의학석사 학위논문

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위험 요인, 임상 특성에 대해

Airway complications after lung transplantation:
risk factors and clinical characteristics

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2022 년 2 월

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ABSTRACT

Background

Recently, lung transplantations have been performed increasingly in Korea, and the outcomes have also been improved over time. However, airway complications after lung transplantation are still associated with considerable morbidity and mortality. The aim of this study was to investigate the incidence, risk factors and clinical impacts of airway complications after lung transplantation.

Methods

The medical records of 154 patients who underwent lung transplantation between 2008 and 2021 were retrospectively reviewed. Patients were divided into two groups: airway complication group, in which patients experienced airway complications after transplantation; non-airway complication group, in which patients did not experience any airway complication during the follow-up period.

Results

The median follow-up period was 20 months. Mean age of patients was 51.3 years and 63.6% was male patients. Of the 154 patients, 31 (20.1%) patients experienced postoperative airway complications, where 123 (79.9%) patients did not. A total of 40 airway complications occurred in 31 patients, and the most common airway complication was stenosis (n = 29), followed by ischemia (n = 7), necrosis (n = 2), and malacia (n = 2). On multivariate Cox analysis, the higher BMI of recipient (Hazard ratio [HR], 1.116; 95% CI, 1.027-1.211; p = 0.009) was a significant

independent risk factor for airway complication with postoperative ECMO (HR, 4.566; 95% CI, 1.472-14.166; p = 0.009). Of the 31 patients who had airway complications, 22 (71.0%) were managed by bronchoscopic intervention, of which 13 (41.9%) underwent an average of 2.1 balloon dilatation, and 9 (29.0%) needed stent insertion after balloon dilatation. There was no significant difference in survival between airway complication group and non-airway complication group.

Conclusions

Our current study revealed a fifth of patients who received lung transplantation experienced airway complication during follow-up period. Patients with higher BMI and postoperative ECMO are a risk factor of airway complication, and close monitoring is warranted in these patients.

Keywords: Airway complication, lung transplantation, incidence, risk factor

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INTRODUCTION

Lung transplantation is a final therapeutic option for end-stage lung disease and has been proven to improve survival and quality of life.[1, 2] The number of lung transplantation has been increasing worldwide, with the most common indications for lung transplantation being interstitial lung disease (ILD), followed by chronic obstructive pulmonary disease (COPD), cystic fibrosis, and pulmonary hypertension,[3] and lung transplantation can also be considered in severe COVID-19 pneumonia.[4] Recently, lung transplantations have also been performed increasingly in Korea, and the outcomes are comparable to other published data.[5] Although the outcomes of lung transplantation have been improved over time, with some differences depending on underlying lung disease, the median survival is still only about 6-7 years.[3, 6]

After lung transplantation, complications such as primary graft dysfunction[7], acute rejection,[8] and chronic lung allograft dysfunction[9] may occur, which are associated with a poor prognosis. Medical complications including infection, renal failure, diabetes, cardiovascular complication, osteoporosis, and malignancy may also occur.[10, 11] In addition to these various complications, airway complication following lung transplantation is associated with considerable morbidity and mortality.[12]

There are several types of airway complications, including dehiscence, granulation, stenosis, tracheobronchomalacia, bronchial fistula and anastomotic infection[13], and the overall incidence of airway complications has been reported from about 2% to 30%.[13, 14] There have been several previous reports about the

incidence[15], risk factors[16], management, and long-term outcome of airway complications[17, 18]. However, results of previous studies are inconsistent, especially in risk factor. In addition, although there have been several studies about airway complication in worldwide[13, 18, 19], previous reports are scarce in Korea.[20, 21] Thus, we aimed to investigate the incidence, risk factors and clinical impacts of airway complications after lung transplantation.

MATERIALS and METHODS

Study population and design

For this single-center, retrospective study, we reviewed the data of 154 patients who underwent lung transplantation [140 bilateral lung transplantation, 12 heart-lung transplantation, and 2 liver-lung transplantation] at Asan Medical center, Seoul, Republic of Korea, between October 2008 and June 2021. Patients were divided into two groups: airway complication group, in which patients experienced airway complications after transplantation; non-airway complication group, in which patients did not experience any airway complication during the follow-up period.

Data about demographics and clinical characteristics were extracted from the medical records. Recipient-related variables included age, gender, body mass index(BMI), height, underlying disease leading to transplantation, smoking status, preoperative infectious episodes, use of corticosteroids and immunosuppressant, duration of mechanical ventilation and extracorporeal membrane oxygenation(ECMO) therapy, and length of intensive care unit(ICU) stay. Donor-related variables included age, gender, and height.

Donor to recipient size mismatching was defined as the case where the donor predicted total lung capacity (pTLC) were not between 75% and 125% of the recipient pTLC, based on the current International Society for Heart and Lung Transplantation(ISHLT) guideline.[22] pTLC was calculated by the European Coal and Steel Community (ECSC) prediction equations.[23] Preoperative steroid use was defined as equivalent dose of methylprednisolone ≥ 0.5mg/kg within a month prior to

transplantation.

The study protocol was approved by the Institutional Review Board at Asan Medical Center, Ulsan university College of Medicine (IRB No. 2021-1324).

Perioperative management and follow-up protocol

All patients received an induction immunosuppression therapy consisting of a high dose of intravenous methylprednisolone and basiliximab before surgery, and maintained standard triple immunosuppression therapy with tacrolimus, mycophenolate mofetil, and methylprednisolone. A target trough level of tacrolimus was 10–15 ng/mL for the first 6 months and 8–12 ng/mL thereafter. Mycophenolate mofetil was adjusted to a target trough level of 1–3 ng/mL.

Several prophylactic regimens were used for the prevention of infection. For the prevention of *Pneumocystitis jiroveci* infection, trimethoprim/sulfamethoxazole 80/400 mg was administered daily. To prevent cytomegalovirus(CMV) infection, 5 mg/kg of ganciclovir was administered intravenously every 24 hours regardless of the CMV serostatus of recipients and donors for 1–4 weeks after transplantation. After that, oral valganciclovir was used until 6 months after transplantation. For antifungal prophylaxis, voriconazole was administered at the target of trough level of 1.5–5.5 mg/dL for 6 months postoperatively. Postoperative antibiotics were routinely adjusted based on preoperative culture data obtained from the donor and the recipient bronchus.

Assessment and management of airway complications

Airway complications were evaluated with flexible bronchoscopy. Flexible bronchoscopy was not routinely performed and was performed when airway complications were suspected based on clinical symptoms, deterioration in lung function, and abnormal finding on chest radiograph or computed tomography(CT). Type of airway complications were classified into five categories: stenosis, ischemia, necrosis, dehiscence and malacia.[13] The treatment plan such as conservative treatment and bronchoscopic intervention was also determined at the time of diagnosis. Bronchoscopic intervention, including balloon dilatation and stent insertion, was performed with flexible or rigid bronchoscopy.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed as percentage. Student's t-test or the Mann-Whitney U test was performed to compare continuous data, and the Chi-square test (or Fisher's exact test) was performed to compare categorical data. Cox proportional hazard regression model was used to find risk factors of airway complications. Variables with P value < 0.2 in univariate analysis were included into the multivariate models. All two-tailed P values of < 0.05 was considered statistically significant. Survival curves were plotted by using the Kaplan-Meier method and compared by using the Gehan-Breslow-Wilcoxon test. The statistical analyses were performed using the SPSS statistics package version 20.0.

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RESULTS

Characteristics of the study population

A total of 154 patients were reviewed, consisting of 98 males (63.6%) and 56 females (36.4%) and the median follow-up duration was 20 months (interquartile range [IQR], 6-43 months). The mean age of the patients was 51.3 ± 13.2 years. The underlying diseases leading to transplantation included idiopathic pulmonary fibrosis (IPF, n = 62), non-IPF ILD (n = 47), pulmonary hypertension (n = 11), bronchiolitis obliterans (n = 9) and others (n = 25). Of the 154 patients, 31 (20.1%) experienced postoperative airway complications, whereas 123 (79.9%) did not. The most common airway complication was stenosis (n = 29), followed by ischemia (n = 7), necrosis (n = 2), and malacia (n = 2). (Table 1) The airway complications tended to predominate on the right side (n = 24, 60%).

Table 1. The incidence of airway complications

	No. of patients (%)
Airway complication	31 (20.1)
Stenosis	24 (15.4)
Ischemia	5 (3.2)
Necrosis	2 (1.3)
Dehiscence	0 (0)
Malacia	2 (1.3)

Data are presented as number (% of total patients)

No.; number

Comparison of characteristics between airway complication group and non-airway complication group

The two groups were not significantly different in most baseline characteristics, however, the mean age (p = 0.041) and the mean BMI (p = 0.016) of the recipients were significantly higher in the airway complication group. Other characteristics, including donor-related variables, preoperative infectious episode and size mismatching, did not show significant differences. (Table 2)

All perioperative variables did not differ significantly between the two groups. There were no significant differences in mean total ischemic time (p = 0.235) and the proportion of patients with preoperative mechanical ventilation (p = 0.524) between both groups. The differences of the proportions of patients with prolonged postoperative intensive care unit (ICU) stay (p = 0.647) and prolonged postoperative mechanical ventilation (p > 0.999) for more than 30 days were also insignificant. (Table 3)

Table 2. Comparison of baseline characteristics airway complication group and non-airway complication group

Characteristic	Total	Airway complication	Non-airway complication	*P* value
Patient numbers	154	31	123	
Recipient Age, years	51.3 ± 13.2	54.9 ±9.9	50.4 ± 13.8	0.041
Male sex	98 (63.6)	23 (74.2)	75 (61.0)	0.172
BMI, kg/m^2	22.1 ± 4.5	23.9 ± 5.5	21.7 ± 4.2	0.016
Donor Age, years	39.2 ± 11.6	38.5 ± 12.4	39.5 ± 11.4	0.653
Donor Male sex	96 (62.3)	20 (64.5)	76 (61.8)	0.779
Diagnosis				0.504
IPF	62 (40.3)	16 (51.6)	46 (37.4)	
Non-IPF ILD	47 (30.5)	9 (29.0)	38 (30.9)	
Pulmonary hypertension	11 (7.1)	2 (6.5)	9 (7.3)	
Bronchiolitis obliterans	9 (5.8)	0 (0.0)	9 (7.3)	
Others	25 (16.2)	4 (12.9)	21 (17.1)	
Diabetes	30 (19.5)	7 (22.6)	23 (18.7)	0.626
Ever-smoker	68 (44.2)	18 (58.1)	50 (40.7)	0.081
Preoperative infection	46 (29.9)	10 (32.3)	36 (29.3)	0.745
Size mismatching	49 (31.8)	9 (29.0)	40 (32.5)	0.709
Donor lobectomy before transplantation	5 (3.2)	2 (6.5)	3 (2.4)	0.264

Data are presented as mean ± standard deviation, median [interquartile range], or number (%)

BMI; body mass index, IPF; idiopathic pulmonary fibrosis, Non-IPF ILD; non-idiopathic pulmonary fibrosis interstitial lung disease

Table 3. Comparison of perioperative management airway complication group and non-airway complication group

Characteristic	Total	Airway complication	Non-airway complication	*P* value
Patient numbers	154	31	123	
Preoperative steroid use	49 (31.8)	12 (38.7)	37 (30.1)	0.357
Preoperative immunosuppressant use	23 (14.9)	6 (19.4)	17 (13.8)	0.412
Preoperative mechanical ventilation	107 (69.5)	23 (74.2)	84 (68.3)	0.524
Duration of preoperative mechanical ventilation (days)	21.0 ± 20.6	24.3 ± 27.7	20.1 ± 18.2	0.390
Preoperative ECMO	90 (58.4)	20 (64.5)	70 (56.9)	0.443
Duration of preoperative ECMO (days)	15.4 ± 12.5	17.5 ± 14.4	14.8 ± 11.9	0.390
Total ischemic time (min)	322.3 ± 101.5	341.7 ± 132.2	317.5 ± 92.2	0.235
Postoperative ECMO	13 (8.4)	4 (12.9)	9 (7.3)	0.297
Duration of postoperative ECMO (days)	10.8 ± 12.7	11.5 ± 14.4	10.4 ± 12.8	0.897
Duration of postoperative mechanical ventilation ≥ 30 days	21 (13.6)	4 (12.9)	17 (13.8)	> 0.999
Length of postoperative ICU stay ≥ 30 days	35 (22.7)	8 (25.8)	27 (22.0)	0.647

Data are presented as mean ± standard deviation, median [interquartile range], or number (%)

ECMO; extracorporeal membrane oxygenation, ICU; intensive care unit

Risk factors for airway complication

The higher BMI of recipient (Hazard ratio [HR], 1.116; 95% CI, 1.027–1.211; $p = 0.009$) was a significantly associated with -airway complications. The patients who required postoperative ECMO support also showed higher rate of airway complication, albeit not statistically significant (HR, 2.827; 95% CI, 0.983–8.134; $p = 0.054$). However, no correlation was found between the airway complication and the age of recipient, preoperative infection and preoperative steroid/immunosuppressant usage.

On multivariate analysis, higher BMI of recipient (HR, 1.123; 95% CI, 1.030–1.224; $p = 0.009$) remained a significant independent risk factor for airway complication. Postoperative ECMO (HR, 4.113; 95% CI, 1.204–14.049; $p = 0.024$) was also independently associated with airway complication (Table 4).

Most characteristics did not show statistically significant difference between patients with BMI $\geq$ 25 and BMI < 25 except preoperative immunosuppressant usage ($p = 0.030$). The disease entities were similar between these groups, and there was no significant difference in sex and age of the recipients. (e-Table 1). However, the disease entities differed significantly depending on the use of postoperative ECMO ($p = 0.011$) and the proportion of pulmonary hypertension was higher in patients with postoperative ECMO (e-Table 2).

As a result of analysis according to the presence of pulmonary hypertension from any etiology, we obtained data for a total of 131 patients, of which 77 (56.6%) had pulmonary hypertension. There was no statistically significant difference between airway complication group and non-airway complication group ($p = 0.573$), and pulmonary hypertension itself was not associated with airway complications (HR, 1.165; 95% CI, 0.528–2.568; $p = 0.706$).

Table 4. Risk factors for airway complication assessed by Cox proportional hazards model

Parameter	Hazard ratio	95% confidence interval	*P* value
Univariate analysis			
Recipient Age, years	1.025	0.994–1.057	0.118
Male sex	1.634	0.731–3.654	0.231
BMI, kg/m^2	1.116	1.027–1.211	0.009
Donor Age, years	0.994	0.964–1.025	0.702
Donor Male sex	1.184	0.567–2.472	0.653
Diabetes	1.134	0.489–2.634	0.769
Ever-smoker	1.795	0.879–3.663	0.108
Preoperative infection	1.139	0.536–2.418	0.736
Preoperative steroid use	1.546	0.750–3.186	0.238
Preoperative immunosuppressant use	1.457	0.598–3.553	0.408
Preoperative mechanical ventilation	1.406	0.628–3.146	0.407
Duration of preoperative mechanical ventilation (days)	1.008	0.992–1.024	0.337
Preoperative ECMO	1.481	0.709–3.093	0.296
Duration of preoperative ECMO (days)	1.019	0.987–1.053	0.247
Total ischemic time (min)	1.003	0.999-1.007	0.115
Postoperative ECMO	2.827	0.983–.8.134	0.054
Duration of postoperative ECMO (days)	1.034	0.950–1.125	0.436
Duration of postoperative mechanical ventilation ≥ 30 days	1.079	0.377–3.087	0.888

Length of postoperative ICU stay ≥ 30 days	1.291	0.577–2.888	0.534
Size mismatching	0.837	0.385–1.819	0.654
Donor lobectomy before transplantation	2.385	0.568–10.019	0.235
Multivariate analysis			
Recipient Age, years	1.019	0.985–1.054	0.281
BMI, kg/m^2	1.123	1.030–1.224	0.009
Ever-smoker	1.853	0.872–3.938	0.109
Total ischemic time (min)	1.001	0.997–1.004	0.660
Postoperative ECMO	4.113	1.204–14.049	0.024

Data are presented as mean ± standard deviation, median [interquartile range], or number (%)

BMI; body mass index, ECMO; extracorporeal membrane oxygenation, ICU; intensive care unit

Characteristics and management of airway complications

The mean time to the first detection was 3.3 ± 2.4 months and 15 patients were diagnosed with airway complications within the first year after transplantation. Of the 31 patients who had airway complications, 9 (29.0%) did not receive any bronchoscopic intervention. A total of 22 (71.0%) were managed with bronchoscopic intervention, of which 13 patients (41.9%) underwent an average of 2.1 balloon dilatation alone and 9 patients (29.0%) needed stent insertion after balloon dilatation. (Table 5) There was no severe adverse event associated with bronchoscopic intervention.

Table 5. Demographic and clinical characteristics of patients with airway complications, management of airway complications

Patient No.	Age/Gender	Underlying disease	Transplant	Detection date (Days)	Airway complication (Location)	Intervention (Total No. of intervention)
1	56/M	IPF	BL	30	Stenosis (Lt.)	Stenting (1)
2	29/F	Humidifier disinfectant related lung disease	BL	84	Stenosis (Rt.)	Ballooning (3), Stenting (1)
3	53/M	Drowning	BL	140	Stenosis (Rt.)	Ballooning (1)
4	55/M	IPF	HL	133	Stenosis (Trachea)	Ballooning (3)
5	61/M	IPF	BL	83	Stenosis (Rt.)	Ballooning (1)
6	56/M	CTD-ILD	BL	56	Stenosis (Rt.)	Ballooning (1)
7	53/M	IPF	BL	115	Stenosis (Rt.)	Ballooning (3), Stenting (1)
8	66/M	IPF	BL	139	Stenosis (Rt.)	None
9	66/M	IPF	BL	55	Necrosis (Lt.)	None
10	50/M	IPF	BL	46	Stenosis (Rt.), Ischemia (Lt.)	Ballooning (2), Stenting (1)

11	56/M	IPF	BL	403	Stenosis (Rt.)	None
12	62/M	IPF	BL	41	Stenosis (Lt.)	Ballooning (1)
13	60/F	IPF	BL	144	Stenosis (Rt.)	Ballooning (2)
14	53/M	NSIP	BL	104	Malacia (Rt.)	Ballooning (1), Stenting (1)
15	64/M	IPF	BL	79	Ischemia (Lt.)	None
16	62/M	CPFE	BL	155	Stenosis (Lt.)	None
17	55/M	IIP	BL	77	Stenosis (Both)	Ballooning (2)
18	56/M	IPF	BL	196	Stenosis (Rt.)	Ballooning (1)
19	56/M	IPF	BL	140	Stenosis (Both)	Ballooning (2), Stenting (1)
20	67/M	IPF	BL	143	Stenosis (Lt.)	Ballooning (4)
21	48/F	IPAH	BL	116	Stenosis (Rt.)	Ballooning (1)
22	59/M	AIP	BL	16	Ischemia (Both)	None
23	54/M	BE, COPD	BL	135	Stenosis (Both)	Ballooning (6)

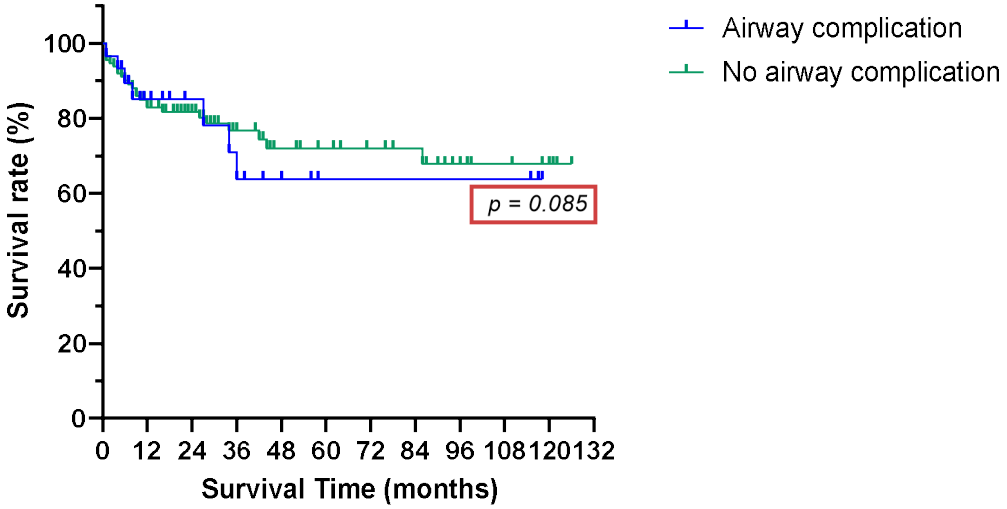
24	32/M	NSIP	BL	99	Stenosis (Rt.)	Ballooning (5), Stenting (1)
25	38/M	CTEPH	BL	15	Necrosis (Lt.)	None
26	65/F	IPF	BL	123	Stenosis (Rt.)	Ballooning (2), Stenting (1)
27	63/F	IPF	BL	95	Stenosis (Rt.)	Ballooning (2), Stenting (1)
28	46/M	OP	BL	21	Ischemia (Both)	None
29	60/F	BE	BL	22	Ischemia (Both)	None
30	65/F	CTD-ILD	BL	42	Stenosis (Both)	Ballooning (3)
31	37/F	NSIP	BL	64	Stenosis (Lt.), Malacia (Rt.)	Ballooning (1)

AIP; acute interstitial pneumonia, BE; bronchiectasis, BL; bilateral, CPFE; combined pulmonary fibrosis and emphysema, CTD; connective tissue disease, CTEPH; chronic thromboembolic pulmonary hypertension, F; female, IIP; idiopathic interstitial pneumonia, IPF; idiopathic pulmonary fibrosis, ILD; interstitial lung disease, Lt.; left, M; male, No.; number, NSIP; non-specific interstitial pneumonia, OP; organizing pneumonia, Rt.; right

Impact of airway complications on survival

A total of 41 patients (26.6%) died during the study, of which 8 (5.2%) experienced airway complications. The overall survival rates after lung transplantation were 79%, 65%, 65%, and 61% at 1, 3, 5, and 7 years, respectively, and there was no significant difference in survival between airway complication group and non-airway complication group ($p = 0.085$) (Figure 1)

Figure 1. Kaplan-Meier survival analysis for patients with airway complication versus without airway complication



DISCUSSION

Our current study showed that airway complication after lung transplantation occurred in a fifth of patients. Higher BMI of recipient and postoperative ECMO seemed to be associated with airway complication, and about 71.0% of patients with airway complication were treated by intervention via bronchoscopy. There was no significant difference in survival according to the airway complication.

Airway complication is associated with significant morbidity in patients who received lung transplantation. [12, 24] Previous studies revealed that incidence of airway complications varies with ranges of 2–30% [17, 25-27], with comparable to our current study. In addition, stenosis was the most common complication in most studies [17, 20, 25, 28], consistent with our results.

Although there are many studies about risk factor of airway complication in patients with lung transplantation[16, 19, 29, 30], prior studies have not shown consistent results. Several reports have been suggested that bronchial ischemia caused by impaired bronchial blood supply during surgery might be associated with airway complication[31, 32]. Otherwise, other studies suggested that donor-recipient height mismatch, primary graft dysfunction, microbiologic infection, especially *Aspergillus fumigatus*, use of sirolimus in the early postoperative period, and prolonged ventilator care are also associated with airway complications. [16, 17, 33] Notably, our current study revealed that higher BMI of recipient and postoperative ECMO were associated with airway complication in post-transplant patients. Previous studies showed obesity of recipient was associated with primary graft dysfunction [34, 35], and several mechanisms have been suggested, such as technically difficult surgery and longer

ischemic time, and decreased respiratory compliance. These disadvantage might influence the development of airway complication. Another possible explanation for the linkage between obesity and airway complication is through pro-inflammatory cytokines from adipose tissue in obesity, which may negatively affect bronchial healing.[36] In addition, ECMO is associated with an inflammatory reaction such as activation of the complement and contact systems, which may lead to disruption of microcirculation and endothelial injury. [37] These reaction might contribute to impaired bronchial healing and result in airway complications.

In our current study, about 71.0% of patients with airway complication received bronchoscopic intervention, such as balloon dilatation and stent insertion. Although there is no gold standard for the management of airway complication, several methods have been proposed for these patients, especially in patients with bronchial stenosis. [13, 38-40] Likewise previous reports [13, 38, 40], 13 of 31 patients (41.9%) received recurrent balloon dilatations and 9 patients (29.0%) required stent insertion for refractory stenosis. There were no serious adverse events directly related to the procedure; therefore, bronchoscopic intervention can be considered as a useful treatment modality in patients with bronchial stenosis. However, in the case of complications except for stenosis, it was difficult to identify optimal treatment because the number of complications was relatively small, as in previous reports. Further research is needed to establish effective therapeutic strategies for these complications.

Previous studies showed conflicting data about the impact of airway complication on survival. Awori *et al.* demonstrated that patients with airway complications had significantly lower survival rates than patients without airway complications.[12] Similarly, an analysis of 312 post-transplant patients showed a

significant increase in mortality in patients with airway complication. [41] On the other hand, Yserbyt *et al*. reported no statistically significant difference in survival according to airway complication.[29] In a retrospective review of 983 recipients, there was no association between airway complication and survival.[42] In the present study, we also observed no statistical differences in survival rates between airway complication group and non-airway complication group. A possible mechanism of these results might be the appropriate management of stenosis, which was the most common airway complication.

Conclusion

In our center, airway complications occurred in a fifth of patients who received lung transplantation. Because higher BMI of recipient and postoperative ECMO support are associated with airway complications, close monitoring would be necessary in these patients. Although optimal management of these patients has not to be elucidated, bronchoscopic intervention might be a useful treatment method, especially in bronchial stenosis.

e-Table 1. Comparison of characteristics between patients with BMI ≥ 25 and patients with BMI < 25

Characteristic	Total	BMI ≥ 25	BMI < 25	*P* value
Patient numbers	154	39	115	
Recipient Age, years	51.3 ± 13.2	49.2 ± 14.0	52.1 ± 12.9	0.238
Male sex	98 (63.6)	28 (71.8)	70 (60.9)	0.220
Donor Age, years	39.2 ± 11.6	37.0 ± 12.8	40.1 ± 11.1	0.154
Donor Male sex	96 (62.1)	24 (61.5)	72 (62.6)	0.905
Diagnosis				0.676
IPF	62 (40.3)	14 (35.9)	48 (41.7)	
Non-IPF ILD	47 (30.5)	14 (35.9)	33 (28.7)	
Pulmonary hypertension	11 (7.1)	4 (10.3)	7 (6.1)	
Bronchiolitis obliterans	9 (5.8)	1 (2.6)	8 (7.0)	
Others	25 (16.2)	6 (15.4)	19 (16.5)	
Diabetes	30 (19.5)	11 (28.2)	19 (16.5)	0.111
Ever-smoker	68 (44.2)	16 (41.0)	52 (45.2)	0.649
Preoperative infection	46 (29.9)	10 (25.6)	36 (31.3)	0.504
Preoperative steroid use	49 (31.8)	15 (38.5)	34 (29.6)	0.303
Preoperative immunosuppressant use	23 (14.9)	10 (25.6)	13 (11.3)	0.030
Preoperative mechanical ventilation	107 (69.5)	28 (71.8)	79 (68.7)	0.716
Duration of preoperative mechanical ventilation (days)	21.0 ± 20.6	17.6 ± 12.7	22.2 ± 22.7	0.304

Preoperative ECMO	90 (58.4)	26 (66.7)	64 (55.7)	0.228
Duration of preoperative ECMO (days)	15.4 ± 12.5	13.1 ± 9.1	16.3 ± 13.6	0.203
Postoperative ECMO	13 (8.4)	2 (5.1)	11 (9.6)	0.518
Duration of postoperative ECMO (days)	10.8 ± 12.7	19.0 ± 19.8	9.3 ± 11.8	0.342
Duration of postoperative mechanical ventilation ≥ 30 days	21 (13.6)	6 (15.4)	15 (13.0)	0.713
Length of postoperative ICU stay ≥ 30 days	35 (22.7)	10 (25.6)	25 (21.7)	0.615
Size mismatching	49 (31.8)	12 (30.8)	37 (32.2)	0.871
Donor lobectomy before transplantation	5 (3.2)	1 (2.6)	4 (3.5)	> 0.999

Data are presented as mean ± standard deviation, median [interquartile range], or number (%)

BMI; body mass index, ECMO; extracorporeal membrane oxygenation, ICU; intensive care unit

e-Table 2. Comparison of characteristics between patients with postoperative ECMO and patients without postoperative ECMO

Characteristic	Total	Postoperative ECMO	No postoperative ECMO	*P* value
Patient numbers	154	13	141	
Recipient Age, years	51.3 ±13.2	50.7 ± 10.9	51.4 ± 13.5	0.859
Male sex	98 (63.6)	5 (38.5)	93 (66.0)	0.069
BMI, kg/m^2	22.1 ± 4.5	21.5 ± 6.4	22.2 ± 4.4	0.620
Donor Age, years	39.2 ± 11.6	38.2 ± 12.2	39.3 ± 11.6	0.735
Donor Male sex	96 (62.3)	11 (84.6)	85 (60.3)	0.133
Diagnosis				0.011
IPF	62 (40.3)	3 (23.1)	59 (41.8)	
Non-IPF ILD	47 (30.5)	5 (38.5)	42 (29.8)	
Pulmonary hypertension	11 (7.1)	4 (30.8)	7 (5.0)	
Bronchiolitis obliterans	9 (5.8)	1 (7.7)	8 (5.7)	
Others	25 (16.2)	0 (0.0)	25 (17.7)	
Diabetes	30 (19.5)	1 (7.7)	29 (20.6)	0.465
Ever-smoker	68 (44.2)	4 (30.8)	64 (45.4)	0.310
Preoperative infection	46 (29.9)	2 (15.4)	44 (31.2)	0.346
Preoperative steroid use	49 (31.8)	5 (38.5)	44 (31.2)	0.756
Preoperative immunosuppressant use	23 (14.9)	2 (15.4)	21 (14.9)	> 0.999
Preoperative mechanical ventilation	107 (69.5)	11 (84.6)	96 (68.1)	0.346
Duration of preoperative mechanical ventilation (days)	21.0 ± 20.6	18.4 ± 13.4	21.3 ± 21.3	0.653

Preoperative ECMO	90 (58.4)	10 (96.9)	80 (56.7)	0.158
Duration of preoperative ECMO (days)	15.4 ± 12.5	16.0 ± 13.2	15.3 ± 12.5	0.866
Duration of postoperative mechanical ventilation ≥ 30 days	21 (13.6)	4 (30.8)	17 (12.1)	0.080
Length of postoperative ICU stay ≥ 30 days	35 (22.7)	6 (46.2)	29 (20.6)	0.075
Size mismatching	49 (31.8)	6 (46.2)	43 (30.5)	0.350
Donor lobectomy before transplantation	5 (3.2)	0 (0.0)	5 (3.5)	> 0.999

Data are presented as mean ± standard deviation, median [interquartile range], or number (%)

BMI; body mass index, ECMO; extracorporeal membrane oxygenation, ICU; intensive care unit

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국문 요약

폐 이식은 말기 폐질환에 대한 유일한 치료 수단이자 장기 생존 및 삶의 질 향상 효과가 입증된 치료로, 최근 한국에서도 그 시행이 점차 증가하고 있다. 시간이 지남에 따라 폐 이식의 예후 또한 점차 향상되고 있으나, 기도 합병증은 여전히 수술 후 주요 합병증으로 남아 폐 이식 후 이환율과 사망률의 주요 원인을 차지한다. 하지만 폐 이식 후 기도 합병증에 대한 연구는 여전히 부족하며, 이전 연구 결과들은 뚜렷한 일관성을 보여주지 못하였다. 이에 본 연구에서는 폐 이식 후 기도 합병증의 위험 인자, 특성 및 임상적 의의를 분석하고자 한다.

본 연구는 2008 년부터 2021 년까지 폐 이식을 시행한 154 명의 환자들을 대상으로 이루어졌으며, 추적관찰 기간 동안 폐 이식 후 기도 합병증이 발생한 기도 합병증 발생군과 발생하지 않은 기도 합병증 비발생군으로 나누어 분석하였다.

환자들의 평균 연령은 51.3 세로, 남성이 63%를 차지하였다. 중앙 추적관찰 기간은 20 개월이었으며, 해당 기간 동안 154 명의 환자 중 총 31 명 (20.1%)이 폐 이식 후 기도 합병증을 경험하였다. 가장 흔한 기도 합병증은 기도 협착이었으며, 기도 허혈, 괴사, 연화증이 뒤를 이었다. 폐 이식 후 기도 합병증 발생 위험인자에 대한 분석 결과, 수혜자의 높은 체질량 지수와 폐 이식 후의 체외막산소요법은 기도 합병증 발생에 대한 유의한 독립적 위험인자로 확인되었다. 기도 합병증이 발생한 31 명 중 22 명 (71.0%)에게 풍선 확장술 혹은 스텐트 삽입술과 같은 기관지내시경 중재술이 시행되었으며, 기관지내시경 중재술 시행과 연관된 심각한 시술 합병증은 발견되지 않았다. 기도 합병증 발생군과 비발생군 사이의 생존율 또한 유의한 차이가 없었다.

이식 후 기도 합병증은 여전히 20% 내외의 발생률과 함께 폐 이식 후 주요 문제로 남아있다. 수혜자의 높은 체질량 지수와 폐 이식 후의 체외막산소요법이 기도 합병증의 위험을 유의하게 높일 수 있으므로 이러한 환자군에서 기도 합병증에 대한 면밀한 관찰이 필요할 수 있다. 하지만 기도 합병증은 보존적 치료 혹은 기관지내시경 중재술에 의해 성공적으로 관리될 수 있으며, 폐 이식 후 기도 합병증의 발생은 생존률에 유의한 영향을 미치지 않았다.