Original Article

Adhesion is a risk factor for postoperative recurrence of spontaneous pneumothorax

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Background: Several risk factors for postoperative recurrence of spontaneous pneumothorax have been reported, but the identified risk factors differed among studies.

Methods: A total of 183 primary spontaneous pneumothorax patients were enrolled in this retrospective study, and the risk factors for postoperative recurrence were evaluated.

Results: Among the patients, more than 80% with ipsilateral postoperative recurrence (IPR) relapsed within 3 years and more than 80% with contralateral postoperative recurrence relapsed within 4 years. Compared with patients without IPR, patients with IPR had significantly more cases with history of pneumothorax (P<0.10), more cases without preoperative drainage (P=0.02), more cases with intraoperative adhesion (P<0.01), greater upward lung volume (P=0.04), more numbers of automatic sutures (P=0.04), and more cases with contralateral recurrence (P<0.01). Furthermore, compared with patients without adhesion, patients with adhesion had significantly older age (P<0.01), and more cases with adhesion on CT images (P<0.01). Patients with adhesion also had significantly greater upward lung volume (P<0.01), more cases that received covering with polyglycolic acid (PGA) sheet covering with fibrin glue (P=0.01), and more cases that received re-do surgery (P=0.04). IPR was significantly more common in the adhesion group (P<0.01), while contralateral postoperative recurrence did not differ significantly between the groups with and without adhesion (P=0.06). Univariate analyses showed that body mass index (BMI) <15.6 kg/m^2 (P<0.01), history of pneumothorax (P=0.01), intraoperative adhesion (P<0.01), upward lung volume >80% (P=0.02), lateral lung volume >80% (P=0.02), 3 fire or more of automatic sutures (P=0.03), and contralateral recurrence (P=0.01) were significant risk factors for IPR. BMI <15.6 kg/m^2 (odds ratio: 20.89; 95% confidence interval: 1.55–280.70; P=0.02) and intraoperative adhesion (odds ratio: 25.58; 95% confidence interval: 1.91–342.39; P=0.01) were identified as risk factors for IPR in a multivariate analysis.

Conclusions: The present findings suggest that low BMI and intraoperative adhesion are risk factors for postoperative recurrence of spontaneous pneumothorax. For such patients, additional intraoperative procedures, such as covering with PGA sheet absorbable oxidized cellulose may be required to reduce postoperative recurrence.

Keywords: Spontaneous pneumothorax; adhesion; postoperative recurrence

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Introduction

Spontaneous pneumothorax can be divided into primary spontaneous pneumothorax (PSP) and secondary spontaneous pneumothorax (SSP). PSP refers to patients with no underlying lung disease, while SSP covers patients with established lung pathology. The annual incidences of PSP were estimated as 18–28/100,000 in men and 1.2–6/100,000 in women (1). In previous studies, SSP was more common than PSP, comprising >60% of cases, and the outcomes of SSP patients were worse than those of PSP patients with higher recurrence rates and longer lengths of hospital stay (2,3).

Sex, young age, no history of smoking, existence of comorbidities, previous surgery for ipsilateral spontaneous pneumothorax, prolonged air leakage after surgery, and no history of pleurodesis were previously identified as risk factors for postoperative recurrence of spontaneous pneumothorax (4-7). Meanwhile, additional intraoperative procedures, such as coverage with polyglycolic acid (PGA) sheet or absorbable sheet with glucose solution for pleural coating, were shown to have potential for reducing postoperative recurrence (8-10).

In the present study, we retrospectively evaluated the risk factors for postoperative recurrence in PSP patients who received surgery in the 15-year period from 2008 to 2022. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1127/rc).

Methods

Patients

Among 280 spontaneous pneumothorax patients who received surgery at Kanazawa Medical University between 2008 and 2022, 8 patients without sufficient data were excluded, 89 SSP patients excluded, and the remaining 183 patients were enrolled in this retrospective study (*Figure 1*). The study was conducted in accordance with the principles of the Declaration of Helsinki (as revised in 2013). The Institutional Review Committee of Kanazawa Medical University approved the study protocol (approval No. I800), and all patients provided written informed consent.

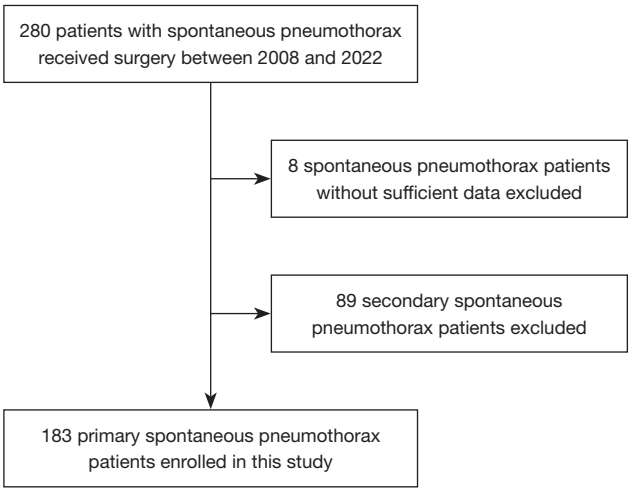

Figure 1 Flow diagram of the patient selection for the study.

Data including clinical characteristics such as sex, age, body mass index (BMI), smoking history, prognostic nutrition index (PNI), season of onset, location of bulla, length of preoperative drainage, adhesion on computed tomography (CT) images, and lung volume on chest roentgen images were collected. Smoking history was assessed using the Brinkman index, calculated as the number of cigarettes smoked per day multiplied by the number of years of smoking (11). PNI was calculated by combining the serum albumin level and the total peripheral lymphocyte count in the peripheral blood (12,13). Season was categorized into four periods: spring, March to May; summer, June to August; autumn, September to November; and winter, December to February. Collapsed lung volumes on a chest X-ray were calculated as shown in *Figure 2*. Upward lung volume was calculated as the lung diameter divided by the hemithorax diameter (*Figure 2A*), and lateral lung volume was calculated as the lung diameter divided by the hemithorax diameter at the level of the cavo-atrial junction (*Figure 2B*).

Highlight box

Key findings
- Low body mass index and intraoperative adhesion are risk factors for postoperative recurrence of spontaneous pneumothorax.

What is known and what is new?
- History of pneumothorax may induce adhesion formation.
- Adhesion may be a landmark for a trend toward recurrence.

What is the implication?
- For such patients, additional intraoperative procedures, such as covering with polyglycolic acid sheet or absorbable oxidized cellulose may be required to reduce postoperative recurrence.

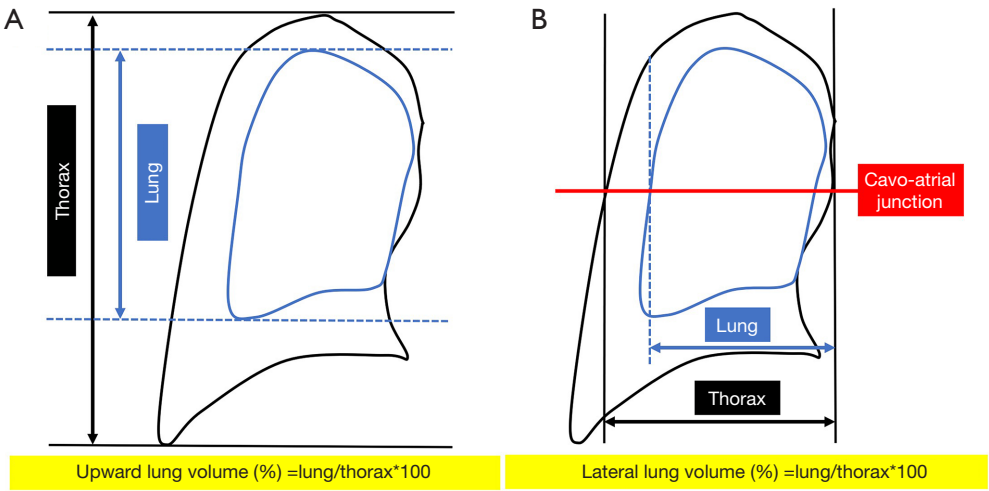

Figure 2 Formulas for calculation of collapsed lung volumes on chest X-rays. (A) Upward lung volume was calculated as the lung diameter divided by the hemithorax diameter; (B) lateral lung volume was calculated as the lung diameter by the hemithorax diameter at the level of the cavo-atrial junction.

Operative findings and factors

Data for intraoperative findings such as air leakage and adhesion, number of patients who received bullectomy, number of automatic sutures, number of patients who received covering, types of covering, and number of patients who received re-do surgery were collected. Types of covering were divided into four categories: absorbable oxidized cellulose with autologous blood or fibrin glue; PGA sheet with saline solution; fibrin glue only; and PGA sheet with fibrin glue. All cases were performed by 3-port video-assisted thoracic surgery. If there is no leak, the drain is removed the next day, and patients were often discharged from the hospital 3 days after surgery. There was an outpatient examination around 10 days after the surgery, and if there were no problems, the treatment was completed.

Statistical analysis

Pearson's chi-square test of independence was used to compare the frequencies of the variables. Cumulative postoperative recurrence was calculated by the Kaplan-Meier method. Cut-off values for the continuous factors associated with postoperative recurrence were calculated using receiver operating characteristic (ROC) curve analyses and used to perform risk analyses. Risk factors for postoperative recurrence were analyzed using Cox proportional hazards regression. A multivariate analysis was performed for the factors that showed significant differences in the univariate analyses. All statistical analyses were two-sided, with the level of accepted statistical significance set at $P<0.05$. The statistical analyses were performed using JMP software v13.2 (SAS Institute Inc., Cary, NC, USA).

Results

Patient characteristics

Comparisons of the PSP patient characteristics between with and without ipsilateral postoperative recurrence (IPR) are shown in *Table 1*. Compared with patients without IPR, patients with IPR had significantly more cases with history of pneumothorax ($P<0.01$), more cases without preoperative drainage ($P=0.02$), more cases with intraoperative adhesion ($P<0.01$), greater upward lung volume ($P=0.04$), more numbers of automatic sutures ($P=0.04$), and more cases with contralateral recurrence ($P<0.01$).

Comparisons of the patient characteristics between patients with and without intraoperative adhesion are shown in *Table 2*. Compared with patients without adhesion, patients with adhesion had significantly older age ($P<0.01$), and more cases with adhesion on CT images ($P<0.01$). Patients with adhesion also had significantly greater upward lung volume ($P<0.01$), more cases that received covering with PGA sheet covering with fibrin glue ($P=0.01$), and more cases that received re-do surgery ($P=0.04$). IPR was significantly more common in the adhesion group ($P<0.01$),

Table 1 Comparison of patient characteristics primary spontaneous pneumothorax with or without ipsilateral postoperative recurrence

Variables	Ipsilateral postoperative recurrence (n=10)	No recurrence (n=173)	P value
Gender (male/female), n	10/0	156/17	0.29
Age (years), median [range]	19 [16–24]	21 [12–83]	0.19
BMI (kg/m^2), median [range]	18.1 [13.5–20.1]	19.1 [12.4–26.1]	0.07
Brinkman index, median [range]	0 (0)	0 [0–640]	0.05
PNI, median [range]	53.0 [43.4–60.0]	53.0 [40.7–69.8]	0.43
History of pneumothorax, n (%)	7 (70.0)	50 (28.9)	<0.01
Preoperative no-drainage cases, n (%)	3 (30.0)	15 (8.7)	0.02
Preoperative drainage length (days), median [range]	4.5 [2–8]	3 [0–16]	0.47
Simultaneous bilateral pneumothorax, n (%)	0	4 (2.3)	0.62
Onset season (Spring/Summer/Autumn/Winter), n	4/2/2/2	45/42/44/42	0.81
Location of bulla (RUL/RML/RLL/LUL/LLL), n	5/0/0/5/0	74/2/4/92/1	0.96
Bilateral bulla on CT, n (%)	6 (60.0)	89 (51.4)	0.59
Preoperative air leakage, n (%)	5 (50.0)	77 (44.5)	0.73
Adhesion on images, n (%)	4 (40.0)	35 (20.2)	0.13
Intraoperative air leakage, n (%)	3 (30.0)	57 (32.9)	0.84
Intraoperative adhesion, n (%)	7 (70.0)	46 (26.6)	<0.01
Upward lung volume (%), median [range]	83.4 [52.0–94.1]	76.4 [38.6–96.2]	0.04
Lateral lung volume (%), median [range]	83.8 [31.0–100]	78.7 [17.6–100]	0.29
Number of automatic sutures, median [range]	2.5 [1–4]	2 [1–5]	0.04
Patients received covering, n (%)	8 (80.0)	147 (84.9)	0.68
Absorbable oxidized cellulose	5 (50.0)	98 (56.6)	0.68
PGA sheet only	2 (20.0)	12 (6.9)	0.13
Fibrin glue only	1 (10.0)	7 (4.0)	0.37
PGA sheet + fibrin glue	0 (0)	31 (17.9)	0.14
Number of patients received re-do surgery, n (%)	0 (0)	4 (2.3)	0.62
Contralateral recurrence, n (%)	3 (30.0)	11 (6.4)	<0.01

BMI, body mass index; PNI, prognostic nutrition index; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; CT, computed tomography; PGA, polyglycolic acid.

while contralateral postoperative recurrence did not differ significantly between the groups with and without adhesion (P=0.06).

Univariate and multivariate analyses

The risk factors for IPR were analyzed (*Table 3*). The cut-off values for factors associated with recurrence were calculated using ROC curve analyses. The following cut-off values were determined: age, 25 years; Brinkman index, 0; BMI, 15.6 kg/m^2; PNI, 54.8; upward lung volume, 80.0%; lateral lung volume, 80.0%; and number of automatic sutures, 3. Univariate analyses showed that BMI (P<0.01), history of pneumothorax (P=0.01), intraoperative adhesion (P<0.01), upward lung volume (P=0.02), lateral lung volume (P=0.02), and contralateral recurrence (P=0.01) were significant risk factors for IPR. BMI <15.6 kg/m^2 (odds ratio: 20.89; 95% confidence interval: 1.55–280.70; P=0.02) and intraoperative

Table 2 Comparison of patient characteristics between with or without intraoperative adhesion

Variables	Intraoperative adhesion (n=53)	Non-adhesion (n=130)	P value
Gender (male/female), n	48/5	118/12	0.96
Age (years), median [range]	25 [12–58]	20 [14–83]	<0.01
BMI (kg/m^2), median [range]	19.2 [12.4–26.0]	19.0 [12.5–26.1]	0.67
Brinkman index, median [range]	0 [0–640]	0 [0–480]	0.06
PNI, median [range]	52.9 [43.4–60.6]	53.0 [40.7–69.8]	0.41
History of pneumothorax, n (%)	21 (39.6)	36 (27.7)	0.11
Preoperative no-drainage cases, n (%)	6 (11.3)	12 (9.2)	0.66
Preoperative drainage length (days), median [range]	3 [0–12]	3.5 [0–16]	0.14
Simultaneous bilateral pneumothorax, n (%)	0 (0.0)	4 (3.1)	0.19
Onset season (Spring/Summer/Autumn/Winter), n	12/13/12/16	37/31/34/28	0.61
Location of bulla (RUL/RML/RLL/LUL/LLL), n	24/1/3/25/0	55/1/1/72/1	0.23
Bilateral bulla on CT, n (%)	31 (58.5)	64 (49.2)	0.25
Preoperative air leakage, n (%)	25 (47.2)	57 (43.8)	0.68
Adhesion on images, n (%)	36 (67.9)	3 (2.3)	<0.01
Intraoperative air leakage, n (%)	17 (32.1)	43 (33.1)	0.89
Upward lung volume (%), median [range]	82.9 [55.9–96.2]	74.3 [38.6–93.7]	<0.01
Lateral lung volume (%), median [range]	79.7 [17.9–100]	79.6 [17.6–100]	0.69
Number of automatic sutures, median [range]	2 [1–4]	2 [1–5]	0.14
Patients received covering, n (%)	46 (86.8)	109 (83.9)	0.61
Absorbable oxidized cellulose	25 (47.2)	78 (60.0)	0.11
PGA sheet only	4 (7.5)	10 (7.7)	0.97
Fibrin glue only	2 (3.8)	6 (4.6)	0.80
PGA sheet + fibrin glue	15 (28.3)	16 (12.3)	0.01
Patients received re-do surgery, n (%)	3 (5.7)	1 (0.7)	0.04
Ipsilateral recurrence, n (%)	7 (13.2)	3 (2.3)	<0.01
Contralateral recurrence, n (%)	1 (1.9)	13 (10.0)	0.06

BMI, body mass index; PNI, prognostic nutrition index; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; CT, computed tomography; PGA, polyglycolic acid.

adhesion (odds ratio: 25.58; 95% confidence interval: 1.91–342.39; P=0.01) were identified as risk factors for IPR in a multivariate analysis.

Postoperative recurrence rate

The ipsilateral and contralateral postoperative recurrence rates are shown in *Figure 3*. More than 80% of spontaneous pneumothorax patients with IPR relapsed within 3 years. More than 80% of spontaneous pneumothorax patients with contralateral postoperative recurrence relapsed within 4 years.

Discussion

In the present study, we retrospectively evaluated the risk factors for IPR in PSP patients who received surgery in the 15-year period from 2008 to 2022. Low BMI and

Table 3 Univariate analysis and multivariate analysis of risk factor for ipsilateral postoperative recurrence

Factor	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Male	NA					
Age <25 years	6.41	0.79–51.76	0.08			
BI =0	NA					
BMI <15.6 kg/m^2	8.20	2.05–32.80	<0.01	20.89	1.55–280.70	0.02
PNI <54.8	5.41	0.67–43.73	0.11			
History of pneumothorax	5.73	1.42–23.08	0.01	2.60	0.48–13.95	0.26
Intraoperative air leakage	0.87	0.21–3.49	0.84			
Intraoperative adhesion	6.44	1.59–25.96	<0.01	25.58	1.91–342.39	0.01
Upward lung volume >80%	5.88	1.21–28.54	0.02	23.38	0.72–755.84	0.07
Lateral lung volume >80%	4.67	1.25–17.37	0.02	2.07	0.29–14.76	0.46
Bilateral bullae	1.41	0.38–5.19	0.60			
Green or black	1.24	0.25–6.14	0.79			
3 fire or more	3.94	1.08–14.37	0.03	3.73	0.71–19.47	0.11
Absorbable oxidized cellulose	0.76	0.21–2.74	0.68			
PGA sheet only	3.35	0.63–17.58	0.15			
Fibrin glue	2.63	0.29–23.78	0.38			
PGA sheet + fibrin glue	NA					
Contralateral recurrence	6.31	1.43–27.83	0.01	20.15	0.95–425.74	0.05

OR, odds ratio; CI, confidence interval; NA, not available; BI, Brinkman index; BMI, body mass index; PNI, prognostic nutrition index; PGA, polyglycolic acid.

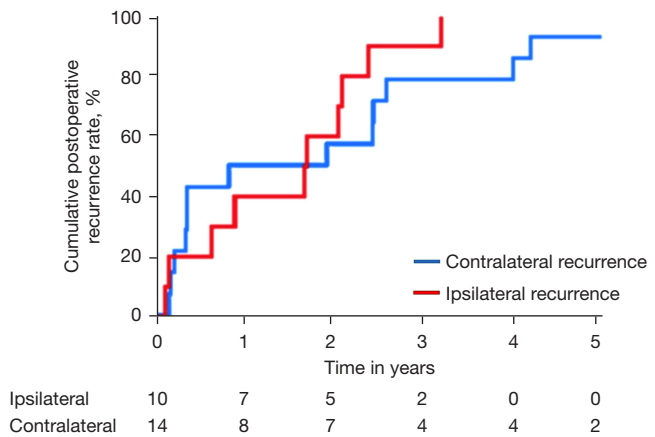

Figure 3 Postoperative recurrence rates. More than 80% of spontaneous pneumothorax patients with ipsilateral postoperative recurrence relapsed within 3 years. More than 80% of spontaneous pneumothorax patients with contralateral postoperative recurrence relapsed within 4 years.

intraoperative adhesion were identified as significant risk factors for IPR. Although low BMI has been previously reported as a risk factor of recurrence in PSP patients, one possible explanation has been reported that low BMI show unbalanced physical development, and this might induce the increase of chest negative pressure, and increase the risk of bleb or bulla formation and pneumothorax (14).

Intraoperative adhesion was identified as risk factors for IPR in the present study. Although history of pneumothorax has been reported as a risk factor of recurrence (6), adhesion has not been reported as a risk factor of recurrence, previously. Because history of pneumothorax may induce adhesion formation, adhesion may be a landmark for a trend toward recurrence. Actually, patients with IPR had significantly more history of pneumothorax and had poorer lung collapse rate due to the presence of adhesions in this study. This result is the new finding for risk factor of recurrence of pneumothorax.

Although young age was previously reported to be a risk factor for postoperative recurrence in PSP patients (5), age was not identified as a significant risk factor for postoperative recurrence in PSP patients in the present study. However, young age might be significant risk factor for postoperative recurrence as the total number of pneumothorax patients increases because postoperative recurrence did not occur in patients older than 25 years in the present study.

Female sex was previously reported to be a risk factor for recurrence of spontaneous pneumothorax (3,4,15). In the present study, sex was not identified as a significant risk factor for postoperative recurrence because postoperative recurrence did not occur in female patients and thus the significance of a difference between the sexes could not be analyzed. The present study was performed at a single institution and the study population was relatively small. The number of female patients with postoperative recurrence may increase as the total number of pneumothorax patients increases.

Additional intraoperative procedures were reported to show potential for reducing postoperative recurrence (8-10). Although coverage with PGA sheet was reported as association with lower recurrence rate, PGA sheet covering with or without fibrin glue was not identified as a significant factor for postoperative recurrence in the present multivariate analysis. However, PGA sheet covering with fibrin glue still has the potential to prevent postoperative recurrence of PSP because patients with ipsilateral recurrence did not receive PGA sheet covering with fibrin glue in the present study (data not shown). Furthermore, covering with absorbable oxidized cellulose with autologous blood or fibrin glue was not identified as a significant factor for postoperative recurrence in the present study. Meanwhile, an absorbable sheet with glucose solution for pleural coating was previously identified as a significant factor for prevention of postoperative recurrence in spontaneous pneumothorax patients (10). Other report showed that there are not significant differences in postoperative pneumothorax recurrence between coverage with PGA sheet and with oxidized cellulose (16). Because oxidized cellulose dissolves more quickly and has lesser foreign-body inflammatory reaction compared with PGA sheet (17,18), oxidized cellulose might be lesser risk of adhesion at the time of re-operation, but future consideration is required.

The present study had several limitations. First, the study was retrospective in nature and potentially included unobserved confounders and/or selection biases. Second, the study was performed at a single institution and the study population was relatively small.

Conclusions

Our findings identified low BMI and intraoperative adhesion as risk factors for postoperative recurrence in spontaneous pneumothorax patients. For such patients, additional intraoperative procedures, such as covering with PGA sheet or oxidized cellulose may be required to reduce postoperative recurrence.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1127/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1127/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1127/coif). The authors have no conflicts of interest to declare.

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 principles of the Declaration of Helsinki (as revised in 2013). The institutional review committee of Kanazawa Medical University approved the study protocol (approval No. I800), and all patients gave written informed consent.

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