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Clinical analysis of patients with idiopathic pulmonary fibrosis concurrent with surgery resectable lung cancer: a retrospective cohort study from perspective of ILD physicians

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Abstract

Background Surgery resection would improve idiopathic pulmonary fibrosis (IPF) patients with early-stage lung cancer (LC). However, most associated studies were published from surgeons. Interstitial lung disease (ILD) physicians involved in perioperative management would be helpful for improving patients with idiopathic pulmonary fibrosis combined with lung cancer (IPF-LC). To enhance the understanding of the clinical characteristics presented by patients with IPF-LC who have undergone surgical resection, and to explore the factors linked to unfavorable prognosis, our ILD physicians conducted this study.

Methods We retrospectively examined clinical records of IPF-LC patients at Peking Union Medical College Hospital from January 2014 to December 2023.Data related to clinical manifestations and treatment methods were collected. Patients underwent routine follow-up through clinical assessments and telephone consultations. The demographic, clinical, and laboratory features of 12 surviving patients and 8 deceased patients were comparatively analysed.

Results There were 30 males and 2 females, aged from 49 years to 82 years. Twenty-eight patients had a history of smoking. Twenty-five patients had at least one comorbidity and emphysema was the most common. IPF was diagnosed before LC in 8 patients but none of them were prescribed with anti-fibrotic medications. Twenty-four patients were simultaneously diagnosed with LC and IPF, and 7 of them were prescribed anti-fibrotic medications. After surgery, 27 patients were pathologically diagnosed with non-small cell lung cancer and 26 patients were classified as stage I or II lung cancer. During follow-up, 8 patients died, 12 patients lost follow-up and 12 patients survived. Among the 8 deceased patients, 5 patients died from acute exacerbation of IPF, one died from cancer progression and 2 died from surgical complications. The serum Cyfra211 level was higher and the lung cancer stage was more advanced in the non-survival group than in the survival group.

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Conclusion Most of our IPF-LC patients were elderly males with a history of smoking and had at least one comorbidity. Most of them were diagnosed with IPF and LC simultaneously. However, only one fifth were prescribed with pirfenidone or nintedanib. Acute exacerbation of IPF was the main cause of death. Similar to the LC patients, higher serum Cyfra211 levels and more advanced lung cancer stages were associated with a poor prognosis for our enrolled IPF-LC patients.

Clinical trial number Not applicable.

Keywords Idiopathic pulmonary fibrosis, Lung cancer, Surgical resection, Retrospective study

Background

The use of antifibrotic medications improve transplantation-free survival in patients with idiopathic pulmonary fibrosis (IPF) [1]. Owing to prolonged survival, comorbidities have become a source of concern for IPF patients. Among these comorbidities, lung cancer is a common potentially fatal comorbidity [2, 3]. Radical surgical intervention is not only an effective strategy for improving outcomes in patients with early-stage lung cancer but also recommended for IPF patients who have concurrent lung cancer (IPF-LC) [4], especially when early-stage lung cancer and mild IPF are suspected. Invasive interventions such as surgery are well-known for their association with acute exacerbation of IPF (AE-IPF), which is a fatal complication for individuals with IPF-LC. However, appropriate perioperative management would improve the prognosis of patients with IPF-LC who undergo pulmonary resection surgery.

The incidence of postoperative AE-IPF in different centers fluctuates from 3 to 32%. The mortality rate of postoperative AE-IPF is between 33.3% and 100%. Additionally, AE-IPF is related to the occurrence of acute respiratory distress syndrome (ARDS) after lung cancer surgery [5]. Furthermore, the deterioration of lung function in IPF-LC patients after surgical resection of the lung segment or lobe where the malignant lesion is located is a source of concern for interstitial lung disease (ILD) physicians, thoracic surgeons, and patients [6]. The number of studies on IPF-LC patients is gradually increasing worldwide. Japanese scholars have focused on the aspects of surgical treatment for IPF-LC. In recent years, researchers have suggested that the preoperative administration of pirfenidone could lower the risk of postoperative AE-IPF [5, 7, 8].

IPF patients diagnosed in the early stages of lung cancer are likely more suitable for radical surgical procedures. Thus, physicians specializing in the treatment of ILD should be involved in the perioperative management of patients with resectable lung cancer. The main objective of this study is to describe the clinical characteristics of patients with IPF concurrent with surgery resectable lung cancer, including epidemiology, comorbidities, laboratory indicators, diagnosis and treatment. The secondary objective is to evaluate the survival status and causes of death, as well as to preliminarily explore the probable associated prognostic factors for them.

Methods

Patients

In total, 144 patients were diagnosed with IPF-LC who were admitted to Peking Union Medical College Hospital from January 2014 to December 2023. Final follow-up date was June 30th 2024. Three researchers (YJ.S., MZ.W. and H.H.) examined their clinical documents (comprising pathological reports) and chest CT images, stored in the hospital's data repository. The inclusion criteria must be met simultaneously as follows: diagnosed with IPF according to the IPF guidelines, pathologically confirmed as lung cancer, and IPC-LC patients who underwent lung cancer surgery. The exclusion criteria include any of the following: IPF-LC patients without surgical resection, incomplete medical records, lack of imaging data, and inaccessible pathological reports. Finally, 32 patients were enrolled in our study after multidisciplinary discussion by four researchers (MZ.W., K.X., C.H. and H.H.). The research received approval from the institutional ethical review board of Peking Union Medical College Hospital (approval number: K4327) in accordance with the Declaration of Helsinki. Our research utilized de-identified healthcare data. The requirement for written informed consent from each participant was waived because the study fulfilled the minimal risk waiver criteria established by the PUMCH Institutional Review Board.

Definitions

Thoracic CT images were evaluated in a blinded fashion by three pulmonologists (YJ.S., MZ.W., and H.H.) and one radiologist (K.X.). The diagnostic criteria for IPF were in accordance with the updated IPF guidelines [9]. The definition of AE-IPF referred to the consensus opinion proposed by the Global AE-IPF Research Group in 2016 [10]. If an IPF patient experienced acute worsening or progression of dyspnea within one month, and the chest CT showed new diffuse GGO and/or consolidation in both lungs, and heart failure or fluid overload was excluded, the cause of death would be classified as AE-IPF. Emphysema was defined as a region of low attenuation without demarcation by visible walls on the

computed tomography image [11]. Typical chest CT images of IPF-LC are presented in Fig. 1.

Statistical analysis

All the data were subjected to analysis by means of the IBM SPSS Statistics version 27.0 software package. Quantitative variables were depicted as the means ± standard deviations (SD) or medians (interquartile ranges [IQRs]), and categorical variables were presented as frequencies and percentages. Comparisons between groups regarding quantitative variables were carried out using the t test or rank sum test, and for categorical variables, the chi-square test was implemented. The statistically significant variables selected through univariate analysis were ultimately evaluated by multivariate analysis. A two-sided P-value < 0.05 was considered statistically significant.

Results

General characteristics of patients with IPF-LC

Among the 32 enrolled patients, 25 patients were older than 59 years. The average age at the time of diagnosis of LC was 66.2 ± 8.3 (range: 49–82) years, and there were 30 males and 2 females. Among them, 28 patients had a history of smoking, with a smoking index of 867.3 ± 546.3 (range: 300–3000). Eighteen patients underwent preoperative pulmonary function tests. Pulmonary function tests revealed that the percentage of predicted value of FVC was 92.0 ± 13.8% (range 70.9-120%), the diffusing capacity for carbon monoxide was 63 ± 15% (range 44-89%), and the FEV1/FVC ratio was >70%. The pulse oxygen saturation was measured at rest in all ward patients not receiving oxygen therapy, and the average saturation was 96.5 ± 3.5% (range 92-100%). The demographic and clinical characteristics and several laboratory parameters of the study participants are presented in Table 1. According to the postoperative staging of lung cancer, 14 patients had stage I lung cancer, 12 patients had stage II, 4 patients had stage III, and 2 patients had stage IV. All patients were pathologically diagnosed with lung cancer, 29 of whom had non-small cell lung cancer (NSCLC) and 3 had small cell lung cancer (SCLC). Among the patients with NSCLC, 16 patients had adenocarcinoma, 11 patients had squamous cell carcinoma (SCC), 1 patient had large cell neuroendocrine carcinoma, and 1 patient had other non-small cell lung cancer (poorly differentiated, partly squamous cell carcinoma). Eight patients with IPF were diagnosed with lung cancer during their follow-up; however, none of them were treated with antifibrotic medications. The remaining 24 patients were diagnosed with IPF and lung cancer simultaneously. Only 7 patients were prescribed antifibrotic medications, 5 of whom were prescribed pirfenidone during the perioperative period and continued treatment after surgery. Two patients were administered nintedanib after surgery.

Comorbidity of patients with IPF-LC

In this study, only 7 patients were comorbidity-free. Ten patients presented with one comorbidity. The remaining patients had two or more comorbidities. Twenty-five patients had at least one comorbidity: emphysema (23 patients), hypertension (14 patients), diabetes (7 patients), coronary heart disease (6 patients),

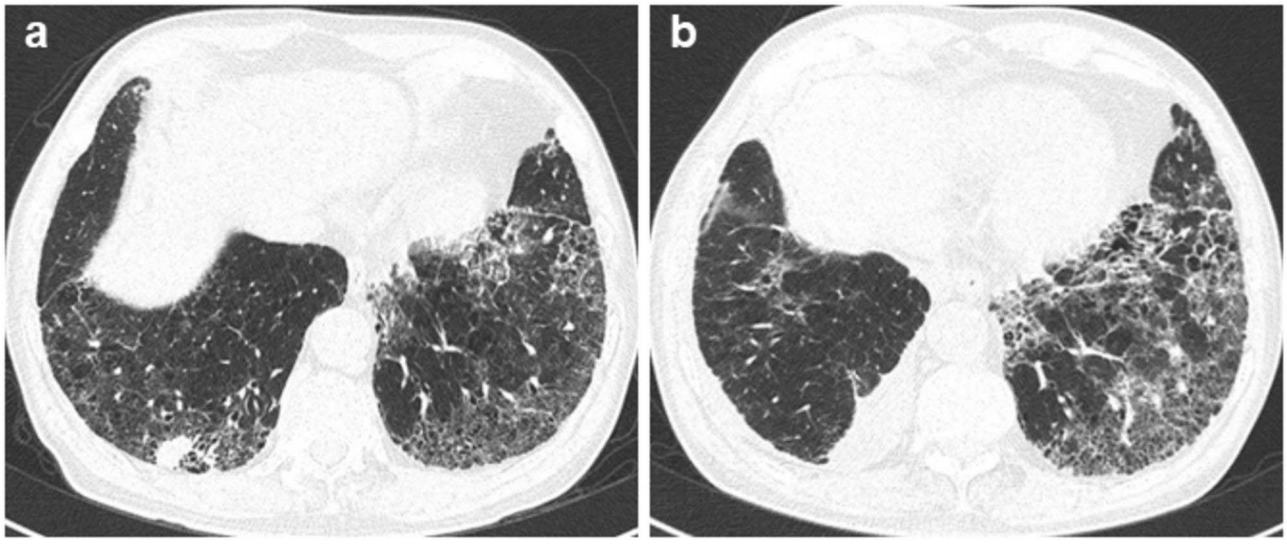

Fig. 1 Typical chest CT images of IPF-LC before and after surgery. (**a**) The preoperative chest CT demonstrated scattered reticular and honeycomb-like shadows in the subpleural areas of both lower lungs, and a solid nodule in the posterior basal segment of the right lower lung. (**b**) The postoperative chest CT indicated that the reticular and honeycomb shadows in the left lower lung were more severe than before, and scattered ground-glass opacities could be observed in both lungs. In the outer basal segment of the right lower lung, there were local reticular or streaky shadows and encapsulated pleural effusion

Table 1 Demographic, clinical and laboratory parameters

Parameter	Result	Normal range
Age (year) [a]	66.2 ± 8.3	NA
Gender [b]		
Male	30 (93.8)	NA
Female	2 (6.3)	NA
BMI (kg/m2) [a]	24.2 ± 2.9	NA
History of smoking [b]	28 (87.5)	NA
Smoking Index [a]	867.3 ± 546.3	NA
Pulmonary function before operation [a]		
FVC / Predicted Value (%)	92.0 ± 13.8	NA
DLCO / Predicted Value (%)	63.0 ± 15.0	NA
SpO2@RA (%) [a]	96.5 ± 3.5	NA
Pathological classification [b]		
Adenocarcinoma	16 (50.0)	NA
Squamous cell carcinoma	11 (34.4)	NA
Small cell lung cancer	3 (9.4)	NA
Large cell neuroendocrine carcinoma	1 (3.1)	NA
Undifferentiated lung cancer	1 (3.1)	NA
Staging of lung cancer [b]		
Stage IA	9 (28.1)	NA
Stage IB	5 (15.6)	NA
Stage IIA	2 (6.3)	NA
Stage IIB	10 (31.3)	NA
Stage IIIA	3 (9.4)	NA
Stage IIIB	1 (3.1)	NA
Stage IVA	2 (6.3)	NA
NSE (ng/ml) [a]	4.8 ± 3.5	0–5
CEA (ng/ml) [a]	4.4 ± 3.0	0-3.5
Cyfra211 (ng/ml) [a]	15.1 ± 3.8	0-16.3
SCCAg (ng/ml) [a]	1.6 ± 1.8	0-2.7
ProGRP (pg/ml) [a]	126.7 ± 336.8	0–50

a, *x*±*s*; b, number of cases (%); c, *M (Q1,Q3)*; **P*<0.05; NA, not available; BMI, body mass index; RA, room air; FVC, forced vital capacity; DLCO, diffusion capacity for carbon monoxide of lung

hyperlipaemia (4 patients), other malignancies (4 patients), or cerebral infarction (2 patients). Four patients had other malignancies, including gastric cancer, esophageal cancer, hypopharyngeal cancer, and colon cancer, 1 of whom was diagnosed with gastric cancer 5 years after surgery for lung cancer, and the other 3 were diagnosed with lung cancer after diagnosis of other malignancies.

Characteristics of patients with IPF-LC in the survival group vs. the non-survival group

As of June 30, 2024, 12 patients were lost to follow-up, whereas 12 patients survived and visited the outpatient department regularly. Eight patients died. Six patients developed AE-IPF, 4 of whom were diagnosed within 90 days after the operation.

Twelve patients were lost to follow-up on day 70, 90, 166, 238, 515, 233, 736, 175, 171, 125, 230, and 679 after surgery. Among these lost-to-follow-up patients, only one patient was lung cancer-free at the last follow-up (125 days after surgery). However, the patient's general condition was poor, requiring bed rest and long-term oxygen therapy. The remaining patients with IPF were in stable condition and had no signs of lung cancer progression at the last follow-up.

Among the 8 deceased patients, 5 patients passed away due to AE-IPF, and 2 patients died from surgical complication (thoracic infection and mediastinal emphysema respectively), one died from lung cancer progression. Among the 3 patients who died within 90 days after surgery, one patient died on the 23rd day after surgery. This patient developed mediastinal emphysema, subcutaneous emphysema, and pneumothorax two weeks after the operation, followed by AE-IPF. The patient's condition deteriorated even with mechanical ventilation, and the patient died. One patient died on the 57th day after the operation. This patient developed pneumothorax after surgery and underwent surgical repair. However, the patient suffered from thoracic infection, tracheoesophageal fistula and AE-IPF, ultimately leading to death. One patient died on the 78th day after the operation. He suffered from an upper respiratory tract infection during postoperative chemotherapy, followed by AE-IPF, respiratory failure and death.

Among the 8 patients in the deceased group, 5 received chemotherapy: 3 received adjuvant chemotherapy and 2 received neoadjuvant chemotherapy. Of these 5 patients, 1 underwent concurrent radiotherapy and 1 received chemotherapy combined with immunotherapy. Among the 24 patients in the survival group, 8 received chemotherapy: 6 received adjuvant chemotherapy and 2 received neoadjuvant chemotherapy. Additionally, 1 patient received concurrent radiotherapy, 1 received simple radiotherapy, and 1 received targeted therapy alone. Among the 8 patients in the death group, 1 received antifibrotic treatment, while among the 24 patients in the survival group, 6 received antifibrotic treatment. Among the 12 patients who are still alive at present, 2 patients have experienced progression of lung cancer. The survival durations of the survival group and the non-survival group were 947 ± 1108 days and 507 ± 1051 days, respectively. Differences in characteristics between the survival and non-survival groups are described in Table 2. The serum Cyfra211 level in the non-survival group was higher than that in the survival group: 3.3 (2.8, 3.7) vs. 4.6 (3.7, 7.4), $p = 0.02$. The lung cancer stage in the survival group is earlier than that in non-survival group: Stage I: 83.3% vs. 14.3%; Stage II: 8.3% vs. 28.6%; Stage III: 8.3% vs. 42.9%; and Stage IV: 0 vs. 14.3%.

Discussion

Most of the IPF patients who underwent surgery for resectable LC included in this study were elderly male smokers. Most of whom (26 patients) were diagnosed

Table 2 Clinical characteristics of survival group and death group

Parameter	Survival group (*n* = 12)	Death group (*n* = 8)	t/Z/χ^2-value	*P*-value
Age (year) [a]	65.3 ± 9.1	68.0 ± 6.1	-0.72	0.48
BMI (kg/m^2) [a]	25.2 ± 2.7	23.4 ± 3.1	1.45	0.17
Gender [b]			-	1.00
Male	11 (91.7)	8 (100.0)		
Female	1 (8.3)	0 (0.0)		
Pathological classification [b]			4.58	0.08
Adenocarcinoma	10 (83.3)	3 (37.5)		
Squamous cell carcinoma	2 (16.7)	4 (50.0)		
Other types	0 (0.0)	1 (12.0)		
History of smoking [b]	9 (75.9)	8 (100.0)	-	0.24
Smoking Index [c]	600 (112.5, 787.5)	850 (600, 1150)	-1.60	0.11
Complicated with emphysema [b]	7 (58.3)	7 (87.5)	-	0.33
SpO2@RA (%) [a]	97.4 ± 1.7	95.3 ± 1.6	2.89	0.10
NSE (ng/ml) [a]	16.0 ± 2.8	15.9 ± 2.6	0.07	0.95
CEA (ng/ml) [c]	3.5 (2.7, 5.7)	3.3 (2.9, 10.8)	-0.50	0.62
Cyfra211 (ng/ml) [c]	3.3 (2.8, 3.7)	4.6 (3.7, 7.4)	-2.31	0.02*
SCCAg (ng/ml) [c]	1.2 (0.8, 1.8)	1.3 (1.0, 2.3)	-1.03	0.31
ProGRP (pg/ml) [a]	55.1 ± 17.2	47.6 ± 24.6	0.78	0.45
Pulmonary function before operation [a]				
FVC / Predicted Value (%)	87.9 (80.5, 98.5)	92.4 (81.3, 105.7)	-0.319	0.75
DLCO / Predicted Value (%)	64.7 (61.1, 68.3)	56 (46, 79)	-0.472	0.64
Staging of lung cancer [b]			8.81	<0.01*
Stage I	10 (83.3)	1 (14.3)		
Stage II	1 (8.3)	2 (28.6)		
Stage III	1 (8.3)	3 (42.9)		
Stage IV	0 (0.0)	1 (14.3)		
Surgical modality [b]				
			-	1.00
VATS	10 (90.9)	8 (100.0)		
VATS - Thoracotomy	1 (9.1)	0 (0.0)		
			-	0.64
Pulmonary lobectomy	9 (75.0)	5 (62.5)		
Wedge resection of pulmonary segment	3 (25.0)	3 (37.5)		
Antifibrotic therapy [b]	6 (25.0)	1 (12.5)	-	0.65

a, *x*±*s*; b, number of cases (%); c, *M (Q1,Q3)*; *, *P*<0.05; BMI, body mass index; RA, room air; VATS, video-assisted thoracic surgery; FVC, forced vital capacity; DLCO, diffusion capacity for carbon monoxide of lung

with early-stage non-small cell lung cancer (stage I or II). Sixteen patients were diagnosed with adenocarcinoma, and 11 patients were diagnosed with squamous cell carcinoma. Comorbidities were common, with emphysema being the most prevalent. IPF was simultaneously diagnosed with LC in 75% of all enrolled patients. The overall mortality rate of this group of patients was 25%. AE-IPF was the main cause of death and 6.3% of patients died from surgery-related complications. The 90-day postoperative mortality rate was 9.4%, which was higher than the overall 90-day postoperative mortality rate of lung cancer patients in our center (about 0.2–0.4%). The proportion of IPF-LC patients who developed AE-IPF after surgery was 15.6%, which was slightly higher than the overall deterioration rate of all the IPF patients we followed up (about 10–15%).

IPF and LC share several common susceptibility factors, such as male, advanced age and smoking history. They also have partially identical pathogenic mechanisms, including epithelial–mesenchymal transition (EMT) and similar genetic susceptibility factors [6, 10]. As a consequence, the incidence of lung cancer among IPF patients is relatively high, ranging from 3 to 22%. The risk of developing LC in IPF patients is five times higher than that in non-IPF patients [2]. IPF patients with concurrent emphysema are more prone to developing lung cancer (OR value is 2.69, 95% CI is 1.78 to 4.05) [12]. A diagnosis of pulmonary fibrosis significantly worsens the prognosis of lung cancer. Additionally, researchers have reported that nintedanib and pirfenidone may lower the risk of LC in IPF patients. Therefore, IPF patients are recommended to receive antifibrotic therapy if they have the financial capability and can tolerate potential adverse effects [13].

In this study, only 8 cases/25% of the patients were diagnosed with LC during the follow-up for IPF. The other patients were diagnosed with both IPF and lung cancer simultaneously, highlighting the need for optimized screening methods for the early diagnosis of IPF. Given the insidious onset and nonspecific clinical manifestations of early-stage or mild-to-moderate IPF, these patients are often missed or misdiagnosed as

common respiratory diseases [14]. Thus, for clinicians, it is necessary to intensify the education and propaganda for patients with respiratory diseases, so as to facilitate their early medical consultation. Additionally, respiratory physicians not specializing in the treatment of ILD need to improve their ability to identify IPF at an early stage. Clinicians should also consider the possibility of ILD in elderly male smokers who present with cough, post-activity dyspnea, crackles on lung auscultation, bilateral subpleural lesions on chest computed tomography and restrictive ventilation dysfunction in pulmonary function. This requires clinicians to arrange high-resolution computed tomography as promptly as possible and, if necessary, refer patients to centers specializing in the treatment of ILD to increase the likelihood of early diagnosis and standardized management of IPF [15].

Postoperative complications and mortality rates are higher in IPF-LC patients than in LC patients without IPF. AE-IPF has the greatest influence on the prognosis of IPF-LC patients. Kushibe et al. reported that the incidences of acute lung injury/acute respiratory distress syndrome (ALI/ARDS) after surgery were 27.3% and 1.3% in IPF-LC patients and LC patients without IPF, respectively ($p < 0.0001$) [16]. However, since the introduction of treatment with antifibrotic drugs, several studies in Japan have revealed that pirfenidone can lower the incidence of AE-IPF after lung cancer resection in IPC-LC patients (7.1 – 32.1% in the treatment group vs. 0-8.3% in the control group). The mortality rate after the occurrence of AE-IPF in the treatment group also decreased (0–23.1% in the treatment group vs. 0–3.1% in the control group) [7]. In this cohort, only a small percentage (15.6%) of patients received pirfenidone treatment before surgery, which may explain the relatively high 90-day postoperative mortality rate in the LC-IPF patients in this study. Sakairi et al. conducted a randomized controlled phase III clinical trial to further validate whether pirfenidone can reduce the incidence of AE-IPF after surgical removal of lung cancer in patients with IPF and NSCLC. Additionally, partial lung resection, low-tidal-volume mechanical ventilation and low-concentration oxygen therapy during operation can potentially reduce the incidence of AE-IPF [17].

The stage of lung cancer is a crucial factor influencing the prognosis of surgically treated IPF-LC patients. In our research, IPF-LC patients in the survival group were diagnosed with an earlier stage of lung cancer, highlighting the importance of early diagnosis. For IPF patients, it is advisable to undergo at least one chest CT examination per year. In the event that small pulmonary nodules are detected, close follow-up and even PET-CT screening are necessary [18]. Surgical treatment remains important for improving the prognosis of IPF-LC patients. In our study, among the IPF-LC patients with complete follow-up data, only 5 presented with progression or recurrence of lung cancer. Therefore, IPF-LC patients without absolute surgical contraindications who are suitable for surgical resection are recommended to undergo surgery as early as possible under close surveillance.

The serum Cyfra211 level of IPF-LC patients in the non-survival group was higher than that in the survival group. Cyfra211 is both a known serum biomarker related to the prognosis of NSCLC and a serum marker related to the progression of IPF. Previous studies revealed that a high serum Cyfra211 level was correlated with a poor prognosis in patients with NSCLC regardless of the planned treatment [19]. On the other hand, the baseline serum concentration of Cyfra211 could predict the risk of 1-year IPF progression and overall mortality [20]. However, multivariate research needs to be conducted in the future to further determine the correlation of serum Cyfra211 levels with prognosis. Moreover, given the relationship between serum Cyfra211 levels and squamous cell carcinoma, the influence of pathological types also requires consideration. Since serum Cyfra211 test is simple, feasible and inexpensive, clinicians might order serum Cyfra211 test during initial and follow-up examinations.

Among the 8 patients who died during the study period, 3 presented with progression or recurrence of lung cancer. Five patients experienced AE-IPF before death, 3 of whom might have triggered by COVID-19 infection. Our previous study revealed that IPF is the type of ILD with the poorest prognosis after COVID-19 infection [21]. Research conducted in Italy revealed that the mortality rate of IPF patients increased after COVID-19 infection [22]. Therefore, in the post-COVID-19 pandemic era, clinicians should aim to prevent COVID-19 infection in IPF patients, especially IPF-LC patients. Patients who present with an upper respiratory tract infection at the follow-up visit should be screened for SARS-CoV-2. If the presence of COVID-19 infection is confirmed, clinicians should prescribe potent anti-COVID-19 medications as soon as possible. Timely removal of other reversible risk factors that may induce acute exacerbation of IPF, such as fatigue, gastroesophageal reflux disease, and bacterial or fungal infections of the respiratory system, may contribute to the prevention of AE-IPF and unfavorable clinical outcomes [23]. However, this study is limited by its single-center design and small sample size. The above conclusions can only reflect the trend of our center and need to be confirmed by larger-scale, multi-center cohort studies.

The main limitations of this study are as follows: Firstly, it is a single-center observational study, which may limit generalizability. Secondly, the sample size of this study is relatively small, which affects statistical power. Thirdly, only small portion of our enrolled

patients were prescribed with anti-fibrotic medications. Finally, approximately one-third of the patients were lost to follow-up, which might affect the accuracy of the conclusion.

This study aims to highlight the current clinical practice, where attention is predominantly focused on lung cancer when IPF and LC are diagnosed concurrently and the LC is resectable. We propose that following the diagnosis of IPF, if conditions permit, patients should initiate anti-fibrotic drug treatment as early as possible and receive regular follow-up and medical guidance from ILD specialists. Simultaneously, these patients should continue to receive appropriate treatment for LC from thoracic oncologists. The integration of these two treatment approaches can contribute to improved patient outcomes, prolonged survival, and enhanced quality of life.

Conclusions

Most of our IPF-LC patients were elderly males with a history of smoking and 78% of them have at least one comorbidity. 75% of the patients were diagnosed with IPF and LC simultaneously and only 22% received pirfenidone or nintedanib treatment. Acute exacerbation of IPF was the main cause of death. Similar to the LC patients, higher serum Cyfra211 levels and more advanced lung cancer stages suggested a poor prognosis for patients with IPF-LC. Clinicians still need to enhance their capabilities in the early diagnosis and standardized treatment of IPF and prevent its acute exacerbation.

Abbreviations

IPF	Idiopathic pulmonary fibrosis
LC	Lung cancer
IPF-LC	Idiopathic pulmonary fibrosis combined with lung cancer
ILD	Interstitial lung disease
ALI	Acute lung injury
ARDS	Acute respiratory distress syndrome
AE-IPF	Acute exacerbation of idiopathic pulmonary fibrosis
CT	Computed tomography
PET-CT	Positron emission tomography-computed tomography
FVC	Forced vital capacity
FEV1	Forced expiratory volume in one second
NSCLC	Non-small cell lung cancer
SCLC	Small cell lung cancer
SCC	Squamous cell carcinoma
EMT	Epithelial–mesenchymal transition
BMI	Body mass index
RA	Room air
VATS	Video-assisted thoracic surgery
DLCO	Diffusion capacity for carbon monoxide of lung
GGO	Ground glass opacity

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Author contributions

H.H took responsibility for the content of the manuscript, including the data and analysis. H. H. and M. W. conceived and designed the study. R. C., J. L., K. X., C. S., M. W. and Z. L. performed the study. Q. C., Y. S. and H. H. analysed the data and wrote the paper. All authors read and approved the final manuscript.

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Data availability

All data generated or analyzed during this study are included in this published article. Besides, any additional data/files may be obtained from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The research received approval by the institutional ethical review board of Peking Union Medical College Hospital (approval number: K4327) in accordance with the Declaration of Helsinki. Our research utilized de-identified healthcare data. The requirement for written informed consent from each participant was waived because the study fulfilled the minimal risk waiver criteria established by the PUMCH Institutional Review Board.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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