

*Original  
Article*

## Incidence of Acute Exacerbation of Interstitial Pneumonia in Operated Lung Cancer: Institutional Report and Review

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**Purpose:** Several small studies have reported that acute exacerbation (AE) of idiopathic interstitial pneumonia (IIP) can occur after lung resection for patients with non-small cell lung cancer, though the incidence rate is unclear.

**Methods:** We examined our institutional data and performed a search of the MEDLINE database for publications regarding AE of IIP following surgery for lung cancer. Studies reporting the incidence rates of IIP and AE were included.

**Results:** Eleven studies including our institutional data were determined to be eligible. Seven studies designated the incidence of IIP. Of 4749 patients (from 7 studies) who underwent lung resection for NSCLC, 277 had IIP, for an incidence rate of 5.8% (range 1.1%–11.7%). Eleven studies designated the incidence of AE from IIP patient, 67 (15.8%) of 424 IIP patients (from 11 studies) developed AE after surgery, of whom 38 (56.7%) died during the postoperative course.

**Conclusion:** Coexistent IIP in patients with lung cancer increases the risk of lung cancer surgery. Furthermore, AE of IIP may be a major cause of operation-related death.

**Keywords:** interstitial pneumonia, idiopathic pulmonary fibrosis, acute exacerbation, lung cancer, complication

### Introduction

Acute exacerbation (AE) of idiopathic interstitial pneumonia (IIP), which is mostly comprised of cases of idiopathic pulmonary fibrosis (IPF), occasionally occurs after lung surgery.<sup>1–4)</sup> We previously reported that some cases of postoperative acute respiratory distress syndrome (ARDS) following thoracic surgery in patients with lung

cancer are AE of obvious or subclinical IPF.<sup>4)</sup> Since IPF is often associated with lung cancer, the indications for surgery must be assessed by giving careful consideration to the risk of AE after surgery. However, the rate of lung surgery in patients with IPF is not clearly known. AE of IIP following lung resection for lung cancer has been documented in several reports, though most are from Japan and the incidence rate is not well recognized. In this study, we report our institutional data and findings of a systematic review of literature regarding the incidence of AE of IIP.

### Subjects and Methods

A total of 443 patients who underwent lung resection due to primary lung cancer from January 2006 through December 2010 at Dokkyo Medical University Hospital

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were investigated in a retrospective manner. Findings of preoperative chest computed tomography (CT) scans that reflected pathological usual interstitial pneumonia (UIP) were double-checked by radiologists. IIP in our patients was diagnosed based on CT findings and not all were diagnosed with IIP before lung cancer surgery. The diagnosis of AE was made from clinical symptoms and chest radiograph, CT scan, and biochemical test results, such as sialylated carbohydrate antigen KL-6 (KL-6) or surfactant protein-D (SP-D) levels.

### Search strategy

We also searched the MEDLINE database using the keywords “interstitial pneumonia,” “lung cancer,” “operation,” and “acute exacerbation or respiratory distress” in studies published between January 2000 and December 2010. When additional information was needed to complete the data collected for this study, the corresponding authors were contacted. If more current data became available, including meeting abstracts, such information was included in the review. For publications that included updates and additions to prior publications, the most current was included.

### Definitions

Several terms such as IIP, interstitial pneumonia (IP), and IPF have been used in reports in regard to this entity. In some, IP was diagnosed as IPF based on pathological findings of UIP, while in others, IP was diagnosed on clinical criteria or clinical findings based on UIP findings of chest CT findings before the operation. Because clinical diagnosis of IP may include non-specific IP (NSIP) or other types of IP, we refer to those as IIP in this study, though most were IPF.

### Inclusion and exclusion criteria

We identified studies that reported incidence of IIP and mortality in all patients and incidence of IIP in patients with lung cancer. Reports focusing on IP in patients with collagen vascular disease (CVD-IP) were excluded. To minimize publication and reporting bias, single case reports or case series comprising of less than 5 analyzable cases were also excluded.

## Results

### Institutional incidence of IIP and AE

Of 443 patients who underwent surgery at our institution for lung cancer, 52 (11.7%) had IIP, of whom 6

**Table 1** Incidence of idiopathic interstitial pneumonia in patients who underwent lung cancer surgery

Study	Total no. of patients	No. of IIP cases	(%)
Osawa (5)	275	3	(1.1%)
Watanabe (6)	673	44	(6.5%)
Takaoka (7)	756	25	(3.3%)
Otani (8)	512	22	(4.3%)
Chida (4)	834	91	(10.9%)
Shintani (9)	1256	40	(3.2%)
Present	443	52	(11.7%)
Total	4749	277	(5.8%)

IIP: idiopathic interstitial pneumonia

(11.5%) had AE of IIP following lung resection. Three (50%) of those 6 patients died in the hospital due to AE of IIP.

### Search results and characteristics of the included studies

Our search strategy yielded a total of 32 articles, all from Japan, of which 20 were relevant reports of patients with both IIP and lung cancer who experienced AE after surgery. Seventeen of the articles contained at least 6 analyzable cases, while 1 report was excluded because the data were updated in a newer report. Eleven of the reports were finally considered eligible, of which 6<sup>4-9)</sup> noted the incidence of IIP in patients with lung cancer who underwent surgery and 10<sup>4,6-14)</sup> reported deaths due to AE during the postoperative course.

### Incidence of AE and IIP

The incidence of IIP in patients with lung cancer who underwent surgery was designated in 7 studies, including the present (**Table 1**). Of a total of 4749 patients in all of the studies, 277 had IIP, for an incidence rate of 5.8% (range, 1.1%–11.7%). Four of those 7 studies also designated the pathological diagnosis of IP as UIP (n = 112), NSIP (n = 3), or CVD-IP (n = 1).

The incidence of AE in patients with IIP who underwent lung cancer surgery was noted in 11 studies, including the present (**Table 2**). A total of 424 patients with IIP who underwent lung resection due to lung cancer were reported. Of those, 67 (15.8%) experienced AE after surgery, of whom 38 (56.7%) with AE died during the postoperative course.

## Discussion

Post-operative ARDS often occurs in patients with IIP

**Table 2 Incidence of acute exacerbation after lung surgery**

Study	No. of IIP cases	No. of cases with AE	Mortality
Koizumi (10)	47	7	2/7 ( 29%)
Imakiire (11)	25	0	0/0 ( 0%)
Watanabe (6)	44	5	5/5 (100%)
Takaoka (7)	25	10	3/10 ( 30%)
Yano (12)	50	12	11/12 ( 92%)
Tanaka (13)	7	1	1/7 ( 14%)
Otani (8)	22	6	0/6 ( 0%)
Muraoka (14)	21	3	1/3 ( 33%)
Chida (4)	91	11	7/11 ( 64%)
Shintani (9)	40	6	5/6 ( 83%)
Present	52	6	3/6 ( 50%)
Total	424	67	38/67 ( 57%)

IIP: idiopathic interstitial pneumonia; AE: acute exacerbation

following surgery for lung cancer. We previously reported that some cases of postoperative ARDS following thoracic surgery in patients with lung cancer are AE of obvious or subclinical IPF, which is a major cause of death after lung cancer surgery.<sup>15)</sup> However, the rates of incidence of IIP in patients with lung cancer and of AE in IIP are not well recognized. We conducted a systematic review of studies found in a world-wide search of MEDLINE and all of the found reports were from Japan. However, we think that AE of IIP following surgery is not a regional issue and should be recognized as a separate entity of postoperative ARDS.

In our review, the incidence of IIP in patients undergoing surgery for lung cancer was 5.8%. Cigarette smoking is a common contributor not only to lung cancer, but also to IIP such as IPF. Although all of the patients in this review underwent surgery, the incidence (5.8%) of IIP found may represent that of patients with lung cancer, regardless of whether they received an operation. Miyazaki et al. reported that 4.5% of patients with small cell lung cancer had interstitial lung disease.<sup>16)</sup>

The therapeutic approach for patients with both lung cancer and IIP is very complex, because of the high rate of post-therapeutic pulmonary complications and mortality. The incidence of AE in patients with IIP was 15.8%, and the rate of mortality in those cases was 56.7%, while the rate of mortality from AE of IIP in all patients who underwent surgery was 0.52%. Mortality in cases of surgery for lung cancer has been reported to be about 1%,<sup>17-20)</sup> thus, AE of IIP is a major cause of operation-related death in patients who undergo surgery for lung cancer. Some cases of post-surgical ARDS are likely AE of IIP and even in those who undergo induction therapy, AE of

IIP is a major cause of post-surgical ARDS following induction therapy.<sup>4)</sup> With developments of surgical devices and perioperative care, deaths owing from technical failure or infection have decreased in recent decades. Nevertheless, the issue of coexistent IIP in patients with lung cancer will be a research theme in this field in the next decade.

## Conclusion

Coexistent IIP in patients with lung cancer increases the risk of lung cancer surgery. Furthermore, AE of IIP may be a major cause of operation-related death.

## Disclosure Statement

None declared.

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