



Interpleural distance predicts persistent air leak after initial primary spontaneous pneumothorax

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Background: Initial surgical intervention for a first episode of primary spontaneous pneumothorax (PSP) is controversial. However, if air leak persists after initial drainage, surgical treatment is recommended. Therefore, we investigated risk factors for persistent air leak (PAL) in patients with a first episode of PSP.

Methods: We retrospectively analyzed 122 patients with a first episode of PSP between January 2011 and April 2019. PAL was defined as air leak lasting 72 hours or longer. Early admission was defined hospital admission within 24 hours of symptom onset. Three methods were used to estimate pneumothorax size on chest X-rays taken at admission: interpleural distance, apex-cupola distance, and Light index.

Results: Among 122 patients, 55 developed PAL (PAL group) and 67 did not (non-PAL group). The size of pneumothorax was significantly larger in the PAL group than in the non-PAL group in all three methods of assessment ($P < 0.001$). Early hospital admission was significantly associated with PAL ($P = 0.026$). Logistic regression analysis revealed that the odds ratio for PAL per unit increase in pneumothorax size evaluated with the interpleural distance was 1.304 ($P < 0.001$). Multivariate logistic regression analysis showed that interpleural distance at the hilum and early admission ($P < 0.001$, $P = 0.008$, respectively) were independent predictors of PAL in patients with a first episode of PSP.

Conclusions: In our study, we demonstrated that the interpleural distance at the hilum is a simple and effective predictor of PAL in patients with a first episode of PSP. Our data may help decision-making for initial surgical treatment in these patients.

Keywords: Primary spontaneous pneumothorax (PSP); persistent air leak (PAL); pneumothorax size; video-assisted thoracoscopic surgery (VATS); first episode

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Introduction

Primary spontaneous pneumothorax (PSP) is defined as an abnormal accumulation of air in the pleural cavity without apparent underlying pulmonary disease. It typically occurs in adolescents who are tall, thin, and who smoke (1). PSP has a high recurrence rate of up to 55% with conservative

treatment. Surgical approaches such as open thoracotomy, transaxillary mini-thoracotomy, and video-assisted thoracoscopic surgery (VATS) are effective and reduce the recurrence rate to 0 to 10% (1-3). Among the three surgical approaches, VATS is recommended in the British Thoracic Society (BTS) guidelines and is commonly used because it is associated with less surgical pain and shorter hospital

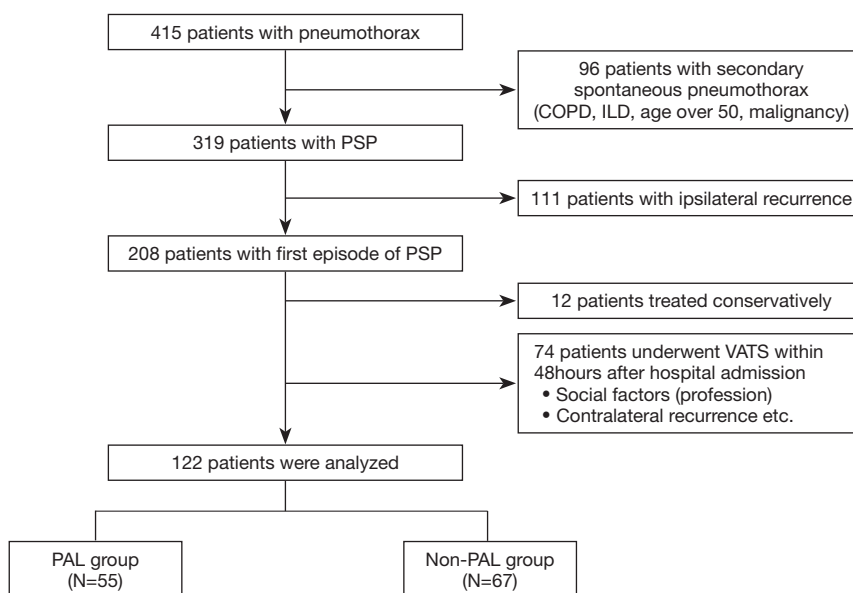


Figure 1 Flow chart of enrolled patients with pneumothorax and treatment decisions. COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease; PSP, primary spontaneous pneumothorax; VATS, video-assisted thoracic surgery; PAL, persistent air leak.

stays than other methods (4). Although, VATS treatment has been demonstrated to be safe, to prevent recurrence (5), and to result in high patient satisfaction of the procedure (6), initial VATS treatment is controversial in patients with a first episode of PSP (7,8).

In the clinical setting, a stepwise approach with an escalating treatment algorithm is followed, in accordance with the guidelines of the BTS and the American College of Chest Physicians (ACCP) (4,9). Initial drainage should be considered if the size of the PSP is “large”; however, what constitutes a large PSP is different in each guideline. BTS guidelines define large as >2 cm of interpleural distance at the hilum, whereas ACCP guidelines define large as ≥3 cm of apex-cupola distance. These guidelines recommend that patients with persistent air leak (PAL) after 3 to 5 days of drainage intervention and those with a second episode of pneumothorax should be treated with surgery.

PAL causes prolonged hospital stays, which burdens patients and consumes medical resources. In addition, there is a report that prolonged delay of intervention decreases the effectiveness of VATS (10). Therefore, in patients with a high risk of PAL, early VATS treatment without waiting more than 3 days for failure of drainage treatment may be a good option. In this study, we used easy and simple methods to estimate pneumothorax size, defined as the distance between the chest wall and collapsed lung according to BTS

and ACCP guidelines,

The purpose of this study was to investigate the risk factors for PAL in patients with a first episode of PSP. This information may promote more effective management of PSP.

Methods

Patients

From January 2011 to April 2019, 415 patients were admitted to Saiseikai Fukuoka General Hospital for treatment of pneumothorax. Ninety-six patients with underlying pulmonary disease (e.g., malignancy, interstitial lung disease, chronic obstructive pulmonary disease) or age over 50 and 111 patients with ipsilateral recurrent pneumothorax were excluded from this study (4). The remaining 208 had a first episode of PSP with initial drainage treatment. Seventy-four patients who underwent surgery within 48 hours after admission because of social factor, contralateral pneumothorax or spontaneous hemothorax and 12 patients who were treated conservatively were excluded; the remaining 122 patients were retrospectively analyzed (Figure 1). Early admission defined as hospital admission within 24 hours of symptom onset (e.g., chest pain, dyspnea, etc.); late admission defined as admission more than a day after symptom onset. The size of PAL was defined as any degree of air leakage lasting more than 72 hours. Low body mass index (BMI)

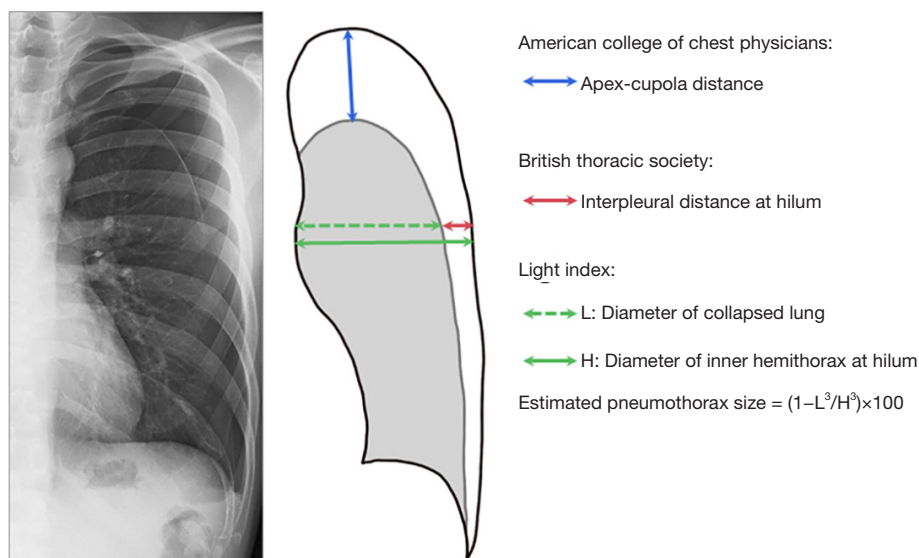


Figure 2 Three methods for estimating the size of pneumothorax.

was defined as BMI less than 18.5 kg/m^2 , consistent with the World Health Organization classification of underweight (11). The study protocol was approved by the institutional review board of Saiseikai Fukuoka General Hospital (IRB approval no., 2019-7-2).

Pneumothorax size

The initial chest X-ray (CXR) was separately examined by two thoracic surgeons (T.A., T.K.) and one resident (A.H.). If the independent assessments did not match, the CXR were reviewed by all three investigators together to reach a consensus. The estimated pneumothorax size on CXR taken at admission was assessed with the following three methods: 1. interpleural distance at the hilum, in accordance with BTS guidelines (4); 2. apex–cupola distance, in accordance with ACCP guidelines (9); and 3. Light index, calculated from the ratio of the diameter of the collapsed lung to that of the hemithorax (12) (*Figure 2*). The estimated pneumothorax percentage = $(1 - L^3/H^3) \times 100$, where H = hemithorax diameter and L = diameter of collapsed lung (*Figure 2*).

Treatment of PSP

Initial chest tube drainage was performed with 8-Fr small-bore aspiration catheters (Aspiration Kit®) or 16-Fr to 20-Fr trocar tubes by pulmonologists or thoracic surgeons.

The chest tube was removed within 24 hours of a negative clamp test. Absence of air leak was defined as no detectable air bubble with deep breathing or coughing and complete lung expansion on CXR. The patients were allowed to leave the hospital after tube removal; however, some patients underwent VATS regardless of the absence of air leaks because of patient preference or a history of contralateral pneumothorax. Some patients refused surgery and therefore did not undergo VATS. VATS was performed with single- or 3-port thoracoscopic technique under general anesthesia with single-lung ventilation. Wedge resection was performed with an endoscopic stapler. The staple line was covered with a polyglycolic acid sheet (NEOVEIL; Gunze, Ayabe, Japan). Chest tubes (20-Fr) were placed routinely after surgery. Neither chemical pleurodesis nor pleurectomy was performed during or after VATS. Postoperative chest tubes were removed within 24 hours of confirmation of the absence of air leaks and full expansion of lung. Patients left the hospital the day after chest tube removal.

Statistical analysis

Clinicopathological variables of patients with versus without PAL were compared with independent-samples Student's *t* test for continuous variables and Fisher's exact test for categorical variables. Odds ratios with 95% confidence intervals were estimated with logistic regression analyses. Univariate and multivariate analyses were performed

Table 1 Characteristics of patients divided according to presence of persistent air leak after intercostal drainage

Factors	Non-PAL group, n=67	PAL group, n=55	P value	All, n=122
Age (years)	28.1±8.9	27.9±9.0	0.934	28.0±8.9
Sex (male), n (%)	60 (89.6)	46 (83.6)	0.422	106 (86.9)
Height (cm)	171.6±7.3	170.3±8.0	0.350	171.0±7.6
Weight (kg)	59.6±10.4	57.0±8.9	0.147	58.4±9.8
BMI (kg/m ²)	20.3±3.1	19.6±2.2	0.168	20.4±2.8
Low BMI status (BMI <18.5 kg/m ²), n (%)	21 (31.3)	20 (36.4)	0.570	41 (33.6)
Smoking (yes), n (%)	36 (53.7)	34 (61.8)	0.462	70 (57.4)
Side of pneumothorax (left), n (%)	36 (53.7)	26 (47.3)	0.584	62 (50.8)
Initial drainage chest tube (aspiration catheter), n (%)	37 (55.2)	27 (49.1)	0.585	64 (52.5)
Hospital admission within 24 hours of symptom onset (Yes), n (%)	21 (31.3)	29 (52.7)	0.026	50 (41.0)
Hospital stay (days)	4.0±1.3	7.4±2.7	<0.001	5.5±2.7
Pneumothorax size				
British thoracic society				
Interpleural distance at hilum (cm)	3.2±2.5	5.5±3.3	<0.001	4.3±3.1
American college of chest physicians				
Apex-cupola distance (cm)	6.9±2.8	9.0±3.5	<0.001	7.9±3.3
Light index				
Estimated pneumothorax size (%)	53.9±22.0	73.9±24.4	<0.001	62.9±26.8

Values shown are mean ± standard deviation or number (percentage). PAL, persistent air leak; BMI, body mass index.

with logistic regression models. All statistical analyses were conducted with JMP version 13 software (SAS Institute, Cary, NC, USA). P values <0.05 were considered statistically significant.

Results

Patient characteristics

As shown in *Figure 1*, 122 patients met the criteria for this study, comprising 55 with PAL (PAL group) and 67 without PAL (non-PAL group). The clinical characteristics of both the PAL and non-PAL groups are shown in *Table 1*. Both groups were composed of young adults (mean age: 28.0±8.9 years) with slender body type (BMI=20.4±2.8 kg/m²). Sixty-four patients (52.5%) were treated with 8-Fr small-bore aspiration catheters. There was no significant difference between the PAL and non-PAL groups with respect to smoking history (P=0.462), the side of pneumothorax (P=0.584), BMI (P=0.570), or the

size of initial chest drainage tube (P=0.585). The number of patients admitted within 24 hours of symptom onset was significantly larger in the PAL group (n=29, 52.7%) than in the non-PAL group (n=21, 31.3%; P=0.026). The size of pneumothorax was significantly larger in the PAL group than in the non-PAL group with all three methods of assessment (P≤0.001). Hospital stays were significantly longer in the PAL group than in the non-PAL group (4.0±1.3 vs. 7.4±2.7 days, P≤0.001). Among the 64 patients who underwent VATS, 61 had their chest tube removed on the first postoperative day, two on the second, and one on the third.

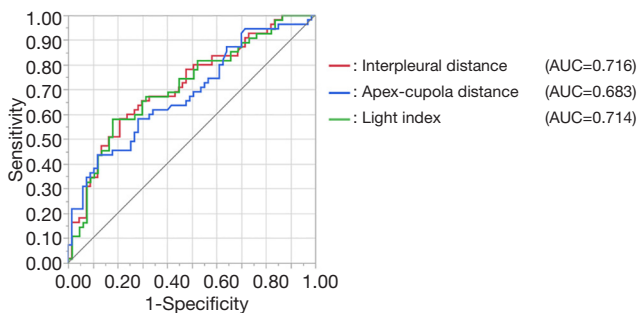
Initial chest tube drainage

We conducted supplementary analysis to compare the characteristics of patients treated with 8-Fr small-bore aspiration catheters (n=64) versus those treated with 16-Fr to 20-Fr trocar tubes (n=58) (*Table S1*). A significantly higher number of the patients treated with aspiration

Table 2 Odds ratios for persistent air leak per unit increase in pneumothorax size

Method of assessing pneumothorax size	OR	(95% CI)	P value
British thoracic society			
Interpleural distance at hilum ^a	1.304	(1.136–1.499)	<0.001
American college of chest physicians			
Apex-cupola distance ^a	1.228	(1.089–1.384)	<0.001
Light index			
Estimated pneumothorax size ^b	1.367	(1.169–1.598)	<0.001

^a, odds ratio per 1-cm increase in distance; ^b, odds ratio per 10% increase in size. OR, odds ratio; CI, confidence interval.

**Figure 3** ROC curve of interpleural distance, apex-cupola distance, and Light index as predictors of persistent air leak. AUC, area under the ROC curve; ROC, receiver operating characteristic.

catheters were never-smokers (n=34, 53.1%), compared with those treated with trocar tubes (n=18, 31.0%; P=0.017). In addition, more female patients were treated with aspiration catheters (n=12, 18.8%), compared with trocar tubes (n=4, 6.9%), though this difference was not significant (P=0.063). The patients treated with aspiration catheters were significantly younger than those treated with trocar tubes (P=0.043). There was no significant difference between groups in the size or side of pneumothorax or in the time from symptom onset to hospital admission.

Pneumothorax size and PAL

Univariate logistic regression analysis revealed that the odds ratios for PAL per unit increase in pneumothorax size according to the BTS (interpleural distance), ACCP (apex-cupola distance), and Light index assessment methods were 1.304, 1.228, and 1.367, respectively (Table 2). Larger

pneumothorax size was associated with a significantly higher risk of PAL. Results of receiver operating characteristic analysis of the studied variables are shown in Figure 3. According to the analysis, the area under the curves of the interpleural distance and Light index were about the same; both were greater than that of the apex-cupola distance. Because measuring the interpleural distance is simple and does not involve calculations (unlike the Light index), we next studied the association between interpleural distance and the risk of PAL.

Interpleural distance as a predictive factor for PAL

Multivariate logistic regression analysis revealed that the following were significant independent predictors of PAL in patients with a first episode of PSP (Table 3): interpleural distance at the hilum and hospital admission within 24 hours of symptom onset (P<0.001, P=0.008, respectively). According to the receiver operating characteristic analysis, the best cutoff value for interpleural distance was 4.3 cm (Figure 3); therefore, we set 4 cm as the cutoff. We classified patients into four groups according to interpleural distance, with distance divided into 2-cm increments. This classification revealed that the larger the interpleural distance, the higher the risk of PAL (Table 4). Multivariate logistic regression analysis revealed that interpleural distance at the hilum greater than 4 cm as well as early hospital admission were independent predictors of PAL in patients with a first episode of PSP (Table S2).

Treatment allocation and recurrence after treatment of first Episode of PSP

Among the 55 patients in the PAL group, eight who refused surgery were treated with drainage alone, whereas 47 underwent VATS (Figure S1). Among the 67 patients in the non-PAL group, sixteen patients underwent VATS despite absence of air leak. Recurrence was more frequent in the drainage-treatment group (15/59, 25.4%) than in the VATS group (6/63; 9.5%). Additionally, among the patients who underwent VATS, recurrence was more frequent in the PAL group (5/16, 31.3%) than in the non-PAL group (1/47, 2.1%) (Figure S1).

Discussion

Surgical intervention is established initial treatment for recurrence of PSP; however, surgical intervention for a first

Table 3 Multivariate logistic regression analysis of risk factors for persistent air leak

Variables	OR	95% CI	P value
Interpleural distance at hilum	1.36*	(1.17–1.57)	<0.001
Hospital admission (early/late)	3.21	(1.36–7.37)	0.008
Sex (male/female)	0.33	(0.09–1.15)	0.081
Smoking (yes/no)	2.28	(0.84–6.16)	0.105
Body mass index (<18.5 kg/m ² /≥18.5 kg/m ²)	1.85	(0.75–4.58)	0.183
Initial drainage chest tube (aspiration catheter/trocar tube)	0.79	(0.34–1.86)	0.600
Side of pneumothorax (left/right)	0.98	(0.43–2.24)	0.966
Age	1.00 [†]	(0.95–1.05)	0.971

*, odds ratio per 1-cm increase in distance; [†], odds ratio per year increase. OR, odds ratio; CI, confidence interval.

Table 4 Relationship between interpleural distance and persistent air leak

Interpleural distance at hilum (cm)	Non-PAL group (n=67), n (%)	PAL group (n=55), n (%)
<2	25 (73.5)	9 (26.5)
2–4	26 (66.7)	13 (33.3)
4–6	9 (39.1)	14 (60.9)
≥6	7 (26.9)	19 (73.1)

Values shown are number (percentage) of patients. PAL, persistent air leak.

episode of PSP remains controversial. Because surgery is recommended for patients with PAL, early surgical treatment can be considered for patients with a high risk of PAL.

Herein, we have shown that interpleural distance was an independent risk factor for PAL. The larger the interpleural distance, the higher the risk of PAL. In addition, hospital admission within 24 hours of symptom onset was a risk factor for PAL.

The finding that the size of pneumothorax was associated with PAL is consistent with two previous studies (13,14). However, unlike previous studies, we estimated the size of pneumothorax not only with the Light index but also with two additional methods, the interpleural distance and apex-cupola distance, which are based on BTP and ACCP guidelines, respectively. The Light index and interpleural distance are both measured at the level of the hilum. Therefore, the finding that the odds ratios and the areas under the curve for the risk of PAL were about the same for these two methods was not surprising. In contrast, the apex-cupola distance was found to be inferior to the other two methods, a finding that may be attributed to adhesions between the lung apex and chest wall resulting

in underestimation of pneumothorax size. The interpleural distance at the level of the hilum is easily measured and pulmonologists are familiar with the definition of “large” pneumothorax described in BTS guidelines. The interpleural distance is therefore the simplest and most useful method for predicting PAL in the clinical setting.

The major problem associated with PAL is that it results in longer hospital stays. Although most air leaks resolve within 7 to 14 days (15), surgical intervention is recommended to reduce the patient’s burden. As expected, our data demonstrated that the length of hospital stay among patients with PAL was 3 days longer than that among patients without PAL. Early surgical treatment of patients with a high risk of PAL would result in shorter hospital stays and benefits for patients.

Our data also provide information for the management of PSP. The BTS guidelines recommend early surgical consultation for patients with PAL. However, in patients with large pneumothorax, the pulmonologist should consult the thoracic surgeon soon after admission without waiting a few days before considering surgical intervention. Waller *et al.* reported that delayed referral to a thoracic surgeon

reduced the success rate of VATS in patients with PAL, a finding that supports our recommendation for early consultation (10).

We also investigated whether the size of the chest tube affected PAL. Whether a pigtail catheter or a large-bore chest tube should be used for drainage is controversial. The size of the catheter used for initial drainage varied according to physician's preference, 8Fr small-bore aspiration catheters tended to be used in young patients, never-smokers, and female patients. However, the size of the chest tube was not a factor in PAL. This finding is consistent with the data from a recent meta-analysis by Chang *et al.*, who found that success rates were similar with the use of a pigtail catheter versus a large-bore chest tube (16).

Another surprising result from our study is that early admission after symptom onset was a risk factor for PAL. In other words, delayed admission increased the success rate of initial drainage treatment. One hypothesis to explain this result is that the amount of air leak might have been smaller among patients with delayed admission than among those with early admission. A smaller amount of air leakage may be more likely to resolve with drainage treatment than larger amounts. Recently, a two-phase (discovery and validation) cohort study demonstrated that a longer time from symptom onset to needle aspiration was associated with treatment success (17). Although the initial treatment approach in the above study differed from that in our study, both findings indicate that the time of symptom onset is an important factor in the treatment of pneumothorax.

We acknowledge that there are several limitations in this retrospective study conducted at a single institution with a small sample size.

The first limitation is that we did not include CT findings in our study. Bullae and blebs are important CT findings that many thoracic surgeons offer VATS because patients with large bullae have a high risk of ipsilateral recurrence of pneumothorax (18,19). In addition, some studies have used the features of bullae on CT to assign lung dystrophy severity scores to determine the indications for PSP treatment (19,20). However, the scoring system is too complicated and prone to observer bias for use in the clinical setting. Moreover, the timing of CT examinations after initial drainage also influences the size of bullae. Therefore, we excluded CT findings from our study.

Nine patients in the present study did not undergo CT scan. No bullae or blebs were detected in 14 cases, whereas 99 patients had some bullae/blebs. Although the statistical power was low, exploratory multivariate analysis

revealed that interpleural distance remained the strongest independent predictor of PAL even when the presence of bullae was included as a factor (data not shown).

The second limitation is that CXRs included both posteroanterior and anteroposterior projections. This difference could affect the quality of pneumothorax size measurement. In addition, it has been reported that CXR evaluation is not an accurate method of measuring pneumothorax size (21). Moreover, CXR is routinely performed in full inspiration. However, chest pain may have prevented full inspiration in some cases, which also may have caused measurement bias. However, in the clinical setting, the priority is not precise measurement of pneumothorax size but rapid decision-making with a simple method based on CXR.

In conclusion, we demonstrated that the interpleural distance at the level of the hilum is a good predictive marker for PAL in patients with a first episode of PSP. This simple and useful method may help promote early referral to thoracic surgeon and decision-making when considering surgical treatment for a first episode of PSP.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/jtd.2020.04.48>). 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. The study protocol was approved by the institutional review board of Saiseikai Fukuoka General Hospital (IRB approval no., 2019-7-2).

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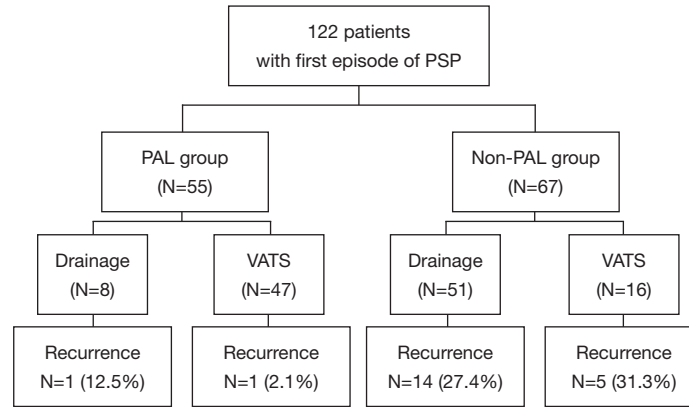


Figure S1 Flow chart of treatment of patients with first episode of primary spontaneous pneumothorax. PSP, primary spontaneous pneumothorax; PAL, persistent air leak; VATS, video-assisted thoracic surgery.

Table S1 Comparison of clinical characteristics according to the type of chest tube

Factors	Aspiration catheter, Group, n=64	Trocar tube, Group, n=58	P value
Age (years)	26.7±7.6	29.5±10.0	0.043
Sex (female), n (%)	12 (18.8)	4 (6.9)	0.063
Low BMI status (BMI <18.5 kg/m ²), n (%)	22 (34.4)	19 (32.8)	0.570
Smoking (No), n (%)	34 (53.1)	18 (31.0)	0.017
Side of pneumothorax (left), n (%)	32 (50.0)	30 (51.7)	1.000
Hospital admission within 24 hours of symptom (Yes), n (%)	38 (59.4)	34 (58.6)	1.000
Hospital stay (days)	5.3±2.6	5.7±2.8	0.368
Pneumothorax size			
British Thoracic Society			
Interpleural distance at hilum (cm)	4.1±2.9	4.5±3.4	0.505
American College of Chest Physicians			
Apex-cupola distance (cm)	7.7±3.2	8.0±3.4	0.586
Light index			
Estimated pneumothorax size (%)	63.1±25.2	62.8±28.7	0.951

Values shown are mean ± standard deviation or number (percentage). BMI, body mass index.

Table S2 Multivariate logistic regression analysis of risk factors for persistent air leak

Variables	OR	95% CI	P value
Interpleural distance at hilum (≥4 cm/<4 cm)	5.30	(2.30–12.22)	<0.001
Hospital admission (early/late)	2.77	(1.20–6.41)	0.017
Sex (male/female)	0.36	(0.10–1.27)	0.112
Smoking (yes/no)	1.79	(0.69–4.64)	0.230
Body mass index (<18.5 kg/m ² /≥18.5 kg/m ²)	1.67	(0.70–4.02)	0.249
Initial drainage chest tube (aspiration catheter/trocar tube)	0.78	(0.34–1.81)	0.564
Side of pneumothorax (left/right)	1.07	(0.47–2.44)	0.868
Age	0.99 [†]	(0.94–1.04)	0.774

[†], odds ratio per year increase. OR, odds ratio; CI, confidence interval.