

**Original
Article**

Analysis of Risk Factors for Bronchopleural Fistula after Surgical Treatment of Lung Cancer

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Purpose: Bronchopleural fistula (BPF) is a potential serious complication of lobectomy or more radical surgery for non-small-cell lung cancer (NSCLC). We aimed to evaluate the risk factors for BPF.

Methods: The study cohort comprised 635 patients who had undergone lobectomy or more radical surgery for NSCLC from March 2005 to December 2017. We examined the following risk factors for BPF: surgical procedure, medical history, preoperative treatment, and surgical management.

Results: In all, 10 patients (1.6%) had developed postoperative BPFs. Univariate logistic regression analysis showed that surgical procedure, medical history (arteriosclerosis obliterans [ASO]), and bronchial stump reinforcement were significant risk factors. Multivariate analysis showed that only surgical procedure (right lower lobectomy, $p = 0.011$, odds ratio = 17.4; right middle lower lobectomy, $p = 0.003$, odds ratio = 59.4; right pneumonectomy, $p < 0.001$, odds ratio = 166.0) was a significant risk factor. Multivariate analysis confined to the surgical procedure of lobectomy showed that right lower lobectomy ($p = 0.011$, odds ratio = 36.5) and diabetes ($\text{HbA1c} \geq 8.0$) ($p = 0.022$, odds ratio = 31.7) were significant risk factors.

Conclusion: When lobectomy or more radical surgery is performed for NSCLC, right lower lobectomy, middle lower lobectomy, and right pneumonectomy are significant risk factors for postoperative BPF. Thoracic surgeons should acquire the techniques of bronchoplasty and angioplasty to avoid such invasive procedures.

Keywords: lung cancer, bronchopleural fistula, risk factors

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Introduction

Bronchopleural fistula (BPF) is a rare complication of lung cancer surgery. However, once this occurs, fatal complications such as empyema, aspiration pneumonia, and bronchopulmonary fistula may be fatal: the mortality rate of BPF is estimated to be 12.5%–71.2%.^{1–5)}

In general, right pneumonectomy, right middle lower lobectomy, and right lower lobectomy are said to be high risk factors for BPF.^{1,6)} Healing of the bronchial stump is reportedly delayed after lymph node dissection because

of impaired blood flow.⁷⁻¹⁰⁾ In addition, neoadjuvant therapy, especially chemoradiotherapy, may inhibit healing of the bronchial stump.

In recent years, sublobar resection for early stage lung cancer has been increasingly performed; however, the standard operation for non-small-cell lung cancer (NSCLC) is lobectomy, bi-lobectomy, or pneumonectomy being necessary for advanced stage NSCLC. It is very important to avoid fatal BPFs, especially after such extended surgery. In this study, we analyzed risk factors for BPF.

Materials and Methods

This study was approved by the Institutional Review Board of the Kochi Health Sciences Center (No. 191065). The study cohort comprised 635 consecutive patients with NSCLC who had undergone lobectomy or more radical surgery in our hospital from March 2005 to December 2017. Lobectomy of the involved lobe was performed, bi-lobectomy or pneumonectomy being performed when indicated by extent tumor invasion or metastases in lymph nodes. Bronchoplasty was performed when possible. Systematic hilar and ipsilateral mediastinal lymph node dissection was performed as part of our standard procedure. Mediastinal lymph node dissection was often limited to sampling in older patients and those with vascular complications or diabetes.

As to specialized perioperative preparation, patients with poorly controlled diabetes mellitus (HbA1c ≥ 8.0) were prescribed appropriate amounts of insulin to stabilize blood glucose concentrations by a diabetologist for 2–4 weeks before surgery. Surgery was performed only when blood glucose concentrations were stable. During the perioperative period, their blood glucose concentrations were maintained under 200 mg/dL by administering insulin on a sliding scale. In contrast, the perioperative treatment of patients with moderately well-controlled diabetes (HbA1c < 8.0 and stable blood glucose concentrations) was managed using a sliding scale without consulting a diabetologist. Incisions have become progressively shorter over time; complete video-assisted thoracoscopic surgery (VATS) having been performed in our institution since 2013. Even in the case of invasive cancer, bi-lobectomy and pneumonectomy were performed with VATS as often as possible.

The bronchial stump was closed as follows. In Method A (stapler), the bronchial stump was closed with a surgical stapler only. This was our standard procedure and

was implemented in most cases. In Method B (suture), the bronchial stump was manually sutured using the Sweet method. This procedure was performed when the surgical margin was poor and changed to bronchoplasty if necessary. In Method C (ligation), the bronchial stump was ligated with 1-0 silk and reinforced by a few simple interrupted stitches with absorbable sutures at intervals of 2 mm distal to the ligation, as described by Nakashima et al.¹¹⁾ Methods B and C were only used in thoracotomies; thus, in VATS procedures, bronchial stumps were closed by stapler only. After closing the bronchial stump by the appropriate method, a sealing test was performed with a pressure up to 25 cm H₂O. If any air leakage was detected, mattress suturing was added using a pair of pledgets; this stopped air leakage in all cases.

The bronchial stump was reinforced when the surgeons had concerns BPF because the patient had received preoperative therapy, had diabetes or cardiorenal or cerebrovascular disease, infection, was receiving a steroid or immunosuppressant, was undergoing pneumonectomy, middle lower lobectomy, or lower lobectomy, or was an older person. In these cases, the stumps were reinforced with pedicled or free pericardial fat pad or an intercostal muscle flap. Intercostal muscle flaps were mainly used for thoracotomy and pericardial fat pads for VATS. BPF was suspected from symptoms or chest X ray or chest CT findings and was confirmed by bronchoscopy.

Risk factors (age, sex, procedure, lymph node dissection, medical history, stump closure, and reinforcement) were assessed by univariate and multivariate logistic regression analyses. Factors shown to be significant using univariate analysis at $p < 0.1$ were included in the multivariate analysis, and independent prognostic factors were considered significant at $p < 0.05$. Statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R Commander that is designed to add statistical functions frequently used in biostatistics.¹²⁾

Results

Table 1 summarizes the characteristics of the 635 study patients. Their median age was 69 years (range: 22–89 years) and 379 were men and 256 women. The tumor was located on the right side in 410 patients and on the left side in 225 the specific locations being the right upper lobe ($n = 225$), right middle lobe ($n = 49$),

Table 1 Clinical characteristics

Factors	n(%)
Age	69 (22–89)
Sex	
Male	379 (59.7)
Female	256 (40.3)
Side of surgery	
Right	410 (64.6)
Left	225 (35.4)
Location of tumor	
Right upper lobe	225 (35.4)
Right middle lobe	49 (7.7)
Right lower lobe	135 (21.3)
Right main bronchus	1 (0.2)
Left upper lobe	123 (19.4)
Left lower lobe	102 (16.0)
Surgical procedure	
Right upper lobectomy	219 (34.5)
Right middle lobectomy	44 (6.9)
Right lower lobectomy	121 (19.1)
Right upper middle lobectomy	5 (0.8)
Right middle lower lobectomy	14 (2.2)
Right pneumonectomy	6 (0.9)
Completion right pneumonectomy	1 (0.2)
Left upper lobectomy	120 (18.9)
Left lower lobectomy	100 (15.7)
Left pneumonectomy	5 (0.8)
Bronchoplasty	
Yes	19 (3.0)
No	616 (97.0)
Lymph node dissection	
ND1b	121 (19.1)
ND2a-1	345 (54.3)
ND2a-2	169 (26.6)
Incision	
Thoracotomy	406 (64.0)
VATS	229 (36.0)
Medical history	
CHF	21 (3.3)
IHD	98 (15.4)
Arrhythmia	46 (7.2)
Hypertension	139 (21.9)
ASO	12 (1.9)
CRF	8 (1.3)
TB	30 (4.7)
Asthma	25 (3.9)
COPD	92 (14.5)
IP	48 (7.6)
CKD	30 (4.7)
Autoimmune disease	32 (5.0)
Steroid/immunosuppressant use	16 (2.5)
Diabetes (HbA1c <8.0)	81 (12.8)
Diabetes (HbA1c ≥8.0)	19 (3.0)
Diabetes (all)	100 (15.7)
CVD	42 (6.6)
Primary cancer in other organs	169 (26.6)
Histology	
Adeno	468 (73.7)
Squamous	110 (17.3)
Others	57 (9.0)

Factors	n(%)
Residual tumor	
R0	633 (99.69)
R1	2 (0.31)
Neoadjuvant therapy	
None	606 (95.4)
Chemotherapy	16 (2.5)
Radiotherapy	0 (0)
Chemoradiotherapy	13 (2.1)
Stump closure	
Stapler	499 (78.6)
Suture	21 (3.3)
Ligation	115 (18.1)
Reinforcement	
Muscle	39 (6.1)
Pericardial fat	129 (20.3)
Pleura	2 (0.3)
Bronchial pleural fistula	
Yes	10 (1.6)
No	625 (98.4)

ASO: arteriosclerosis obliterans; CHF: chronic heart failure; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CVD: cerebrovascular disease; IHD: ischemic heart disease; IP: interstitial pneumonia; TB: tuberculosis; VATS: video-assisted thoracoscopic surgery

right lower lobe (n = 135), right main bronchus (n = 1), left upper lobe (n = 123), and left lower lobe (n = 102). The surgical procedures were right upper lobectomy (n = 219), right middle lobectomy (n = 44), right lower lobectomy (n = 121), right upper middle lobectomy (n = 5), right middle lower lobectomy (n = 14), right pneumonectomy (n = 6), completion right pneumonectomy (n = 1), left upper lobectomy (n = 120), left lower lobectomy (n = 100), and left pneumonectomy (n = 5). Preoperative treatment was administered to 29 patients (chemotherapy, n = 16; chemoradiotherapy, n = 13). Bronchoplastic surgery was performed on 19 patients (lobectomy 18; pneumonectomy 1). Lymph node dissection was ND1 (hilar lymph nodes, n = 121), and ND2 (mediastinal lymph nodes, n = 514). The methods of stump closure were stapler (n = 499), suture (n = 21), and ligation (115). The stump was reinforced in 170 patients (intercostal muscle 39; pericardial fat pad 129; parietal pleura 2). In all, 10 patients (1.6%) developed postoperative BPFs; eight of them were men and two were women. BPF occurred in two patients who had undergone right pneumonectomy (20.0%), two middle lower lobectomy (20.0%), five right lower lobectomy (50.0%), and one left lower lobectomy (10.0%). Regarding lymph node dissection, one of these patients had undergone ND1 and nine ND2. The methods of stump closure were stapler in nine patients and suture in one. The stump was

reinforced in seven of these patients (intercostal muscle five; pericardial fat pad two). BPF developed between 14 and 391 days after surgery (median 221 days), three of them developing within 30 days of surgery. Five patients received only conservative management and closure of the stump was achieved in three of them. The remaining five patients required aggressive interventions. Two of them underwent direct omentoplasty. Another two underwent thoracic fenestration, one of whom also underwent omentoplasty. The fifth patient underwent transbronchial treatment. Closure was achieved in three of the five patients; however, one of them died of BPF-related complications. **Table 2** shows the results of univariate and multivariate analyses of risk factors for BPF in all cases. Logistic regression analysis showed that age, sex, side of surgery, bronchoplasty, lymph node dissection, thoracotomy or VATS, residual tumor, stump closure, and preoperative treatment were not significant risk factors. Univariate analysis showed that the surgical procedure (right lower lobectomy; right middle lower lobectomy; right pneumonectomy), medical history (arteriosclerosis obliterans [ASO]), and bronchial stump reinforcement were significant risk factors. Multivariate analysis showed that the surgical procedure (right lower lobectomy $p = 0.011$, odds ratio = 17.4; right middle lower lobectomy, $p = 0.003$, odds ratio = 59.4; right pneumonectomy, $p < 0.001$, odds ratio = 166.0) was a significant risk factor. Because right pneumonectomy and right middle lower lobectomy showed higher odds ratios than right lower lobectomy, a further analysis of only patients who had undergone lobectomy was performed (**Table 3**). Multivariate analysis showed that right lower lobectomy ($p = 0.011$, odds ratio = 36.5) and diabetes ($\text{HbA1c} \geq 8.0$) ($p = 0.022$, odds ratio = 31.7) were significant risk factors within this subgroup.

Discussion

BPF is a rare complication of lung cancer surgery, reportedly occurring in 3% or less of patients.¹⁾ However, once it occurs, BPF can cause empyema and aspiration pneumonia and may be fatal, the estimated mortality rate being 12.5%–71.2%.^{1–5)} Ten of our study patients (1.6%) developed BPF after lung cancer surgery, and the death rate from BPF was 10% (one patient).

The causes of BPF fall into two groups: surgery-related and non-surgery-related factors. Surgery-related factors include the surgeon's experience, means of closure of the bronchial stump, lymph node dissection, residual tumor in

the bronchial stump, side of surgery, reinforcement of the stump, and lobe resected, whereas non-surgery-related factors include age, sex, preoperative treatment, and medical history.

The relative merits of various means of achieving bronchial closure are as follows. An automatic suturing device is expected to achieve complete adherence of the mucosal surfaces and has the advantage of being simple and inducing few foreign body reactions¹³⁾; such devices have been increasingly used with improvements in them and the increasing implementation of VATS. It is thought that the influence of the surgeon's experience on the rate of occurrence of BPF has decreased in parallel with increasing use of such devices. In a study on adult mongrel dogs, Moriyama reported the usefulness of tightly joining the mucosal surfaces and of using an automatic stapling device in regard to bronchial stump healing following pneumonectomy.¹³⁾ The dogs were divided into three groups: in group A, interrupted sutures were used; in group B, mattress sutures plus interrupted sutures; and in group C, an automatic stapling device. Mucosal adhesion was poor and cysts composed of mucosal epithelium and sinuses were noted at the site of contact of the mucosal surfaces in all groups. These results suggest that there is a negligible difference in bronchial stump healing between automatic stapling devices and hand suturing, that tight joining of the mucosal surfaces does not result in mucosal adhesion, and that mucosal adhesion is poor with all closure methods.¹³⁾ In our study, the incidence of BPF did not differ significantly between means of bronchial closure (automatic stapling device, suture, or ligation); however, there were no BPFs in the ligation group. According to a report by Sato et al.,¹⁴⁾ the advantages of bronchial stump ligation are as follows: (1) equivalent pressure applied around the bronchial stump, so there is less deformity, (2) because no sutures are exposed in the bronchial stump cavity, infections are less likely to occur. In addition, Nakashima et al. reported that no BPFs occurred in 715 patients who underwent lobectomy and bronchial ligation method, despite VATS.¹¹⁾ Given that there is no evidence that use of a stapling device has a positive effect on bronchial mucosal adhesion, bronchial ligation may be needed whenever the patient is considered at risk of postoperative BPF, regardless of whether a thoracotomy or VATS procedure is being performed.

If there is residual tumor in the bronchial stump, the bronchial closure becomes loose and a stump fistula develops as the residual tumor grows. We were unable to assess this phenomenon in the present study because

Table 2 Results of univariate and multivariate analysis of risk factors for BPF (all cases)

Risk factors		Univariate			Multivariate		
		OR	95% CI	P value	OR	95% CI	P value
Age		1.03	0.97–1.09	0.426			
Sex	Male	2.76	0.58–13.10	0.201			
Side of surgery	Right	5.03	0.63–39.90	0.127			
Surgical procedure	Right upper lobectomy	–	–	0.989			
	Right middle lobectomy	–	–	0.992			
	Right lower lobectomy	4.39	1.25–15.40	0.021	17.40	1.94–156.00	0.011
	Right upper middle lobectomy	–	–	0.994			
	Right middle lower lobectomy	12.80	2.45–66.6	0.003	59.40	4.12–856.00	0.003
	Right pneumonectomy	38.80	6.19–243.00	<0.001	166.00	9.64–2850.00	<0.001
	Completion right pneumonectomy	–	–	0.994			
	Left upper lobectomy	–	–	0.992			
	Left lower lobectomy	0.59	0.07–4.71	0.619			
	Left pneumonectomy	–	–	0.994			
Bronchoplasty	Yes	3.75	0.45–31.20	0.222			
Lymph node dissection	ND2 (mediastinal lymph node)	2.14	0.27–17.00	0.473			
Incision	Thoracotomy	0.84	0.24–3.02	0.794			
Medical history	CHF	–	–	0.992			
	IHD	1.38	0.29–6.59	0.688			
	Arrhythmia	1.43	0.18–11.60	0.736			
	Hypertension	1.54	0.39–6.04	0.535			
	ASO	6.20	0.72–53.30	0.096	4.43	0.37–53.70	0.242
	CRF	–	–	0.992			
	TB	–	–	0.990			
	Asthma	–	–	0.991			
	COPD	1.49	0.31–7.11	0.620			
	IP	1.37	0.17–11.00	0.769			
	CKD	2.28	0.28–18.60	0.441			
	Autoimmune disease	–	–	0.990			
	Steroid/immunosuppressant use	–	–	0.993			
	Diabetes (HbA1c <8.0)	0.76	0.09–6.05	0.793			
	Diabetes (HbA1c ≥8.0)	3.75	0.45–31.20	0.222			
	Diabetes (all)	1.34	0.28–6.43	0.711			
	CVD	–	–	0.993			
Primary cancer in other organs	1.19	0.30–4.64	0.807				
Residual tumor	R1	–	–	0.994			
Neoadjuvant therapy	Chemotherapy	–	–	0.993			
	Radiotherapy	–	–	–			
	Chemoradiotherapy	–	–	0.994			
Stump closure	Stapler	2.48	0.31–19.70	0.391			
	Suture	3.36	0.41–27.80	0.261			
	Ligation	–	–	0.992			
Reinforcement	Yes	6.61	1.69–25.90	0.007	1.84	0.34–9.90	0.476

ASO: arteriosclerosis obliterans; CHF: chronic heart failure; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CRF: chronic respiratory failure; CVD: cerebrovascular disease; IHD: ischemic heart disease; IP: internal pneumonia; TB: tuberculosis; VATS: video-assisted thoracoscopic surgery

Table 3 Results of univariate and multivariate analysis of risk factors for BPF (lobectomy only)

Risk factors		Univariate			Multivariate		
		OR	95% CI	P value	OR	95% CI	P value
Age		1.03	0.96–1.12	0.409			
Sex	Male	3.57	0.42–30.80	0.246			
Side of surgery	Right	2.89	0.34–24.90	0.334			
Surgical procedure	Right upper lobectomy	–	–	0.993			
	Right middle lobectomy	–	–	0.993			
	Right lower lobectomy	20.80	2.40–180.00	0.006	36.50	2.22–600.00	0.011
	Left upper lobectomy	–	–	0.992			
	Left lower lobectomy	1.01	0.12–8.72	0.994			
Bronchoplasty	Yes	–	–	0.993			
Lymph node dissection	ND2 (mediastinal lymph node)	1.70	0.21–13.90	0.622			
Incision	Thoracotomy	0.95	0.22–4.00	0.942			
Medical history	CHF	–	–	0.992			
	IHD	2.68	0.48–14.80	0.259			
	Arrhythmia	–	–	0.993			
	Hypertension	0.71	0.08–6.10	0.752			
	ASO	10.70	1.15–99.10	0.037	3.77	0.31–46.60	0.301
	CRF	–	–	0.993			
	TB	–	–	0.994			
	Asthma	–	–	0.994			
	COPD	2.98	0.54–16.50	0.212			
	IP	2.40	0.28–21.00	0.429			
	CKD	3.92	0.44–34.70	0.219			
	Autoimmune disease	–	–	0.994			
	Steroid/immunosuppressant use	–	–	0.993			
	Diabetes (HbA1c <8.0)	–	–	0.994			
	Diabetes (HbA1c ≥8.0)	6.84	0.76–61.74	0.087	31.70	1.65–611.00	0.022
	Diabetes (all)	1.09	0.13–9.40	0.940			
	CVD	–	–	0.993			
Primary cancer in other organs	1.36	0.25–7.48	0.726				
Residual tumor	R1	–	–	0.994			
Neoadjuvant therapy	Chemotherapy	–	–	0.994			
	Radiotherapy	–	–	–			
	Chemoradiotherapy	–	–	0.994			
Stump closure	Stapler	–	–	0.992			
	Suture	–	–	0.992			
	Ligation	–	–	0.992			
Reinforcement	Yes	6.36	1.15–35.11	0.034	3.65	0.57–23.40	0.172

ASO: arteriosclerosis obliterans; BPF: Bronchopleural fistula; CHF: chronic heart failure; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CRF: chronic respiratory failure; CVD: cerebrovascular disease; IHD: ischemic heart disease; IP: interstitial pneumonia; TB: tuberculosis

only two of our 635 patients had residual tumor in the bronchial stump.

In general, healing of the bronchial stump is strongly affected by the adequacy of blood supply to the bronchial stump postoperatively. Lymph node dissection and

preoperative therapy, especially chemoradiotherapy, are risk factors for BPF.^{7–10} Lymph node dissection blocks blood vessels around the bronchus, thus reducing blood flow. In addition, preoperative treatment, especially chemoradiotherapy, causes fibrosis of the peribronchial

tissue, reducing blood flow and resulting in failure of the bronchial stump to heal, leading to disaggregation of the stump. However, in our study, we detected no significant impact of lymph node dissection or preoperative therapy on the incidence of BPF, possibly because we try to preserve the peribronchial tissue as much as possible when performing lymphadenectomy, regardless of the extent of dissection. Also, patients who receive preoperative treatment often have advanced stage disease and lymph node metastases. Therefore, lymphadenectomy at the time of pulmonary resection is essential; however, we think that it is important to preserve the peribronchial tissue as much as possible and maintain blood flow to the stump. Some would say that the above method has the potential to leave cancer cells in the peribronchial tissue. We hope that any such cells have already been killed by preoperative chemoradiotherapy and prioritize prevention of postoperative BPF.

According to data from a national clinical database in Japan, interstitial pneumonia, central nerve system disorder, autoimmune disease, and smoking habit are reported risk factors for BPF.¹⁵⁾ In this study, the only risk factor for BPF identified by multivariate analysis in patients undergoing lobectomy was diabetes (HbA1c ≥ 8.0). Moreover, although ASO was not identified by multivariate analysis, it is also a possible risk factor. Some authors list diabetes as one of the risk factors for postoperative BPF.^{4,16,17)} Both diabetes and ASO are related to blood flow, supporting the contention that an adequate blood supply is essential for bronchial stump healing.

Unfortunately, there is one medically unavoidable factor and that is an anatomical one. Right pneumonectomy, right middle lower lobectomy, and right lower lobectomy have been reported as risk factors for postoperative BPF,^{1,6)} and these three factors were also found to be independent significant risk factors in this study. In pneumonectomy, the right main bronchus is wider and more vertical than the left, resulting in greater accumulation of secretions in the bronchial stump.¹⁸⁾ The left main bronchial stump tends to be under the cover of the aortic arch, whereas the right main bronchus is not covered with mediastinal tissue and therefore more likely to be exposed to the thoracic free space. In addition, the right bronchus is supplied with only one bronchial artery, whereas the left bronchus is supplied with two arteries.¹⁹⁾ If the single artery of the right bronchus is damaged during lymphadenectomy, the right bronchial stump becomes ischemic.^{18,20)} The above factors may also account for the high incidence of postoperative BPF

after middle lower lobectomy. In the case of right lower lobectomy, preserving the middle lobe bronchus makes the distance from the bifurcation to the stump longer, possibly rendering it more ischemic than the left. Thus, there is a combination of contributing factors, the most important of which we believe to be whether the blood flow around the bronchial tissue, especially the bronchial artery, can be preserved.

Our findings in this study that the odds ratio for right pneumonectomy was about tenfold that of right lower lobectomy and that of middle lower lobectomy about threefold indicate that these procedures should be avoided as much as possible. How can these treatments be avoided? We believe they can best be avoided by performing bronchoplasty or angioplasty. For example, in the case of hilar lung cancer at the upper lobe bronchial entrance, sleeve upper lobectomy can avoid right pneumonectomy and when the cancer is in the intermediate bronchus, sleeve middle lobectomy can avoid middle lower lobectomy. In patients whose cancers are invading the left upper lobe bronchus and pulmonary artery, pneumonectomy may be avoided by performing bronchoplasty and angioplasty. After lobectomy or pneumonectomy, the relevant bronchus is closed with the mucosal surfaces in contact with each other and a stump formed. In contrast, in bronchoplasty, of the bronchus is connected layer-to-layer, enabling primary healing of the anastomosis. We consider that this can lead to a better healing process than occurs after lobectomy or pneumonectomy. Endo et al. reported risk factors for BPF drawn from a national clinical database in Japan.¹⁵⁾ Regarding surgical procedure, right pneumonectomy was a stronger risk factor (odds ratio 11.1) than bronchoplasty with segmentectomy or lobectomy (odds ratio 5.4). Admittedly, advanced techniques are required for plastic surgery. We consider that thoracic surgeons should acquire the ability to perform bronchoplasty or angioplasty to avoid more invasive surgery and reduce the incidence of postoperative BPF.

Many thoracic surgeons reinforce the bronchial stumps to prevent postoperative BPF. Sonobe et al. recommended covering the stump with a pedicled intercostal muscle flap after previous ipsilateral thoracotomy and induction therapy.¹⁾ Some authors suggest routinely covering the bronchial stump with surrounding tissue in all patients, whereas others recommend this only for right pneumonectomy.^{21–23)} However, there is no evidence to support reinforcement of the bronchial stump.¹⁵⁾ The most common materials used to reinforce it are adipose tissue and muscle. For adipose tissue, pedicled or free

pericardial fat pad can be easily obtained from the thoracic cavity.^{24,25} We often use the pericardial fat pad for reinforcement during VATS. As to muscle tissue, the latissimus dorsi, serratus anterior, pectoralis major, or intercostal muscles can be collected and used. Okuda et al.²⁶ reported that both pedicled fat and free fat remain free of degeneration for a long time, whereas muscle tissue shortens and relaxes if not used for contraction. We therefore think that a muscle flap may be effective in maintaining blood flow; however, it may be difficult to isolate it from surrounding tissues. Although the omentum is considered the most effective material for preventing BPF, it can only be obtained by performing abdominal surgery.^{27,28} Because it is so invasive to perform omentoplasty routinely, a more practical approach would be to use omentum as a covering material only when a BPF develops postoperatively. Our present data provide no basis for recommending reinforcement of the bronchial stump. Indeed, univariate analysis identified reinforcing the bronchial stump as a risk factor. Our practice is to reinforce bronchial stumps in patients with risk factors such as preoperative therapy, diabetes or cardiorenal cerebrovascular disease, infection, use of steroids or immunosuppressants, undergoing pneumonectomy, middle lower lobectomy, or lower lobectomy, and older age. Because anatomical factors are likely greater risk factors than the effect of covering the bronchial stump, it is possible that bronchial reinforcement does not contribute to preventing BPF. The role of bronchial reinforcement remains controversial and a prospective comparative trial is needed to determine whether the bronchial stump should be reinforced. In the meantime, we plan to continue to reinforce the bronchial stump in the hope that it does reduce the risk of BPF.

Conclusion

When lobectomy or more radical surgery is performed for treatment of NSCLC, right lower lobectomy, middle lower lobectomy, and right pneumonectomy are significant risk factors for postoperative BPF. Additionally, in the subgroup undergoing lobectomy, right lower lobectomy and diabetes (HbA1c ≥ 8.0) are significant risk factors. We found no good evidence for reinforcement of the bronchial stump. Postoperative BPF may be prevented by bronchial ligation and preserving peribronchial blood flow. Thoracic surgeons should acquire the techniques of bronchoplasty or angioplasty to avoid more invasive procedures and thus minimize the risk of BPF.

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Disclosure Statement

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