospective analysis was waived.

Results

During the study period, a retrospective analysis of 1,234 surgeries was conducted. The PDL group included 31 patients, whereas the non-PDL group included 247 patients. The results of the univariate analysis are presented in *Table 1*. Chronic lung diseases, such as emphysema and interstitial lung disease, were more prevalent in the PDL

Table 1 Clinical characteristics of patients with progressive destroyed lung and control patients

Characteristics	Non-PDL (n=247)	PDL (n=31)	P
Age (years)	71 [65–75]	72 [68–75]	0.26
Sex			<0.001
Male	137 (55.5)	27 (87.1)	
Female	110 (44.5)	4 (12.9)	
Smoking			0.005
Yes	97 (39.3)	27 (87.1)	
No	150 (60.7)	4 (12.9)	
COPD or ILD			0.003
Yes	88 (35.6)	20 (62.5)	
No	159 (64.4)	11 (35.5)	
Tb/NTM			0.24
Yes	28 (11.3)	6 (19.4)	
No	219 (88.7)	25 (80.6)	
DM			0.31
Yes	38 (15.4)	7 (22.6)	
No	209 (84.6)	24 (77.4)	
Pathology			<0.001
Ad	197 (79.7)	13 (41.9)	
Sq	37 (15.0)	17 (54.9)	
Other	13 (5.3)	1 (3.2)	
Stage			0.02
I	156 (63.2)	14 (45.2)	
II	48 (19.4)	5 (16.1)	
III	43 (17.4)	12 (38.7)	
Side			0.55
Left	88 (35.6)	13 (41.9)	
Right	159 (64.4)	18 (58.1)	
Surgical procedure			0.80
Lobectomy (+α)	204 (82.6)	25 (80.6)	
Sublobar resection	43 (17.4)	6 (19.4)	
Surgical approach			0.003
VATS	101 (40.9)	4 (12.9)	
Thoracotomy	146 (59.1)	27 (87.1)	
Acute pneumonia			<0.001
Yes	14 (5.7)	11 (35.5)	
No	233 (94.3)	20 (64.5)	
Chronic pneumonia			<0.001
Yes	12 (4.9)	19 (61.3)	
No	235 (95.1)	12 (38.7)	
Air leak			0.001
Yes	19 (7.7)	9 (29.0)	
No	228 (92.3)	22 (71.0)	
Recurrence			0.45
Yes	102 (41.3)	15 (48.4)	
Locoregional	30 (12.1)	10 (32.3)	
Distant organ	61 (24.7)	4 (12.9)	
Both	11 (4.5)	1 (3.2)	
No	145 (58.7)	16 (51.6)	
Chemotherapy			0.57
Yes	119 (48.2)	17 (54.8)	
CT	100 (40.5)	15 (48.4)	
TKI	9 (3.6)	1 (3.2)	
ICI	2 (0.8)	0	
CT + TKI	5 (2.0)	1 (3.2)	
CT + ICI	3 (1.2)	0	
No	128 (51.8)	14 (45.2)	
Radiation therapy			<0.001
Yes	25 (10.1)	11 (35.5)	
LF	16 (6.5)	4 (12.9)	
MS	1 (0.4)	5 (16.1)	
CW	2 (0.8)	0	
LF + MS	4 (1.6)	2 (6.4)	
LF + CW	2 (0.8)	0	
No	222 (89.9)	20 (64.5)	

Values are presented as median [IQR] or n (%). PDL, progressive destroyed lung; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease; Tb, tuberculosis; NTM, non-tuberculous mycobacteria; DM, diabetes mellitus; Ad, adenocarcinoma; Sq, squamous cell carcinoma; VATS, video-assisted thoracoscopic surgery; CT, cytotoxic drug; TKI, tyrosine kinase inhibitor; ICI, immune checkpoint inhibitor; LF, lung field; MS, mediastinum; CW, chest wall; IQR, interquartile range.

Table 2 Multivariable analysis of risk factors for progressive destroyed lung in all patients

Variables	Odds ratio	95% CI	P
Sex			0.80
Male	1.3	0.2–6.6	
Female	1.0		
Smoking			0.93
Yes	1.1	0.2–5.8	
No	1.0		
COPD or ILD			0.65
Yes	1.3	0.4–4.4	
No	1.0		
Surgical approach			0.07
Thoracotomy	3.4	0.9–12.6	
VATS	1.0		
Acute pneumonia			0.03
Yes	3.5	1.1–11.2	
No	1.0		
Chronic pneumonia			<0.001
Yes	31.4	9.9–100.0	
No	1.0		
Air leak			0.001
Yes	7.2	2.2–23.8	
No	1.0		
Radiation therapy			<0.001
Yes	10.5	3.4–32.6	
No	1.0		

CI, confidence interval; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease; VATS, video-assisted thoracoscopic surgery.

group than in the non-PDL group. More surgeries were performed via an open-chest approach in the PDL group than in the non-PDL group. Postoperative complications, including acute pneumonia, chronic pneumonia (involving *Aspergillus* infection and aspiration pneumonia), and persistent or delayed air leak, and a history of radiation therapy after lung cancer surgery were more common in the PDL group than in the non-PDL group.

We conducted a multiple logistic regression analysis considering multicollinearity for the significant factors in *Table 1*. We selected sex, smoking history, background lung disease (chronic obstructive pulmonary disease/interstitial lung disease), pathology, surgical approach (thoracotomy/VATS), acute pneumonia, chronic pneumonia, air leak, and a history of radiation therapy after considering multicollinearity. Acute pneumonia (OR: 3.5, 95% CI: 1.1 to 11.2), chronic pneumonia (OR: 31.4, 95% CI: 9.9 to 100.0), air leak (OR: 7.2, 95% CI: 2.2 to 23.8), and radiation therapy (OR: 10.5, 95% CI: 3.4 to 32.6) emerged as independent risk factors for PDL (*Table 2*).

For all enrolled patients, median follow-up was 57 months. No significant difference in overall survival (OS) and recurrence-free survival (RFS) was observed between the PDL group and the non-PDL group (*Figure 3A,3B*). However, a significant difference was observed in disease-specific survival (DSS) between these two groups, as expected (*Figure 3C*).

Subsequently, to analyze surgical and postoperative effects, we performed a case-control study in which preoperative factors with P values of <0.1 were matched between the cohorts. Acute and chronic pneumonia were identified as risk factors in this matched case-control study (*Table 3*).

After a multiple logistic regression analysis of the two risk factors, only chronic pneumonia (OR: 10.1, 95% CI: 2.9 to 35.8) emerged as an independent risk factor for PDL (*Table 4*).

Among propensity score-matched patients, the median follow-up period was 54 months. No significant differences were observed in OS and RFS between the PDL group and the non-PDL group (*Figure 4A,4B*). However, there was a difference, although not a statistically significant one, in DSS between these two groups (*Figure 4C*).

Regarding the localization of the destroyed lung, all cases were on the resected side, with the most common location being the right upper lobe after right lower lobectomy (including bilobectomy) in ten cases (32%). Following this, there were six cases (19%) of destroyed lung in the left lower lobe after left upper lobectomy (*Table 5*). No cases of destroyed lung were observed in the right lower lobe after right upper lobectomy.

Discussion

Key findings

In this study, we focused on postoperative residual lungs, at times referred to as "destroyed lungs". Specifically,

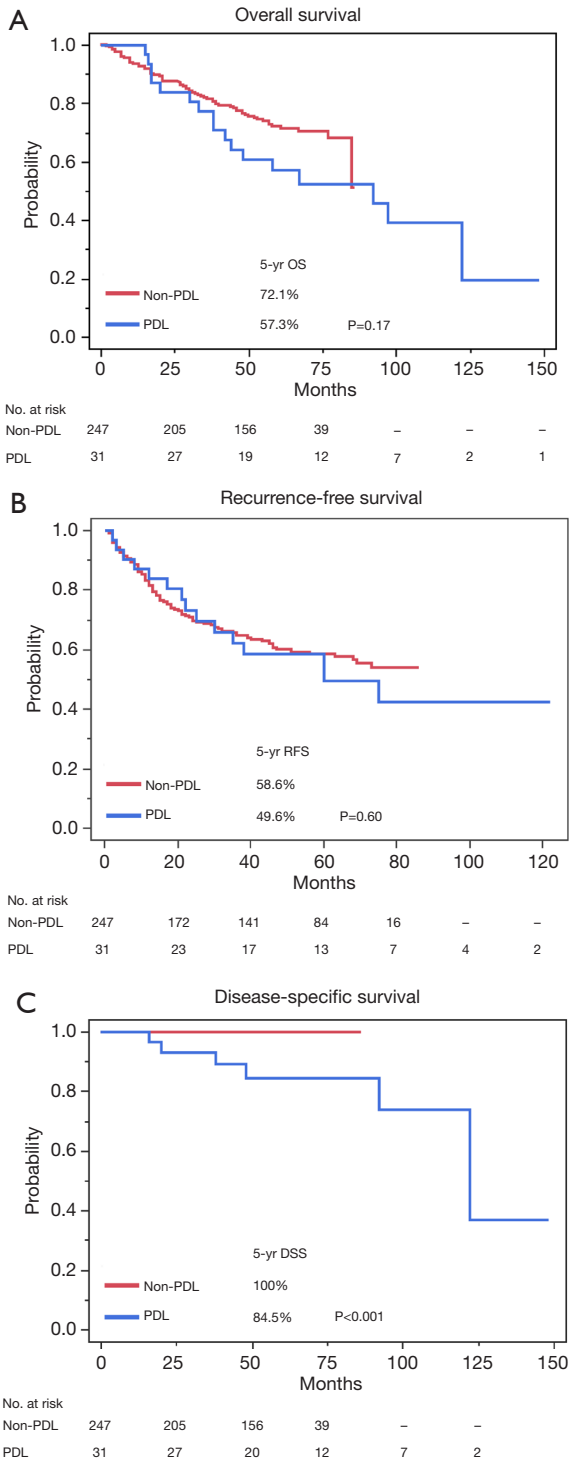

Figure 3 Kaplan-Meier curves for (A) OS, (B) RFS and (C) DSS comparing PDL group and non-PDL group. No., number; PDL, progressive destroyed lung; OS, overall survival; RFS, recurrence-free survival; DSS, disease-specific survival.

we conducted a retrospective analysis of cases involving lung cancer surgery, which is a common lung resection procedure. Limited to cases of lung cancer surgery performed at our institution, our analysis revealed that postoperative acute pneumonia, chronic pneumonia including aspiration pneumonia and *Aspergillus* infection, persistent or delayed air leak, and radiation therapy were independent risk factors for the development of destroyed lung. In a post-matching case-control study focusing on postoperative factors, only chronic pneumonia was identified as an independent risk factor for PDL. Among the 31 cases of PDL in our study, episodes of aspiration were observed in five (16%) cases, and *Aspergillus* infection was observed in 13 (42%) cases. PDL progresses slowly, so there may be a possibility of a short observation period, resulting in no significant impact on OS. However, there was a tendency for a difference to be observed in DSS. Furthermore, regarding the localization of the destroyed lung, all cases were on the resected side. On the right side, the right upper lobe was the most commonly affected after right lower lobectomy or middle-lower lobectomy; conversely, on the left side, the left lower lobe was the most commonly affected after left upper lobectomy.

Strengths and limitations

Although significant findings were obtained, this study had some limitations. First, this was a small-scale, retrospective study conducted at a single institution. Second, owing to data discrepancies and differences in the follow-up period caused by disease-specific factors, the selection periods for the patient and control groups differed. Therefore, long-term progression of lung destruction may not have occurred in the control group. Third, open thoracotomy tended to be an independent risk factor for PDL in the entire cohort. However, surgical techniques have transitioned from open thoracotomy to VATS over time, with open thoracotomy increasingly being chosen for more extensive surgeries; thus, this limitation seems important.

Comparison with similar researches and explanations of findings

This study indicated that infections, primarily pneumonia, and impairment caused by radiation triggered lung damage. Identifying persistent or delayed air leakage as a risk factor

Table 3 Clinical characteristics of patients with progressive destroyed lung and control patients after propensity score matching

Characteristics	Non-progressive destroyed lung (n=31)	Progressive destroyed lung (n=31)	P	SMD
Age (years)	71 [67–77]	72 [68–75]	0.91	0.029
Sex			>0.99	<0.001
Male	27 (87.1)	27 (87.1)		
Female	4 (12.9)	4 (12.9)		
Smoking			>0.99	<0.001
Yes	27 (87.1)	27 (87.1)		
No	4 (12.9)	4 (12.9)		
COPD or ILD			>0.99	<0.001
Yes	20 (62.5)	20 (62.5)		
No	11 (35.5)	11 (35.5)		
Tb/NTM			0.26	0.392
Yes	2 (6.5)	6 (19.4)		
No	29 (93.5)	25 (80.6)		
DM			>0.99	0.079
Yes	6 (19.4)	7 (22.6)		
No	25 (80.6)	24 (77.4)		
Pathology			>0.99	<0.001
Ad	13 (41.9)	13 (41.9)		
Sq	17 (54.9)	17 (54.9)		
Other	1 (3.2)	1 (3.2)		
Stage			0.14	0.523
I	19 (61.3)	14 (45.2)		
II	7 (22.6)	5 (16.1)		
III	5 (16.1)	12 (38.7)		
Side			>0.99	<0.001
Left	13 (41.9)	13 (41.9)		
Right	18 (58.1)	18 (58.1)		
Surgical procedure			>0.99	0.079
Lobectomy (+α)	24 (77.4)	25 (80.6)		
Sublobar resection	7 (22.6)	6 (19.4)		
Surgical approach			0.07	0.547
VATS	11 (35.5)	4 (12.9)		
Thoracotomy	20 (64.5)	27 (87.1)		

Table 3 (*continued*)

Table 3 (*continued*)

Characteristics	Non-progressive destroyed lung (n=31)	Progressive destroyed lung (n=31)	P	SMD
Acute pneumonia			0.01	0.763
Yes	2 (6.5)	11 (35.5)		
No	29 (93.5)	20 (64.5)		
Chronic pneumonia			<0.001	1.422
Yes	2 (6.5)	19 (61.3)		
No	29 (93.5)	12 (38.7)		
Air leak			0.21	0.404
Yes	4 (12.9)	9 (29.0)		
No	27 (87.1)	22 (71.0)		
Recurrence			>0.99	0.065
Yes	14 (45.2)	15 (48.4)		
Locoregional	6 (19.4)	10 (32.3)		
Distant organ	7 (22.6)	4 (12.9)		
Both	1 (3.2)	1 (3.2)		
No	17 (54.8)	16 (51.6)		
Chemotherapy			0.61	0.194
Yes	14 (45.2)	17 (54.8)		
CT	11 (35.5)	15 (48.4)		
TKI	1 (3.2)	1 (3.2)		
ICI	0	0		
CT + TKI	1 (3.2)	1 (3.2)		
CT + ICI	1 (3.2)	0		
No	17 (54.8)	14 (45.2)		
Radiation therapy			0.15	0.454
Yes	5 (16.1)	11 (35.5)		
LF	3 (9.7)	4 (12.9)		
MT	0	5 (16.1)		
CW	1 (3.2)	0		
LF + MT	0	2 (6.4)		
LF + CW	1 (3.2)	0		
No	26 (83.9)	20 (64.5)		

Values are presented as median [IQR] or n (%). SMD, standardized mean difference; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease; Tb, tuberculosis; NTM, non-tuberculous mycobacteria; DM, diabetes mellitus; Ad, adenocarcinoma; Sq, squamous cell carcinoma; VATS, video-assisted thoracoscopic surgery; CT, cytotoxic drug; TKI, tyrosine kinase inhibitor; ICI, immune checkpoint inhibitor; LF, lung field; MT, mediastinum; CW, chest wall; IQR, interquartile range.

Table 4 Multivariable analysis of risk factors for progressive destroyed lung after propensity score matching

Variables	Odds ratio	95% confidence interval	P value
Acute pneumonia			0.53
Yes	1.5	0.4–5.3	
No	1.0		
Chronic pneumonia			<0.001
Yes	10.1	2.9–35.8	
No	1.0		

further suggests that poor expansion due to pneumothorax and adhesions during pneumothorax healing may cause lung destruction. Previous reports have indicated that lung collapse can lead to pulmonary infections (16). Although not identified as a risk factor in this study, a similar impact may be considered for open thoracotomy, where a tendency for it to be a risk factor was observed. The effects of complex lung resections and extensive chest wall damage, which result in restricted chest wall movement, as well as the potential for impaired lung expansion due to lung adhesion to the chest wall, could contribute to these effects.

Pleuroparenchymal fibroelastosis (PPFE) is similar to or related to destroyed lung. PPFE is characterized by predominant fibrotic lesions in the upper lungs on both sides, and idiopathic PPFE is considered a rare form of interstitial pneumonia. The term "PPFE" was coined by Frankel *et al.* in 2004, characterizing the clinical, radiographic, physiologic, and pathologic findings of the disease entity (17). Although pathological characterization of destroyed lung was impossible in this study because of the lack of biopsy, radiographic features of destroyed lung including irregular nodular consolidations adjacent to the pleura at the lung apex, linear or reticular opacities, and often accompanied by traction bronchiectasis within the shadows were similar to or consistent with those of PPFE. Indeed, according to multiple reports by Sekine *et al.* since 2017, patients with a history of open thoracic surgery for lung or esophageal cancer have been known to develop unilateral (surgical side) upper lung field pulmonary fibrosis (upper PF) with clinical, radiological, and pathological features common to those of idiopathic PPFE during the postoperative remote period (18,19). These patients exhibited fibrosis leading to flattening of the upper lungs,

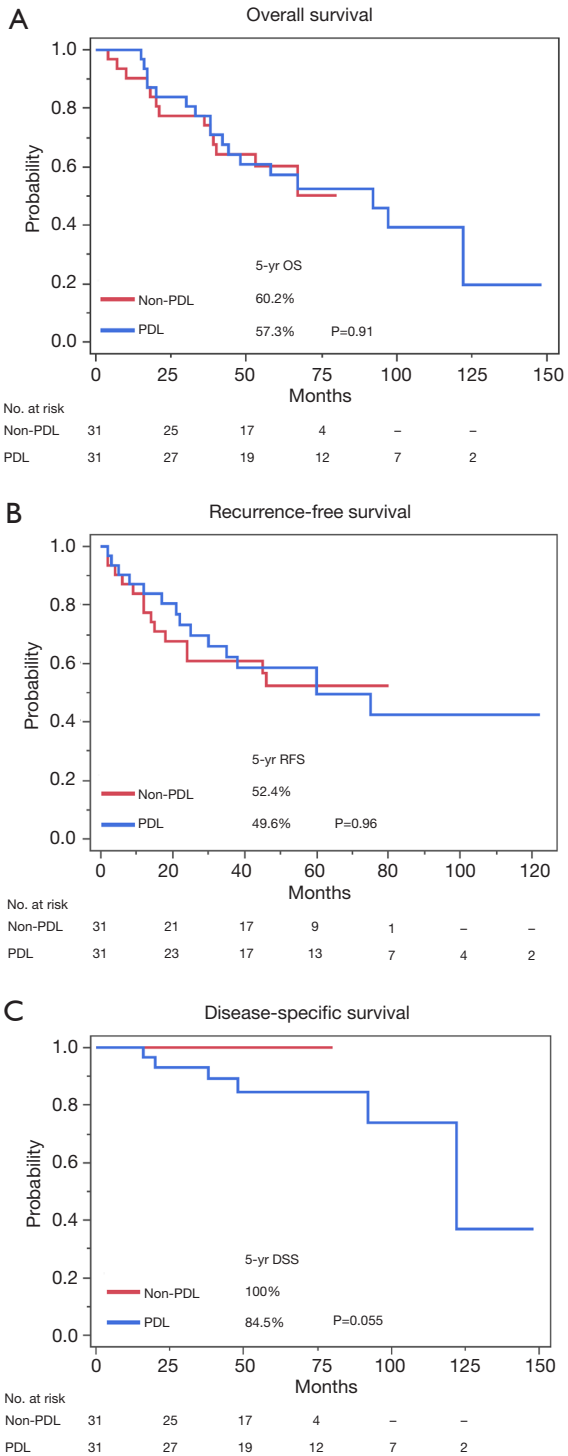

Figure 4 Kaplan-Meier curves after propensity score matching for (A) OS, (B) RFS and (C) DSS comparing PDL group and non-PDL group. No., number; PDL, progressive destroyed lung; OS, overall survival; RFS, recurrence-free survival; DSS, disease-specific survival.

Table 5 Location of progressive destroyed lung and surgical procedure

Location	Surgical procedure	Number of patients (n=31)
Right upper lobe	Right lower lobectomy	5
	Right middle and lower lobectomy	5
	Right segmentectomy	2
	Right wedge resection	1
Right middle lobe	Right upper lobectomy	4
	Right lower lobectomy	1
Left upper lobe	Left lower lobectomy	4
Left lower lobe	Left upper lobectomy	6
	Left segmentectomy	2
	Left wedge resection	1

progressing to fibrosis that elevates the lung hilum (similar to in PPFE). Furthermore, the same research group has recently reported that 25/587 patients (4.3%) who underwent lung resection for lung cancer were diagnosed with unilateral upper PF, or "radiographic PPFE" (20).

Chest wall movement disorders on the surgical side were observed, and an association with chronic inflammation due to aspiration was also noted. Restricted chest wall movement exacerbates airway clearance impairment, and repeated episodes of aspiration pneumonia may lead to rapid progression of PPFE changes in the remaining lung on the surgical side (19). Most cases involved the right side, and in cases without emphysema, the unilateral lung apex gradually transformed into cystic lesions, with multiple cases developing *Aspergillus* infection. Patients with idiopathic PPFE may exhibit common features, such as subpleural cystic changes and pulmonary aspergillosis (21). In our study, 13 (41%) cases of PDL occurred in the right upper lobe, all of which showed findings that did not allow PPFE to be ruled out. It is challenging to determine whether *Aspergillus* infection is a risk factor or whether it occurs in the lungs, showing changes similar to PDL. Furthermore, a history of postoperative air leakage was identified as a risk factor in the PDL group, supporting its association with pleuroparenchymal fistulas, as suggested in unilateral upper PF cases.

As shown in *Table 5*, there was a tendency for upper-lobe involvement on the right side and lower-lobe involvement on the left side. The lesions tended to occur in the apical part of the remaining lung lobes, again showing a pattern similar to that of idiopathic PPFE. It is possible that "destroyed lung" after lung resection for lung cancer in this study and PPFE have at least some overlap. Further research seeking pathological evidence for PPFE is required in the future, to better characterize destroyed lung.

Implications and actions needed

Progressive destruction of the lung following lung cancer surgery involves various factors, particularly postoperative complications such as chronic infections occurring after 3 months, postoperative acute pneumonia, air leaks, and radiation exposure. Understanding the mechanisms and factors influencing the progression of lung destruction, especially interventions and preventive measures for postoperative complications (such as chronic infections), can improve patient outcomes. However, the effectiveness of these interventions needs to be corroborated by further research.

Conclusions

In this study, progressive destruction of the remaining lung after lung cancer surgery was found to be primarily associated with postoperative chronic pneumonia, *Aspergillus* infection, and aspiration pneumonia. Additionally, it was observed to occur more frequently in the upper lobe on the right side and the lower lobe on the left side of the

remaining lung, with a tendency to occur in the apical part of the lung lobes.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-452/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of the National Hospital Organization Tokyo National Hospital (No. 220036) and the requirement for individual consent for this retrospective analysis was waived.

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