



# Pulmonary resection using polyglycolic acid sheet without fibrin glue and its surgical complications

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**Background:** After pulmonary resection, fibrin glue is usually used with a polyglycolic acid (PGA) sheet around the staple line of the residual lung to prevent air leakage and pulmonary fistula. At our institution, a PGA sheet is attached to the surface of the lung or staple line with blood, saline, or lavage, and fibrin glue is not used. This study aimed to reveal the efficacy of PGA sheets without fibrin glue for pulmonary resection and to compare the postoperative drainage period with or without reinforcement.

**Methods:** We retrospectively analyzed 483 major lung resections (lobectomies and segmentectomies) and their postoperative clinical course. The effectiveness of reinforcement methods for air leakage on drainage or duration of hospital stay was investigated. The effects of fibrin glue on air leakage reinforcements methods were determined.

**Results:** Seven re-operations (1%) were performed because of broncho-pleural fistulas (n=1) and pulmonary fistulas (n=6). The average drainage period was 2.9 days, and the postoperative hospitalization period was 7.3 days. Eleven patients (1.7%) required a prolonged drainage period because of air leakage, and five patients returned to the hospital after discharge because of subcutaneous emphysema.

**Conclusions:** Although there might be some points to note, pulmonary resection without fibrin glue could be considered an alternative method.

**Keywords:** Polyglycolic acid sheet (PGA sheet); fibrin glue; air leakage

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## Introduction

In 2016, in Japan, 31,365 and 5,136 cases of anatomical pulmonary resections via lobectomies and segmentectomies, respectively, were performed (1). Prolonged air leakage (PAL) is one of the most common complications of pulmonary resections. In the 1990s or 2000s, several randomized studies on synthetic sealants (2-4) and fibrin glue in lung surgery revealed the significance of fibrin glue in terms of postoperative air leakage (4). Recently, fibrin glue has been used with polyglycolic acid (PGA) sheets to prevent air

leakage and pulmonary fistulas after pulmonary resections. Visceral pleural repairs using PGA combined with fibrin glue were reported to be tolerable at bursting pressures higher than 40 cmH<sub>2</sub>O (5). However, the efficacy of PGA sheets or oxidized regenerated cellulose (ORC) mesh was reported without fibrin glue and autologous blood (6). If fibrin glue is not always necessary, a postoperative course without it would be acceptable, and the medical cost and blood donation could be reduced.

At our institution, a PGA sheet is attached to the surface of the lung or staple line with blood, saline, or lavage, and

fibrin glue is not used due to infectious concerns, complicated procedures, and medical costs [The redemption price of Neobeil sheet is 167 yen per 1 cm<sup>2</sup> (10×5 cm; 8,350 JY). If fibrin glue is used, usually a 3ml kit with 33,459 JY cost is needed].

This study aimed to retrospectively reveal the efficacy of PGA sheets without fibrin glue for pulmonary resections and to compare the hospital period with or without reinforcement. Thus, a comparison between whether using a PGA sheet with fibrin glue or covering a PGA sheet without suturing pleural defects is sufficient. We present this article in accordance with the STROBE reporting checklist (available at <https://vats.amegroups.com/article/view/10.21037/vats-23-51/rc>).

## Methods

This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional review board of Saku Central Hospital (No. R201907-07) and individual consent for this retrospective analysis was waived. We retrospectively reviewed 659 consecutive operations from 2013 to 2018 and the clinical courses after pulmonary resections. The inclusion criteria were operations for lung tumors, and the exclusion criteria were pneumonectomies or partial resections (wedge resections), and operations for infectious lesions. The patients who were complicated with postoperative chylothoraces were also excluded, and a total of 483 patients were enrolled in this study. The clinical data

analyzed included age, sex, smoking history, comorbidities [chronic obstructive pulmonary disease (COPD) or interstitial pneumonia], type of operation, histopathological diagnoses, chest drainage duration, and length of hospital stay. For logistic regression analysis, patients were divided into two groups: those whose respiratory function test was graded as Global Initiative for Chronic Obstructive Lung Disease (GOLD) and GOLD 2 or more. Interstitial pneumonia was judged as the usual pneumonia pattern, ground-glass opacity, and honeycomb appearance on computed tomography (CT).

The surgical procedures were as follows: in lobectomy or segmentectomy, auto-suture devices were used for interlobar fissure or segmental formation (resection) and resection of the bronchus and pulmonary artery or vein. After pulmonary resection and lymph node dissection, a sealing test (leak test) was performed at inspiratory pressures of 15–20 cmH<sub>2</sub>O. If air leakage was observed, mattress sutures with pledget sheets holding the leak point were performed, and the surgeon applied sutures only or covered the pleural injury with a PGA sheet after the 2<sup>nd</sup> or 3<sup>rd</sup> sealing tests. If minor air leakage was observed, covering the staple line with a PGA sheet was selected. If no air leakage was observed, the surgeon applied no reinforcements at all. The PGA sheet was 5×10 cm in size, 0.3 mm in thickness (Neoveil sheet<sup>®</sup> NV-M-3G, Gunze, Osaka, Japan), and was usually cut into four pieces. Each piece was approximately 5×2.5 cm in size. Usually, fibrin glue was not used to fix the PGA sheet; instead, the PGA sheet was fixed with intrathoracic blood or lavage. A cotton stick was not adequate for intertangles because they catch and intertangle with each other; therefore, an opposite stick, an outer cylinder (Endo Finger<sup>®</sup>, Kenzmedico, Saitama, Japan), was used to catch and release a small amount of saline or blood for adopting the PGA sheet. However, fibrin glue was used during the reoperation, and a fibrin sealant patch (TachoSil<sup>®</sup> CSL Behring K.K., PA, USA) was used for pulmonary artery bleeding. Another type of PGA sheet (Neoveil Nano<sup>®</sup>, Gunze) was not used during this period.

For postoperative management, a 20-Fr chest tube (Argyle, Cardinal Health Inc., OH, USA) was placed, and a chest drainage bag (Sumitomo Bakelite Co., Tokyo, Japan) was kept under water pressure as a sealant if the subcutaneous emphysema was tolerable. Otherwise, reinsertion of the chest drainage tube from the anterior and superior intercostal spaces was required. Talc or adhesive materials were not used, and reoperation was performed to close the pulmonary fistula if the patient accepted it after

### Highlight box

#### Key findings

- Pulmonary resection without fibrin glue could be considered an alternative method.
- Prolonged air leakage (PAL) for >7 days including six cases that required reoperation cases: 5.0%.

#### What is known and what is new?

- A fibrin glue has been used with polyglycolic acid (PGA) sheets to prevent air leakage and pulmonary fistula after pulmonary resections; however, comparisons of outcomes with or without fibrin glue have not been reported.
- Postoperative complications of pulmonary resection using PGA sheet without fibrin glue: 2.4% (readmissions and re-operations).

#### What is the implication, and what should change now?

- Pulmonary resections using PGA sheets without fibrin glue could be one of the options for preventing PAL.

**Table 1** Demographic characteristics of 483 patients

Variable	No. of patients
Age (years), median [range]	72 [21–88]
Sex	
Female	175
Male	308
Smoking	
Never smoker	160
Smoker	323
Underlying disease	
COPD	72
UIP (fibrosis)	23
Surgery	
Open bilobectomy	7
Thoracoscopic lobectomy	342
Open lobectomy	38
Thoracoscopic segmentectomy	91
Thoracoscopic lobectomy + segmentectomy	5
Pathological diagnosis	
Lung cancer	454
Adenocarcinoma/MIA/AIS	257/39/18
Squamous cell carcinoma	94
LCNEC <sup>†</sup> /small/carcinoid	12/11/5
Adenosquamous/pleomorphic <sup>‡</sup>	8/10
Metastatic lung tumor	27
Colorectal cancer	18
Other organ cancer	9
Others <sup>§</sup>	2

<sup>†</sup>, LCNEC includes large cell carcinoma; <sup>‡</sup>, pleomorphic (n=8), anaplastic (n=1), pulmonary blastoma (n=1); <sup>§</sup>, B-cell lymphoma (n=1), and sclerosing hemangioma (n=1). COPD, chronic obstructive pulmonary disease; UIP, usual interstitial pneumonia; MIA, minimally invasive adenocarcinoma; AIS, adenocarcinoma in situ; LCNEC, large cell neuroendocrine carcinoma.

7–10 days of observation.

### Statistical analysis

For comparisons between methods using PGA sheets and drainage or hospital stay, statistical analyses with a *t*-test

or the Kruskal-Wallis test were performed. Associations between PAL for >7 days and clinicopathological variables were analyzed using the chi-squared test for categorical variables. The significance of clinicopathological variables in differentiating risk factors for PAL was assessed using logistic regression analysis. Multivariate logistic regression analysis was performed to identify significant clinicopathological variables ( $P < 0.1$ ) in the univariate analysis. For all analyses, statistical significance was set at  $P < 0.05$ . JMP software (13.1.0 SAS Institute, Cary, NC, USA) was used for all analyses.

## Results

### Patient population and procedures

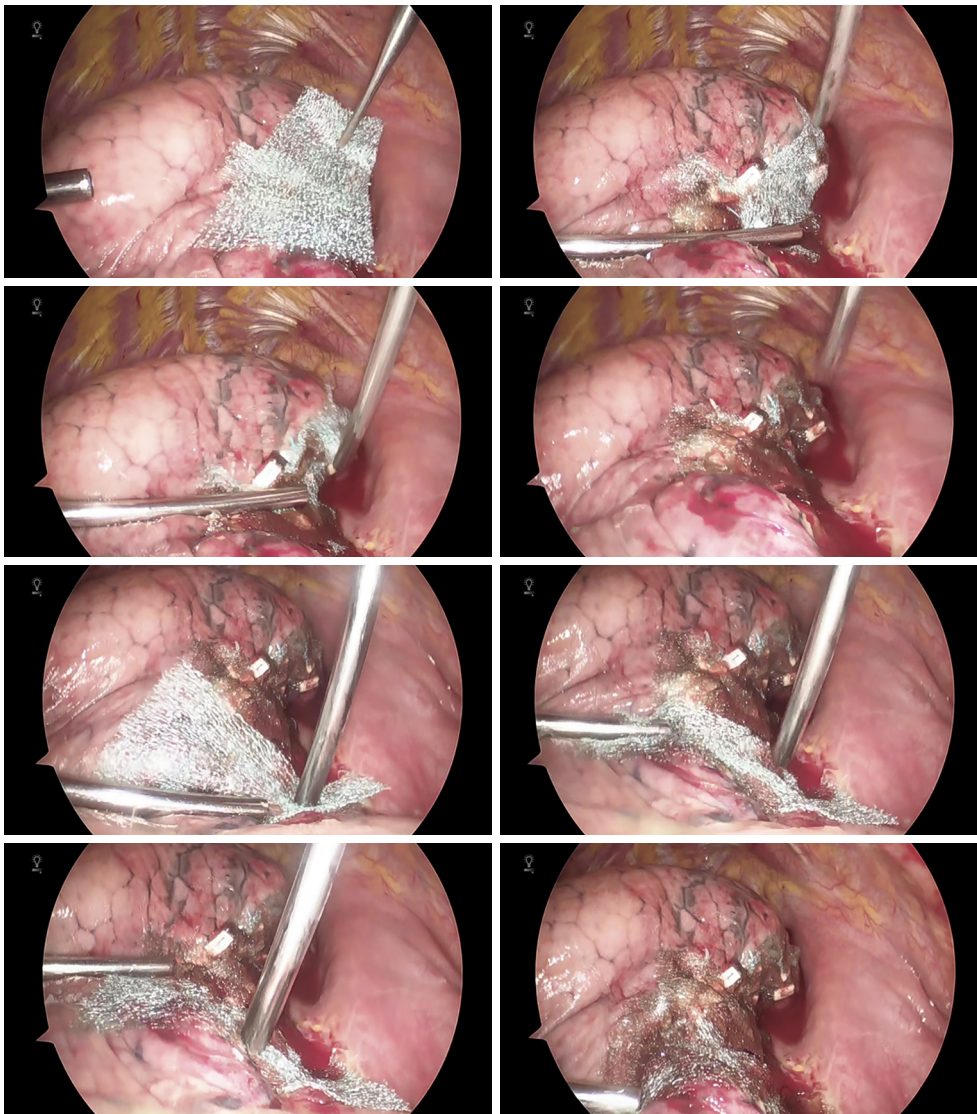
The demographic characteristics and histopathological diagnoses of the 483 patients are shown in *Table 1*. There were 454 cases of lung cancer (adenocarcinoma, 257; adenocarcinoma in situ, 18; minimally invasive adenocarcinoma, 39; squamous cell carcinoma, 94; adenosquamous, 8; pleomorphic carcinoma, 8; anaplastic carcinoma, 1; pulmonary blastoma, 1; large cell carcinoma and large cell neuroendocrine carcinoma, 12; small cell carcinoma, 11; carcinoid, 5), 27 cases of metastatic tumors (colorectal cancer, 18; other organ cancer, 9), and 2 cases of other lung tumors (B-cell lymphoma, 1; sclerosing hemangioma, 1). *Figure 1* shows the technique used to patch the PGA sheet around the pulmonary staple stump.

### Postoperative results

Of the 483 major lung resections, thoracoscopic lobectomy was performed in 342 cases, thoracoscopic segmentectomy in 91, thoracoscopic lobectomy + segmentectomy in 5, open lobectomy in 38, and bilobectomy in 7. Total complications associated with air leakage, including readmission caused by subcutaneous emphysema, were seen in 29 cases (6.0%).

### Complications details and rates

There were 5 readmissions for subcutaneous emphysema (1.0%) and 7 re-operations (1.4%) for one case with a broncho-pleural fistula and six cases of pulmonary fistulas. The average postoperative drainage duration was 2.9 (median 2) days, and the average postoperative hospital stay was 7.3 (median 6) days. PAL for >7 days was observed in 24 cases (5.0%), including six cases that required



**Figure 1** Polyglycolic acid sheet was covered around the staple line or suturing point with a pledget sheet and fixed with intrathoracic blood or lavage using a cylinder (Endo Finger<sup>®</sup>) without a cotton stick. Because no fibrin glue was used, careful observation is needed when placing the drainage tube and inflating the lung.

reoperation. The postoperative drainage period for patients in whom the PGA sheet was used was longer than that for patients in whom reinforcement was not needed (3.00 days for PGA sheet *vs.* 2.49 days for no use,  $P=0.0429$ , *t*-test; 3.13 days for suture + PGA sheet *vs.* 2.49 days for no use,  $P=0.0034$ ), although there was no difference between that for patients whom the PGA sheet was used and that for patients in whom the PGA sheet was not used (3.00 days for PGA sheet *vs.* 2.98 days for suture only,  $P=0.9535$ , *t*-test; 3.13 days for suture + PGA sheet *vs.* 2.98 day for suture only,

$P=0.0034$ ). The number of PALs was significantly lower (2–8% *vs.* 1–5%) in groups without a PGA sheet (*Table 2*).

#### **Regression analysis on complications of PAL**

Univariate logistic regression analysis showed that PAL of >7 days was more often observed in male patients [odds ratio (OR) =14.04, 95% confidence interval (CI): 2.92–252.2,  $P=0.0001$ ], smokers (OR =5.774, 95% CI: 1.67–36.3,  $P=0.0032$ ), or patient with interstitial pneumonia



**Table 2** Difference in surgical method and postoperative duration of air leakage (483 cases)

Variable	None (n=103)	Suture only (n=58)	Suture + PGAS (n=217)	PGAS (n=105)	P value
Drainage duration (days)	2.5±0.9	3.0±1.6	3.1±1.9	3.0±2.3	0.0249
Air leakage of >7 days	1 (1.0)	3 (5.2)	18 (8.3)	2 (1.9)	0.0137
Hospital days	6.3±2.9	8.6±12.0	8.6±12.0	6.8±4.6	0.3090

Data are presented as No. (%) or mean ± standard deviation. P values were calculated using the Kruskal-Wallis test. PGAS, PGA sheet patching without fibrin glue.

(OR =4.632, 95% CI: 1.26–13.8, P=0.0241). The multiple logistic regression analysis did not include the use of PGA sheets without fibrin glue, but male sex was identified as a significant risk factor (OR =8.95, 95% CI: 1.40–180.2, P=0.0164) and the presence of interstitial pneumonia was a borderline significant risk factor (OR =3.57, 95% CI: 0.94–11.2, P=0.0608) (Table 3).

## Discussion

PAL is the most common complication of pulmonary resection. Dezube *et al.* reported that 5.4% of 2,384 patients who underwent lobectomies, segmentectomies, or wedge resections had PAL for more than 5 days, 22.5% of them required interventions, and 55% required reoperations (7). Hoeijmakers *et al.* reported that the incidence of PAL for >5 days was 9.0% in 12,382 patients, and intraoperative preventive measures varied between hospitals; in an online survey in the Netherlands, 17.6% of the surgeons used sealants [TachoSil 64.4%, Tissucol (fibrin glue) 76.3%, Neoveil 20.3%, etc.], while 13.2% never used sealants (8).

Pulmonary resection using fibrin glue has been established in the past 20–30 years (2), and a randomized, blinded study showed a lower incidence of alveolar air leakage and shorter duration of chest tube placement and postoperative length of hospital stay. Fibrin glue consists of fibrinogen and thrombin, and its combination with a PGA sheet is thought to be an indispensable agent for pulmonary resection. There have been some reports that compared using PGA sheets with fibrin glue or fibrin glue only; however, no reports have been published to compare PGA sheets with fibrin glue or PGA only (9). Sakai *et al.* reported that a method using PGA and fibrin glue showed higher bursting pressures than a method using ORC mesh and fibrin glue, ORC mesh only, or fibrin glue alone (5). However, a general concern with fibrin glue is the transmission of blood-borne diseases. Kawamura *et al.* reported a 20% transmission rate of human parvovirus B19

as a potential pathogen in immunocompromised hosts (10).

Kawai *et al.* reported a better method of combining PGA sheets with fibrin glue, with a postoperative drainage period of 3.1–4.67 days, and the frequency of air leaks for >7 days was 13.5% (17/126) (11). Kawashima *et al.* reported the feasibility of autologous fibrin glue with a postoperative drainage period of 3.17–3.23 days, and PAL was observed in 12.8–16.7% of cases (12). In the National Clinical Database in Japan, postoperative PAL of >7 days has been reported in 4.5–5.3% of cases (13). In the present cases, the frequency of PAL for >7 days was 5.0% (24/483), which may be different considering whether the pleural defect was sutured or not. We usually suture pleural defects in which an air leak is observed and possibly thread the edge of the pleura to the opposite pleura to shut the air leak point with a pledget sheet. This might be useful to seal air leaks, although it affects postoperative pulmonary function to a lesser extent than that of the PGA patch to the pleural defect with fibrin glue. However, air leakage was not observed at inflation pressures >20 cmH<sub>2</sub>O, and postoperative air leakage was sometimes observed after extubation. When postoperative air leakage occurs, a PGA sheet may be useful to patch or accelerate adhesion. In some cases of reoperation for PAL, the PGA sheet was not shifted or removed but attached to the pulmonary parenchyma, and the air leak was conducted just under the PGA sheet.

Recently, a linear staple device with bioabsorbable PGA was used for pulmonary wedge resection with emphysema, and postoperative air leakage following pulmonary lobectomy was significantly less frequent in the stapler with PGA group than in the stapler-only group (14).

In surgery for primary spontaneous pneumothoraces, a PGA patch after bullectomy was associated with lower rates of postoperative recurrence and PAL than the non-PGA approach in 1,095 patients, as reported in a systemic review (15). Ozawa *et al.* reported that the recurrence rate of covering PGA sheets after bullectomy was less than that of covering ORC mesh (post-drainage period, 2.4±1.0 days). In

**Table 3** Probability for prolonged drainage period (total 483 cases)

Variables	n	Univariate LR		Multivariate LR	
		OR (95% CI)	P value	OR (95% CI)	P value
Sex					
Female	175	1	0.0001	1	0.0164
Male	308	14.04 (2.92–252.2)		8.95 (1.40–180.2)	
Age (years)					
≤71	245	1	0.7292		
≥72	238	1.156 (0.51–2.68)			
Smoker					
Never	160	1	0.0032	1	0.7121
Smoker	323	5.774 (1.67–36.3)		1.36 (0.31–10.0)	
COPD					
–	411	1	0.0666	1	0.2987
+	72	2.496 (0.93–6.03)		1.68 (0.61–4.26)	
IP (fibrosis)					
–	460	1	0.0241	1	0.0608
+	23	4.632 (1.26–13.8)		3.57 (0.94–11.2)	
Surgery					
Segmentectomy	96	1	0.3275		
Lobectomy	387	1.779 (0.60–7.64)			
Surgical site					
Upper lobe	260	1	0.4210		
Middle/lower	223	1.401 (0.61–3.25)			
PGA sheet					
–	159	1	0.0659	1	0.1027
+	324	2.549 (0.94–8.88)		2.36 (0.85–8.41)	

LR, logistic regression; OR, odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; IP, interstitial pneumonia; PGA, polyglycolic acid.

these cases, no fibrin glue was used after lung resections, such as bullectomies (6). Fibrin glue is not necessarily required to fix the PGA sheet and prevent pulmonary fistulas. Pulmonary resection without fibrin glue could be considered an alternative method, although there might be some points to note: (I) the interlobular fissure should be separated to a depth that does not damage the pleura of the remaining pulmonary lobe; (II) a stapler device of appropriate height should be selected; (III) the interlobular fissure should be divided on the remaining pulmonary lobe's

side to avoid leaving a defect.

This study had some limitations. This study is not a prospective comparative analysis between the use of the fibrin glue group and the without fibrin glue group. This study had a retrospective design, was conducted at a single institute, and had a small sample size. In this study, a comparison between using a PGA sheet with fibrin glue or covering a PGA sheet without suturing pleural defects was not sufficient, as cases that required a suture were present in patients with an important intraoperatively identified

air leak (Table 2). In severe emphysema cases, rupture of the residual lung is sometimes observed even with a lower pressure inflation test, and these cases should be treated with PGA sheet with fibrin glue to avoid postoperative severe subcutaneous emphysema.

## Conclusions

We would not contradict the use of fibrin glue; however, this study concluded that pulmonary resections using PGA sheets without fibrin glue might be tolerable in terms of the postoperative drainage duration and hospital stay.

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional review board of Saku Central Hospital (No. R201907-07) and individual consent for this retrospective analysis was waived.

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