Outcomes after lung transplantation among Chinese patients with connective tissue disease-associated interstitial lung disease and pulmonary hypertension: a retrospective cohort study

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Abstract

Objective

The present study aimed to compare the post-lung transplant survival and complications of connective tissue disease (CTD)-related interstitial lung disease (ILD) and/or pulmonary arterial hypertension with idiopathic pulmonary fibrosis (IPF).

Methods

The clinical data of patients with CTD-ILD or IPF who received lung transplantation between 2015 and 2020 were retrospectively reviewed. Cumulative survival rates after transplantation were estimated using the Kaplan-Meier method.

Results

The study included 31 patients with confirmed CTD-ILD and 98 with IPF. Patients with CTD-ILD were significantly younger (53.2 ± 13.7 vs. 62.3 ± 7.2 years, p=0.001) and more likely female (61.3% vs. 7.1%, p<0.001) than patients with IPF. No significant difference was noticed in the 1-year and 5-year survival rates between CTD-ILD and IPF patients (1-year, 73.2% vs 71.4%, p=0.76; 5-year, 69.1% vs. 39.5%, p=0.21). The incidence of primary graft dysfunction was significantly higher in CTD-ILD patients (90.3% vs. 70.4%, p=0.03), while there was no significant difference in primary graft dysfunction-related mortality (6.5% vs. 6.1%, p=0.95) between the two groups.

Conclusion

There was no significant difference in post-lung transplant survival and complications between CTD-ILD and IPF.

Key words

connective tissue disease, interstitial lung disease, lung transplantation, idiopathic pulmonary fibrosis, pulmonary arterial hypertension, survival

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Introduction

Interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH) are common manifestations of connective tissue disease (CTD). Respiratory failure secondary to ILD and/or PAH is a major cause of morbidity and mortality (1-3). Lung transplantation is the only effective treatment for end-stage CTD-ILD and severe respiratory failure. However, there is concern about post-lung transplant survival in patients with CTD due to the extra risks of systemic autoimmune disease and extrapulmonary involvement (4-6). Many transplantation centers do not offer lung transplantation to CTD patients for reasons of extrapulmonary involvement, such as severe renal insufficiency.

There is scarce data on post-lung transplant survival in CTD-ILD. Merely 1% of lung transplantations worldwide were performed on patients with CTD-ILD between 1995 and 2016, according to a report from the International Society for Heart and Lung Transplantation (ISHLT) registry (7). The survival and outcomes of these patients after lung transplantation have been reported differently (8-10). The prevalence of CTD in China ranges from 11.6% to 46.4%, varying by locality, study protocol, and age of the people surveyed (11, 12). Despite a previous attempt to conduct lung transplantation in this population (13, 14), few reports have focused on outcomes of lung transplantation in CTD-ILD patients. Moreover, no data have been reported about the outcome of lung transplantation in Chinese patients with CTD-PAH, let alone heart-lung transplantation in CTD patients with severe PAH and resultant right heart failure.

The primary objective of our study was to compare the post-lung transplant survival in CTD-ILD with IPF. The secondary aim was to investigate the overall effects, such as lung function and exercise capacity, of lung transplantation in CTD-ILD compared to IPF.

Materials and methods

Design and study population

This retrospective cohort study was conducted at a secondary lung transplantation center in China. We evaluated data from all patients who underwent lung or heart-lung transplantation between January 2015 and December 2020 at the First Affiliated Hospital of Guangzhou Medical University, which is affiliated to the state Key Lab and Institute of Respiratory Disease. The inclusion criteria were as follows: (1) age ≥18 years, (2) lung or heart-lung transplants, with lung transplants including single- or double-lung transplants, and (3) the primary indication for lung or heart-lung transplantation was ILD (15). The exclusion criteria were as follows: (1) incomplete medical history data, (2) the primary indication for lung or heart-lung transplantation was an ILD other than IPF or CTD-ILD (patients with pneumocystis, sarcoidosis, or drug-associated ILD were excluded), and (3) survival time ≤1 day post-transplantation. The study was designed by the First Affiliated Hospital of Guangzhou Medical University and approved by the Ethics Committee (approval number: 2021K-31). The distribution and donation of every organ were processed within the judicial system for all study patients, as voluntary citizen-based deceased organ donation systems have been adopted since January 2015 in China (16). Written informed consent was obtained from living donors or family members of brain-dead donors.

Diagnosis of PAH

PAH was defined as a mean pulmonary arterial pressure ≥25 mmHg at rest as assessed by right heart catheterisation. Pre-capillary PAH was defined by a pulmonary artery wedge pressure ≤15 mmHg and a pulmonary vascular resistance >3 Wood units in the absence of other causes of PAH (17). Only part of the patients was examined by right heart catheterisation because some of them may not tolerate the procedure.

Immunosuppressive scheme

Patients older than 70 years or those who had pulmonary infection within the last 2 weeks before the transplantation did not receive the induction therapy. There were 27 (87.1%) patients in the CTD group and 85 (86.73%) in the IPF group who received induction therapy and routine triple immunosuppression

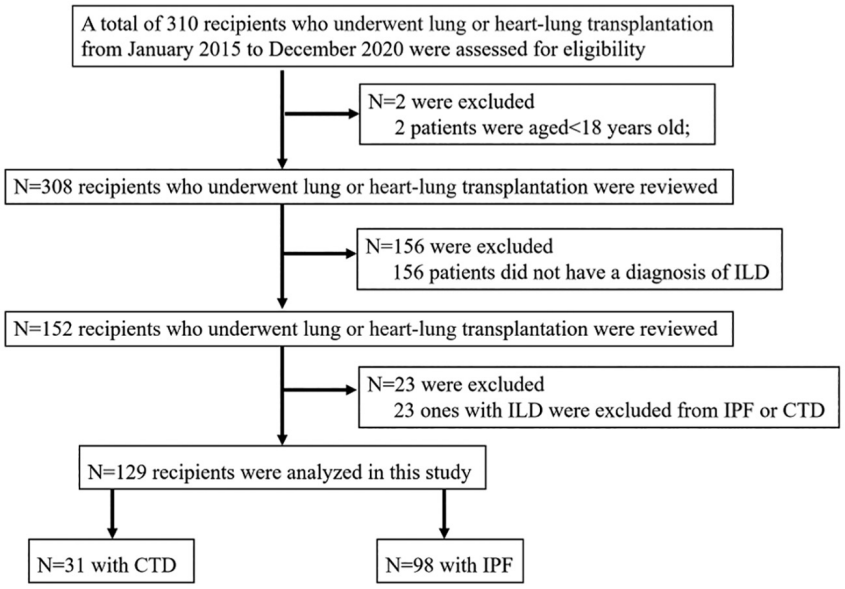

Fig. 1. A flowchart of patient inclusion.

maintenance therapy. Induction was performed with basiliximab 20 mg IV on days 0 and 4. Patients with bronchiectasis or at a lower risk of rejection did not receive either basiliximab or rabbit antithymocyte globulin (r-ATG) induction, and those at highest risk received r-ATG induction instead of basiliximab. Tacrolimus was administered at 0.075 mg/kg twice daily to achieve initial levels of 13–17 ng/mL for the first month, 12–16 ng/mL for the second month, and 11–15 ng/mL for the third month. Methylprednisolone 500 mg was administered at induction, and oral/IV steroids were titrated to 15 mg daily for 1 week and then maintained at 15 mg thereafter. T cell-depleting antibodies were routinely prescribed for rejection prophylaxis or treatment.

Data collection

All CTD diagnoses were confirmed based on existing criteria (18), and relevant clinical data and laboratory testing were reviewed and verified by rheumatologists. Guidelines similar to those of well-known ILD were used as the criteria for selecting lung transplant recipients with CTD. The following data were obtained: age at transplantation; date of transplantation; date of birth; weight and height at transplant; chest high-resolution computed tomography (CT) before and after lung transplantation; maximum panel reactive antibody status; recipient and donor cytomegalovirus serology status; pulmonary function tests; right heart catheterisation measurements; induction therapy (interleukin-2 receptor antibody or T cell-depleting antibody); immunosuppression prescribed at 0, 3, and 6 months and at each year post-transplant; whether or not the patient died (until December 2020); and the date of death. In addition, our transplant team reviewed the histological patterns of lung pathology specimens from each patient's explant. All patients were followed up continuously until December 2020 or death.

Clinical outcomes

The primary outcome was cumulative survival (at 30 days, 6 months, 1 year, 3 years, and ≥5 years) for each patient after lung transplantation. The secondary outcomes included the incidence and severity of primary graft dysfunction (PGD), intensive care unit (ICU) days, post-transplant hospital days, pulmonary function, and exercise capacity. PGD was assessed during the first 72 h post-transplantation, and the severity of PGD was graded based on the ratio of arterial oxygen pressure to inspired oxygen concentration (PaO_2/FiO_2) and the presence of infiltration on chest radiography according to the ISHLT criteria (19). Pulmonary function and exercise capacity were assessed by best performance on pulmonary function and the 6-min walk distance tests at 1 year post-transplant. CTD flares were determined by both our transplant team and rheumatologists based on the patient's clinical history, assessment, and response to treatment. CTD flares were defined as a new or progressive condition that was consistent with the underlying CTD (20).

Statistical analysis

Statistical analysis was performed using SPSS software (v. 19.0; IBM Corp., Armonk, NY, USA), and data were plotted using GraphPad Prism 5 software (GraphPad Software, Inc., San Diego, CA, USA). Normally distributed continuous data are expressed as mean ± standard deviation, and categorical variables are described using counts and percentages. The pre-transplant and post-transplant characteristics of the recipients with CTD-ILD were compared to those of recipients with IPF using Fisher's exact test for categorical variables and the Mann-Whitney U-test or Student's t-test for continuous variables. The log-rank test was used to compare the Kaplan-Meier survival curves. Risk factors associated with survival were analysed using the multivariate analysis. Hazard ratios were expressed as relative risks with 95% confidence intervals. Statistical significance was set at $p<0.05$.

Results

Baseline demographic and clinical characteristics

The patient inclusion and exclusion process are shown in Figure 1. The final analysis included 129 patients, comprising 31 (24%) patients with CTD-ILD and 98 (76%) patients with IPF. A patient with systemic lupus erythematosus (SLE) in the CTD group who underwent combined heart-lung transplantation was not excluded from this study because the primary indication was SLE-associated PAH and severe right heart failure.

Table I shows the baseline characteristics and clinical variables of the patients. Patients with CTD-ILD were significantly younger (53.2±13.7 *vs.* 62.3±7.2 years, $p=0.001$) and more likely female (61.3% *vs.* 7.1%, $p<0.001$) than patients

Table I. Baseline demographic and clinical characteristics of the study patients.

	CTD-ILD (n=31)	IPF (n=98)	*p*-value
Female, n (%)	19 (61.3)	7 (7.1)	<0.001
Age, years	53.2 ± 13.7	62.3 ± 7.2	0.001
Body mass index, kg/m^2	21.62 ± 3.40	20.83 ± 2.72	0.29
Current smoker, n (%)	2 (6.5)	7 (7.1)	1
Pulmonary function test			
Patients able to perform the test, n (%)	13 (41.9)	52 (53.1)	0.55
FVC, %	33.4 ± 4.9	37.7 ± 9.8	0.14
FEV_1, %	45.3 ± 8.6	48.1 ± 8.2	0.27
FEV_1/FVC	74.5 ± 11.5	79.3 ± 19.7	0.43
Patients able to perform DLCO, n (%)	7 (22.6)	37 (37.8)	0.49
DLCO%	18.8 ± 8.0	27.7 ± 7.6	0.016
Serum creatinine, umol/L	67.7 ± 12.9	71.2 ± 11.0	0.42
6-minute walk distance test			
Patients able to perform the test, n (%)	13 (41.9)	68 (69.4)	0.008
Walk distance, m	150.1 ± 70.7	132.1 ± 42.7	0.37
Echocardiogram			
Left ventricular ejection fraction, %	70.9 ± 6.1	71.7 ± 5.9	0.53
Pulmonary artery systolic pressure >40 mmHg, n (%)	17 (54.8)	31 (31.6)	0.02
Pulmonary artery systolic pressure, mmHg	50.4 ± 29.1	47.1 ± 17.3	0.57
Right ventricular diameter, mm	22.14 ± 4.12	21.71 ± 5.49	0.66
Right atrial diameter, mm	33.8 ± 4.8	33.5 ± 7.3	0.78
Right heart catheterisation			
Patients who had catheterisation, n (%)	17 (54.8)	63 (64.3)	0.25
Pulmonary arterial hypertension confirmed by catheterisation, n (%)	16 (94.1)	34 (54.0)	0.002
Pulmonary arterial pressure, mmHg	40.8 ± 20.2	27.7 ± 11.9	0.02
Right ventricular systolic pressure, mmHg	19.9 ± 12.7	17.2 ± 7.4	0.27
Pulmonary capillary wedge pressure, mmHg	7.1 ± 4.7	9.8 ± 5.1	0.05
Cardiac index, L/min/m^2	2.99 ± 0.95	2.82 ± 0.71	0.49
Respiratory support			
Nasal oxygen, n (%)	13 (41.9)	37 (37.8)	0.78
Non-invasive mechanical ventilation/nasal intermittent positive pressure ventilation, n (%)	8 (25.8)	36 (36.8)	0.42
Invasive mechanical ventilation, n (%)	7 (22.6)	14 (14.3)	0.36
Extracorporeal membrane oxygenation, n (%)	3 (9.7)	11 (11.2)	0.83

CTD-ILD: interstitial lung disease related to connective tissue diseases; IPF: idiopathic pulmonary fibrosis; DLCO: diffusing capacity of lung for carbon monoxide; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity.

Table II. Symptoms, signs, and autoantibodies of the underlying connective tissue disease.

Connective tissue disease	Symptoms and signs	Autoantibodies
Systemic lupus erythematosus (9)	Cutaneous lupus (8), renal damage (6)	Anti-nuclear (7), anti-dsDNA (6), anti-Smith (3)
Mixed connective tissue disease (5)	Renal damage (5), cutaneous lupus (2), joint deformity (1)	Anti-U1 RNP (5), anti-nuclear (4)
Systemic sclerosis (5)	Scleroderma and muscle rigidity (5), gastroesophageal reflux (1)	Anti-topoisomerase 1 (4), anti-fibrillarin (3)
Polymyositis/dermatomyositis (5)	Raynaud's phenomenon and mechanic's hands (5)	Anti-(t)RNA synthetases (5), anti-Jo-1 (4), anti-MDA5 (1)
Rheumatoid arthritis (4)	Joint deformity (4)	Rheumatoid factor (4), cyclic citrullinated peptide (4)
Sjögren syndrome (3)	Dry eyes, photophobia, and joint deformity (3)	Anti-nuclear (3), anti-SS-B/La (3)

Numbers in brackets denote the affected patients.

with IPF. The multivariate showed that age was independently associated with lower odds of survival time (OR: 11.4; 95% CI: 3.5–19.3; p=0.005).

The symptoms, signs, and autoantibodies of the underlying CTD are shown in Table II. The types of ILD included nonspecific interstitial pneumonia in 15 patients, usual interstitial pneumonia in 12, organising pneumonia in 2, and fibrotic nonspecific interstitial pneumonia in 2.

Previous medications

Immunosuppressive therapy was used to manage the underlying CTD in the 31 ILD patients, with 17 patients receiving glucocorticoid monotherapy and 14 patients receiving glucocorticoids and other immunosuppressive medications, such as cyclophosphamide, azathioprine, and tacrolimus. All immunosuppressants were discontinued at least 1 month before the transplantation.

Anti-fibrotic medications were also used to treat CTD-ILD, including pirfenidone (400–600 mg tid) in 18 patients and nintedanib (150 mg bid) in 4 patients. The PAH medications included 1) endothelin receptor antagonists, such as bosentan and macitentan; 2) compounds targeting the prostacyclin pathway, such as subcutaneous treprostinil, and selective oral prostacyclin, such as selexipag; 3) phosphodiesterase-5 inhibitors, such as tadalafil and sildenafil; and 4) soluble guanylate cyclase stimulators, such as riociguat.

Type of transplantation

Table III shows clinical variables including the types of transplantation in both groups. Unilateral and bilateral lung transplants were performed in 38.7% and 58.1% of CTD-ILD patients, respectively, and similar proportions (41.8% unilateral and 58.2% bilateral) were found in IPF patients. Notably, one patient with SLE underwent combined heart-lung transplantation for the primary indication of progressive right heart failure and respiratory failure, which were resulted from SLE-PAH and SLE-ILD. Before transplantation, thoracic CT found diffuse pulmonary fibrosis with honeycombing and interstitial thickening, suggestive of ILD and PAH (Supplementary Fig. S1). In addition, the pulmonary artery trunk was significantly thickened, indicating severe PAH.

In terms of induction therapy, one-third of the patients in both groups received basiliximab prior to transplantation, and >50% of the recipients in both groups received r-ATG induction therapy as rejection prophylaxis during the early days post-transplantation (Table III).

Pathological findings suggestive of collagen vascular disease involvement of the lung, including lymphoid follicles with usual interstitial pneumonia or fibrosing nonspecific interstitial pneumonia, were found in 20 of 31 patients with CTD-ILD, while usual interstitial pneumonia was identified in all patients with IPF. The pathological characteristics of the lung tissue and pulmonary vasculature of the patient who received combined heart-lung transplantation are shown in Supplementary Figure S2.

Table III. Peri-transplant clinical characteristics.

	CTD-ILD (n=31)	IPF (n=98)	*p*-value
Pre-transplant CMV-IgG match			
Donor+/Recipient-, n (%)	2 (6.5%)	7 (7.2%)	0.90
Recipient+, n (%)	25 (80.6%)	80 (81.6%)	0.97
ECMO assisted, n (%)	14 (45.2%)	48 (48.9%)	0.83
Type of transplantation			0.20
Single, n (%)	12 (38.7%)	41 (41.8%)	
Bilateral, n (%)	18 (58.1%)	57 (58.2%)	
Heart-lung combination, n (%)	1 (3.2%)	0 (0.0%)	
Induction therapy			
Basiliximab, n (%)	7 (22.6%)	36 (36.7%)	0.29
r-ATG, n (%)	20 (64.5%)	53 (54.1%)	0.60

CMV: cytomegalovirus; ECMO: extracorporeal membrane oxygenation; r-ATG: rabbit antithymocyte globulin; CTD-ILD: interstitial lung disease related to connective tissue diseases; IPF: idiopathic pulmonary fibrosis.

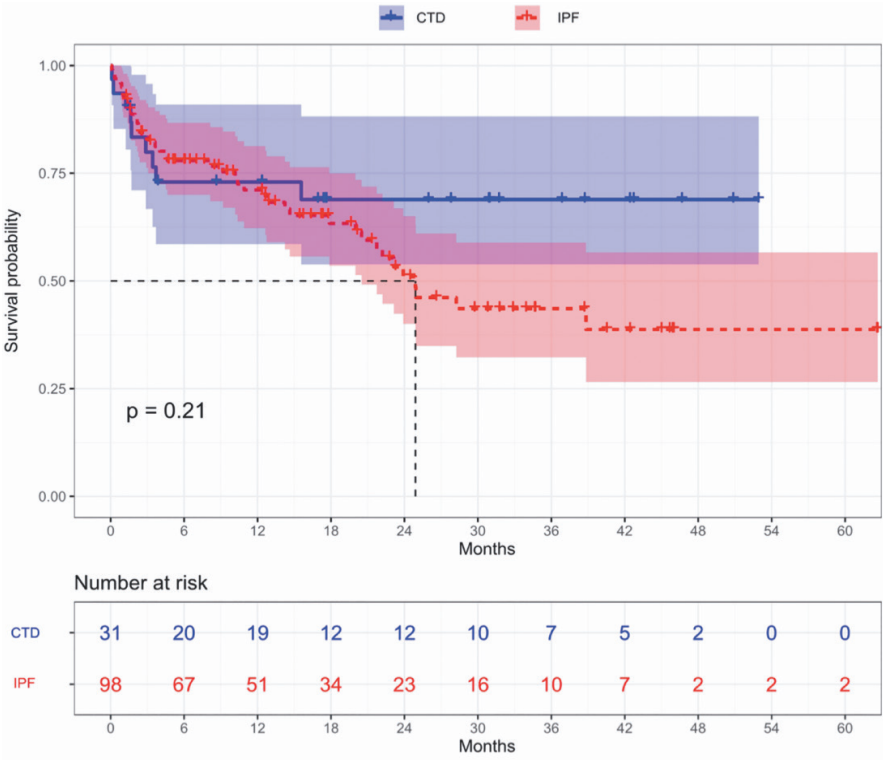

Fig. 2. Kaplan-Meier survival curves comparing the survival rates between connective tissue disease-related interstitial lung disease (CTD-ILD) and idiopathic pulmonary fibrosis (IPF) (p=0.21).

Overall outcomes of lung transplantation

The median follow-up durations for CTD-ILD and IPF patients were 31.1 and 27.2 months, respectively (Fig. 2). There was no significant survival difference between CTD and IPF patients (p=0.21), although the 1-year, 3-year, and about 5-year cumulative survival rates of patients with CTD-ILD were all slightly higher than those of IPF patients (Fig. 2, Table IV). The longest survival time was 4.5 years. The numbers of death in patients with CTD-ILD at post-transplant 1 year, 3 years, and 5 years were 8 (25.8%), 9 (29.03%), and 9 (29.03%), respectively. The numbers of death in the IPF patients at post-transplant 1 year, 3 years, and 5 years were 29 (29.6%), 41 (41.8%), and 42 (42.8%), respectively.

Significantly increased lung function was observed in both groups when compared to pre-transplantation. Percentage of predicted forced vital capacity (FVC%) increased 1.2-fold in the

IPF group and 1.34-fold in the CTD-ILD group, and percentage of predicted diffusing capacity of lungs for carbon monoxide (DLCO%) increased 1.57-fold in the IPF group and 1.87-fold in the CTD-ILD group. There were no significant differences in the levels of increase of FVC% and DLCO% between the two groups, with *p*-values of 0.08 and 0.083, respectively. Additionally, exercise capacity improved in both groups when compared to pre-transplantation, with 6MWT increasing 3.08-fold in the CTD-ILD group and 2.57-fold in the IPF group; there were no significant differences in the improvement of exercise capacity between the two groups at 1 year post-transplant (p=0.79).

Early post-transplant complications

Table IV presents the post-transplant complications in both groups. During the first month, PGD was significantly more common in the CTD-ILD patients than in the IPF patients (90.3% *vs*. 70.4%, p=0.03). However, there was no significant difference in the proportions of patients who died of PGD between the CTD-ILD group and the IPF group (6.5% *vs*. 6.1%, p=0.95). During the first 3 months post-transplant, the all-cause death rates were similar between the two groups, irrespective of whether the cause was infection-related or not. Moreover, there were no significant differences in postoperative ICU or hospitalisation days between the two groups. Two patients experienced CTD flares, one with polymyositis/dermatomyositis and the other with rheumatoid arthritis.

Table IV. Outcomes and complications after transplantation.

	CTD-ILD (n=31)	IPF (n=98)	*p*-value
Primary graft dysfunction (PGD), n (%)	28 (90.3)	69 (70.4)	0.03
PGD grade 0, n (%)	3 (9.7)	29 (29.6)	0.03
PGD grade 1, n (%)	4 (12.9)	25 (25.5)	0.06
PGD grade 2, n (%)	14 (45.2)	21 (21.4)	0.64
PGD grade 3, n (%)	10 (32.3)	23 (23.5)	0.79
Died of PGD, n (%)	2 (6.5)	6 (6.1)	0.95
PaO_2/FIO_2 ratio			
24-h PaO_2/FIO_2 ratio	208.4 ± 79.4	268.5 ± 109.8	0.16
48-h PaO_2/FIO_2 ratio	277.9 ± 99.0	269.9 ± 89.3	0.68
72-h PaO_2/FIO_2 ratio	267.5 ± 86.8	268.0 ± 85.6	0.98
Cause of death within 3 months post-transplant			
Infectious disease, n (%)	2 (6.5)	4 (4.1)	0.6
Non-infectious disease, n (%)	5 (16.1)	12 (12.2)	0.63
Post-transplant ICU days, median [IQR]	10 [6–29]	8 [6–27]	0.32
Post-transplant hospital days, median [IQR]	31 [19–51]	28 [17–59]	0.12
Lung function test at 1 year post-transplant			
FEV1 (%)	74.0 ± 19.2	81.0 ± 15.5	0.08
FVC (%)	74.1 ± 16.7	77.7 ± 16.6	0.38
FEV1/FVC (%)	82.9 ± 10.9	82.8 ± 8.7	0.96
DLCO%	57.0 ± 12.7	64.8 ± 14.2	0.12
6MWT at 1 year post-transplant, m	509.1 ± 76.4	462.9 ± 106.5	0.10
Cumulative survival rate			0.21
1 month	90.3	90.8	
6 months	73.2	86 (87.9)	
1 year	23 (74.2)	69 (70.4)	
3 years	22 (70.0)	57 (58.2)	
5 years	22 (70.0)	56 (57.1)	

DLCO%: percentage of predicted diffusing capacity of lungs for carbon monoxide; FEV1%: percentage of predicted forced expiratory volume in 1 s; FVC%: percentage of predicted forced vital capacity; PGD: primary graft dysfunction; 6MWT: 6-minute walk distance test; CTD-ILD: interstitial lung disease related to connective tissue diseases; IPF: idiopathic pulmonary fibrosis: IQR: interquartile range.

Discussion

Three important points are noted in our study. First, consistent with previous studies (21-23), our study found that SLE is the most common underlying disease in Chinese patients with CTD-PAH. On the contrary, systemic sclerosis (SSc) is the most common CTD in European countries (4, 6, 9, 24-26). Second, CTD-associated severe PAH was an important but overlooked indication for lung transplantation. Third, there was no significant difference in the 5-year cumulative survival rates after lung transplantation between CTD and IPF.

Previous studies have shown comparable post-lung transplant survival between CTD and IPF, with reported 5-year survival rates ranged from 42.4% to 55% in CTD and from 46.6% to 65.8% in IPF (10, 13, 14, 25-27). Similarly, our study found no significant difference in post-lung transplant 5-year survival between CTD and IPF, although it was slightly higher in CTD than in IPF (70% *vs*. 57.1%). On the contrary, a study by Prieto-Peña *et al*. found that the 5-year cumulative survival rates after lung transplantation was lower in CTD-ILD compared to IPF (42.4% *vs*. 65.8%), although not reaching statistical significance (p=0.075) (27). The discrepancy between the two studies may be attributable to the significantly younger ages of the CTD patients compared to the IPF patients in our study.

Notably, the survival curve of the CTD patients dropped more rapid in the early stage than that of the IPF patients, but maintained stable thereafter. On the contrary, the survival curve of the IPF patients dropped constantly in the first 2 years of follow-up. Despite the discrepancy in early-stage survival between CTD and IPF after lung transplantation, longer follow-up showed overall comparable survival between CTD and IPF and supported the use of lung transplantation in CTD patients.

Significant differences in age and sex were noted between patients with CTD and those with IPF in our study. CTD is more likely to occur in females and more often attacks multiple organs at an early age, including the pulmonary parenchyma and vasculature. Both the CTD group and the IPF group had decreased lung function at baseline, while only DLCO% was significantly lower in the CTD patients compared to the IPF patients. This may be associated with the significantly higher proportion of PAH in the CTD patients.

SLE accounted for a plurality of patients (29%) in our study, and CTD-PAH was confirmed in 88% (7/8) of patients with

SLE. Among these patients with SLE, a 23-year-old woman had severe PAH and right heart failure; thus, heart-lung transplantation was performed, as suggested by an American specialist. After the heart-lung transplantation, she experienced acute rejection in the early stage, although she survived after treatment with methylprednisolone and r-ATG. The patient has been enjoying a high quality of life with the 6-min walk distance test >550 m during the follow-up period. Similar results have been observed for CTD-PAH in SSc (23, 24). Bernstein *et al*. (28) performed a retrospective cohort study of CTD patients with PAH and IPF who underwent lung transplantation in the United States and demonstrated that SSc patients showed a slight increase in the 1-year mortality rate compared to non-SSc-related ILD patients, although the difference did not reach significance. Consistently, the mean pulmonary arterial pressure was significantly higher in the CTD patients than in the IPF patients in our study, while there was no significant survival difference between patients with CTD and IPF after lung transplantation.

In our CTD cohort, there were four patients with SSc. Oesophageal dysmotility and gastroesophageal reflux disease have been reported as common in SSc patients (29). However, only one patient in our study suffered from gastroesophageal reflux disease. The patient reported reflux symptoms early after lung transplantation; however, CT images showed no oesophageal dilatation, and no oesophageal dysfunction was observed on manometry. The symptoms resolved gradually but relapsed 6 months after lung transplantation. There was no suspicion of reflux-associated complications such as bronchiolitis obliterans syndrome. The other three patients with SSc did not report symptoms of oesophageal dysfunction, and no oesophageal dilatation was shown on CT images. They survived without complications after transplantation and had significant improvement in quality of life. Moreover, all four patients with SSc survived, with the longest survival time of 2 years 5 months. Nevertheless, long-term survival should be confirmed with more patients in China.

Limitations

First, the CTD-ILD patients were significantly younger than the IPF patients in our study, which may have biased the survival outcomes. Second, PAH was only diagnosed in part of the patients, thus the real prevalence of PAH in our study was unknown. This may also contribute to the bias in patient survival. Third, the small sample size and the single-centre design may compromise the representativeness of our study.

Conclusions

SLE was the most prevalent subtype of CTD-ILD and/or CTD-PAH requiring lung transplantation in China. The post-lung transplant survival in CTD-ILD was comparable to IPF. The incidence of complications, post-operative ICU stay, and hospital stay were also comparable between CTD and IPF. There was no significant difference in the improvement in exercise capacity and lung function between the two groups at 1 year post-transplant.

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