Impact of Treatment on Cessation of Air Leakage and Recurrence of Spontaneous Pneumothorax: A Case Control Study

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Abstract

Background: Conservative observation with/without oxygen supplementation, aspiration, or tube drainage is selected as an initial treatment for spontaneous pneumothorax. In this study, we have examined the efficacy of initial management for cessation of air leak and prevention of recurrence separately, with consideration of the degree of lung collapse.

Methods: Spontaneous pneumothorax in patients who underwent initial management in our institute between January 2006 and December 2015 were included in this retrospective, single-institutional study. Multivariate analyses were conducted to identify risk factors related to the persistent air leak after initial treatment and those related to ipsilateral recurrence after last treatment.

Results: In the multivariate analysis for predicting persistent air leak after first treatment, repeated episode of ipsilateral pneumothorax ($p = 0.0022$), high degree of lung collapse ($p = 0.032$), and bulla formation ($p < 0.0001$) were the statistically significant risk factors for treatment failure. Recurrence of ipsilateral pneumothorax was observed in 126 cases. In the multivariate analysis for predicting the recurrence, repeated episode of ipsilateral pneumothorax was the significant risk factor ($p = 0.0032$).

Conclusions: Predicting factors for persistent air leak after initial treatment were recurrence of ipsilateral pneumothorax, high degree of lung collapse, and radiological evidence of bullae. The predictive factor for recurrence after the last treatment was recurrence of ipsilateral pneumothorax. Selection of either observational or interventional approach at initial management did not affect the outcomes evaluated. Therefore, because of treatment invasiveness, observation is recommended to be attempted first in cases sans risk factors.

Trial Registration: retrospectively registered

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Introduction

Patients with spontaneous pneumothorax generally have a favourable prognosis, and only rarely develop fatal respiratory distress [1, 2]. Clinical treatment for this disease is commonly well performed; however, standardisation of initial management protocol is required, especially for physicians who are not specialists of this disease. Treatment options performed in initial management comprises of conservative observation with/without oxygen supplementation, aspiration, and tube drainage; but the indication for each of these is different among the published guidelines [3, 4]. Moreover, selection of the initial treatments generally depends on the size of the pneumothorax. Previous reports detailing initial management mainly focused on the comparison between aspiration and tube drainage [5, 6]. Recent reports had referred to the efficacy of conservative observation [7–10].

We have discussed previously about the objectives of the treatments as proper outcomes for the evaluations and proposed that management of air leak and recurrence should be assessed separately [11]. The efficacy of initial treatments has not been well assessed on each outcome (air leak and recurrence, independently). Observation has been considered less effective treatment, mainly based on previous reports of the recurrence [12, 13]. However, initial treatment is essentially considered to be performed for management of air leak [11]. Thus, evaluation of initial treatments is not favourable with only secondary outcome: recurrence. Some reports indicated that observation in specific situations of pneumothorax was safe even for the patients with a high risk of lung collapse [14]. There were some reports that degree of lung collapse in spontaneous pneumothorax has been found to be an independent risk factor of treatment failure [15], although the impact was not clearly examined.

To evaluate appropriate impact of initial treatments and pneumothorax size, related risk factors were not clearly demonstrated. In this study, we retrospectively examined the efficacy of initial management for spontaneous pneumothorax in achieving cessation of air leak and prevention of pneumothorax recurrence separately, with consideration of the degree of lung collapse.

Methods

Ethical statement

This study was approved by the Institutional Review Board of Kansai Medical University (approval date: May 28 3, 2018; approval number: 2017320). The requirement for informed consent was waived because of the retrospective nature of the study.

Study design and population

Spontaneous pneumothorax in patients who underwent initial management in the outpatient clinic or were admitted to our hospital between January 2006 and December 2015 were included and analysed in this retrospective, single-institutional study. Initial treatment was selected by each attending doctor. Patients with primary spontaneous pneumothorax (PSP) and secondary spontaneous pneumothorax (SSP) were included. SSP was defined as pneumothorax in patients with an obvious underlying lung disease or those older than 50 years of age. Patients of first and repeated episodes were included in this study.

Classification of lung collapse

Degree of lung collapse was categorised according to the chest radiographic appearance as low, middle, or high as per the definition proposed by The Japan Society for Pneumothorax and Cystic Lung Disease (JSPCLD) as follows: 1) low: apex is at the same level or higher than the clavicle, 2) high: total or almost total collapse, and 3) middle: the degree between low and high. High and middle degrees of lung collapse defined by JSPCLD are almost equivalent to large pneumothorax defined by the British Thoracic Society

(BTS) and the American College of Chest Physician (ACCP) guidelines [3, 4], and low degree of pneumothorax to small pneumothorax.

Definition of terms

In this report, initial treatments denoted treatments firstly performed for pneumothorax and indicated the following three methods: observation, needle aspiration, or tube drainage. To evaluate efficacy of the initial treatment, “success” and “failure” were defined as follows. When initial treatment achieved lung re-expansion and no lung collapse in following observation, or did not show air leak, the treatment was evaluated as a “success.” When a patient did not achieve stable lung re-expansion, or showed persistent air leak after initial treatment, the treatment was considered as a “failure.” In failure of initial treatments, further treatments were performed to cease air leak. To evaluate success and failure, the durations required for each treatment was not specified in this study, because of retrospective analysis. In some of the successful cases, additional treatments were performed to prevent recurrence even after cessation of air leak. Further, additional treatments included surgery and chemical pleurodesis in addition to the three initial treatments. To evaluate recurrence, last treatment was analysed. When patients achieved success with initial treatment and did not undergo additional treatment for prevention of recurrence, the initial treatment was also counted as the last treatment. When patients needed further treatments to cease air leak after the initial treatment, the initial treatment was recorded as a failure, and the second or third treatment to finally cease air leak (without any additional treatment) was counted as the last treatment. When additional treatment was performed, the final one was counted as the last treatment. Recurrence on the ipsilateral side was only counted as recurrence.

Data collection

The following clinical data and radiological findings were collected from patients’ medical records and chest X-rays: age, sex, smoking history, previous episode of ipsilateral pneumothorax, side of pneumothorax, underlying lung disease, degree of lung collapse, radiological finding of bulla formation or pulmonary fibrosis, intervention for pneumothorax, and recurrence of pneumothorax. Information of the intervention from the initial management was collected along with the patient’s time line as follows: 1) initial treatments; 2) further treatments to cease air leak in cases of failure, including second and third treatments; and 3) additional treatments to prevent recurrence after cessation of air leak. Recurrence-free interval was defined as the period between the day of the last treatment and the day of recurrence. When the patient was managed by only observation and cured, recurrence-free interval was defined as the period of radiographically evaluated day between full expansion of the lung and the day of recurrence.

Statistical analysis

Analysis of treatment efficacy to manage air leaks was performed by initial treatment and that of recurrence was performed by last treatments. Continuous variables were reported as a mean with standard deviation, and categorical variables were expressed as number of patients. Statistical analysis was performed to investigate the risk factors for persistent air leak on initial treatment and those for recurrence of ipsilateral pneumothorax after the last treatment. The Wilcoxon rank-sum test and the Fisher exact test were used to compare continuous data and categorical data, respectively. Logistic regression analysis was used in univariate and multivariate analyses. Factors with a p-value < 0.2 in univariate analyses were used in multivariate analyses. A Cox proportional hazard model was used to estimate the recurrence risk. The cumulative recurrence rate was estimated by the Kaplan–Meier method. A p-value < 0.05 was considered statistically significant. All statistical analyses were performed using JMP software version 13.2.1 (SAS Institute, Inc., Cary, NC, USA).

Results

Study subjects

This study included 668 episodes of 522 patients. Treatments performed for the 668 pneumothoraces and evaluation of the initial treatments are summarised in Fig. 1. Of them, 198 events were initially treated by observation, 22 by aspiration, and 448 by tube drainage, and pneumothorax was cured in 170 (85.9%), 18 (81.8%), and 289 (64.5%) events, respectively. Success of the aspiration group required a maximum of 2 times of aspiration. When the air leak persisted after the initial treatment, further treatment was performed to manage the air leak. Except in 2 patients who died due to exacerbation of pneumonitis and progression of malignant tumor, air leak ceased by initial or further treatments. After the pneumothorax was cured, additional treatments, surgery and pleurodesis, were performed for 47 and 11 patients, respectively, to prevent recurrence.

Initial treatments to manage air leak

Characteristics of the 3 groups classified according to the initial treatments were shown in Table 1. Clinical backgrounds of the 3 groups were significantly different in age ($p < 0.0001$), sex ($p < 0.0001$), smoking history ($p < 0.0001$), type of spontaneous pneumothorax ($p < 0.0001$), degree of lung collapse ($p < 0.0001$), and bulla formation ($p = 0.0013$). Aspiration or tube drainage was selected as initial treatment in most cases (88.3%) of high and middle degrees of pneumothorax, and observation was selected as the initial treatment in cases (73.3%) of low degree of pneumothorax.

Results of univariate and multivariate analyses for predicting the cessation of air leak by initial treatment are shown in Table 2. In the univariate analysis, age ($p < 0.0001$), sex ($p = 0.049$), smoking history ($p < 0.0001$), repeated episode of ipsilateral pneumothorax ($p < 0.0001$), type of spontaneous pneumothorax ($p < 0.0001$), high and middle degrees of lung collapse ($p < 0.0001$ and 0.0009, respectively), and treatment option of tube drainage as initial treatment ($p < 0.0001$) were statistically significant. However, in the multivariate analysis, repeated episode of ipsilateral pneumothorax ($p = 0.0022$), high degree of lung collapse ($p = 0.032$), and bulla formation ($p < 0.0001$) were the statistically significant risk factors for treatment failure. No treatment showed a significant difference for the outcome in multivariate analysis.

Recurrences after the last treatments

Recurrences of ipsilateral pneumothorax after the last treatments are shown in Table 3. Recurrence of ipsilateral pneumothorax was observed in 126 cases; 18 in the observation group, 3 in the aspiration group, 67 in the tube drainage group, 15 in the pleurodesis group, and 23 in the surgery group. Mean follow-up period was 18.4 months (range: 0-124 months). Figure 2 shows the Kaplan-Meier curve of recurrence according to the last treatments in all 666 pneumothoraces; the curve of the recurrence rate in the observation group overlaps with that in the surgery group. Statistical analysis by the log-rank test showed a significant relationship between the 2 groups of observation and tube drainage ($p = 0.0029$), tube drainage and surgery ($p < 0.0001$), and pleurodesis and surgery ($p = 0.0024$).

Results of univariate and multivariate analyses for predicting the recurrence of ipsilateral pneumothorax according to the last treatment are shown in Table 4. In univariate and multivariate analyses, repeated episode of ipsilateral pneumothorax was the significant risk factor for recurrence ($p = 0.047$ and 0.0032, respectively). Tube drainage as the last treatment was a significant risk factor for recurrence in univariate analysis but not in multivariate analysis ($p = 0.0029$ and 0.10, respectively). Degree of lung collapse was not a significant risk factor for recurrence in univariate and multivariate analyses.

Discussions

In this study, we retrospectively evaluated risk factors of initial treatments in management of air leak and that of recurrence independently. Thus, the first analysis identified risk factors to predict persistent air leak in initial treatments, and the second analysis identified risk factors to predict recurrence after last treatments.

The first multivariate analysis for predicting persistent air leak after initial treatments, which required additional treatment to cease air leak, showed statistical significances in repeated episode of ipsilateral pneumothorax, high degree of lung collapse, and radiological finding of bulla formation. Initial treatment was not an independent risk factor for the outcome of air leak in this study. This result is not consistent with findings in previous reports [7, 16]. And there are very few reports that evaluated success in cessation of air leak in comparison between observation and invasive treatment [7, 17]. Those studies did not adjust the outcomes with the degree of lung collapse that was used as indication of those treatments. Lung collapse on chest X-ray does not always represent persistent air leak, although a high degree of lung collapse was a risk factor for persistent air leak in this study. Recent researches reported that observation was safe even for patients with moderate to large collapse in specific situation [8, 14]. Moreover, less invasive management of patients with use of ambulatory device was reported to be effective [18]. Further research is needed to determine whether some large pneumothoraces could be treated with conservative observation or if all large pneumothoraces should be treated by any interventions. On the other hand, tube drainage carries a risk of critical complication [10, 19], Based on the findings of our analysis, less invasive treatments, conservative observation, would be firstly attempted in patients of mild and moderate lung collapse without risk factors, i.e., repeated episode, and bulla formation.

The second analysis of recurrence showed that repeated episode of ipsilateral pneumothorax was the only risk factor for ipsilateral recurrence. Kaplan-Meier analysis showed that observation and surgery were superior to tube drainage among the last treatments. When adjusted by clinical background factors in multivariate analysis, tube drainage showed a high hazard ratio for recurrence but not statistically significant. Those findings were not consistent with some of the previous studies wherein patients treated with observation showed a higher recurrence rate than those with tube drainage [12, 13]. Further, large pneumothorax was not an independent risk factor of recurrence. As we consider that initial management is intended to manage air leak [11], prevention of recurrence should be additionally followed if necessary. Tube drainage showed a high hazard ratio of recurrence, although it was not statistically significant. Therefore, among patients with a repeated episode of ipsilateral pneumothorax, those cured in air leak with tube drainage may be recommended to be treated with additional treatment to prevent recurrence.

Our study included PSP and SSP. SSP has been reported to be associated with a higher morbidity and mortality than PSP [20], and the BTS guideline states that distinction between PSP and SSP should be made at the time of diagnosis to guide appropriate management [4]. In clinical practice, we sometimes encounter difficulty in distinguishing PSP from SSP. Recent reports pointed out that spontaneous pneumothorax should be initially treated the same way regardless of PSP or SSP distinction [6, 21]. Here, we included patients with various underlying lung diseases, such as chronic obstructive lung disease and interstitial pneumonia as SSP. The types of pneumothorax (PSP and SSP) were not risk factors for cessation of air leak and prevention of recurrence.

Our study has several limitations. Body mass index and smoking habit during the follow-up period, which were reported as risk factors for recurrence of PSP in several studies [22, 23], were not available in most patients of this study, and therefore, were not examined. Moreover, as this was a retrospective study from a single institution, unknown confounding factors may affect the prognosis. Several studies reported that the water seal setting was favourable in cessation of air leak compared to continuous suction [24–26] and the data regarding this was unavailable. Thus, we could not separately evaluate the two types of management of tube drainage. A recent study of ours showed that measurement of the intrapleural pressure is useful for predicting persistent air leak determining the indication for initial intervention in pneumothorax [27]. In this study, presumption of air leak was determined clinically by the presence of symptoms and chest radiography findings. Consideration of the measurement of the intrapleural pressure in a future study may facilitate more appropriate management of air leaks.

Conclusions

The multivariate analyses with clinical background factors including size of the pneumothorax showed that risk factors for persistent air leak were repeated episode of ipsilateral pneumothorax, high degree of lung collapse, and radiological bulla formation. The risk factor for recurrence after the last treatment was repeated episode of ipsilateral pneumothorax. Selection of observational or interventional treatments did not affect the outcomes of persistent air leak and recurrence. Owing to treatment invasiveness, observation is recommended to be firstly attempted in patients without risk factors.

Abbreviations

ACCP; The American College of Chest Physician

BTS; The British Thoracic Society

JSPCLD; The Japan Society for Pneumothorax and Cystic Lung Disease

PSP; primary spontaneous pneumothorax

SSP; secondary spontaneous pneumothorax

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Kansai Medical University (approval date: May 28 3, 2018; approval number: 2017320). The requirement for informed consent was waived because of the retrospective nature of the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

TN conducted data collection and statistical analysis of this study. TN drafted, KH revised, and MT supervised the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1
Patient characteristics by each initial treatment

	Observation (n = 198)	Aspiration (n = 22)	Drainage (n = 448)	p-value
Age (years), mean ± SD	39.7	44.3	51.3	< .0001
≥ 50 years, n (%)	64 (68.1)	8 (36.4)	249 (55.6)	< .0001
Sex, n (%)				< .0001
Male	141 (71.2)	14 (63.6)	383 (85.5)	
Female	57 (28.8)	8 (36.4)	65 (14.5)	
Smoking history, n (%) (n = 584)				< .0001
≥ 10 packs-year	35 (21.2)	6 (40.0)	183 (46.0)	
< 10 packs-year	130 (78.8)	15 (60.0)	215 (54.0)	
Previous episode of ipsilateral pneumothorax, n (%)	59 (29.8)	11 (50.0)	147 (32.8)	0.15
Side, n (%)				0.55
Right	99 (50.0)	11(50.0)	244 (54.5)	
Left	99(50.0)	11(50.0)	204 (45.5)	
Type of spontaneous pneumothorax, n (%)				< .0001
PSP	109 (55.1)	9 (40.9)	156 (34.8)	
SSP	89 (44.9)	13 (59.1)	292 (65.2)	
Degree of lung collapse defined by JSPCLD, n (%) (n = 654)				< .0001
High	3 (1.5)	0 (0.0)	171 (39.1)	

SD: standard deviation, PSP: primary spontaneous pneumothorax, SSP: secondary spontaneous pneumothorax
JSPCLD: Japan Society for Pneumothorax and Cystic Lung Disease
ACCP: American College of Chest Physician

	Observation (n = 198)	Aspiration (n = 22)	Drainage (n = 448)	p-value
Middle	51 (25.9)	17 (77.3)	219 (50.1)	
Low	143 (72.6)	5 (22.7)	47 (10.8)	
Degree of lung collapse defined by ACCP, n (%) (n = 654)				
Large	54 (27.4)	17 (77.3)	389 (89.2)	< .0001
Small	143 (72.6)	5 (22.7)	47 (10.8)	
Radiological finding, n (%)				
Bulla formation	99 (50.0)	14 (63.6)	293 (65.4)	0.0013
Pulmonary fibrosis	15 (7.6)	1 (4.5)	18 (4.0)	0.16
SD: standard deviation, PSP: primary spontaneous pneumothorax, SSP: secondary spontaneous pneumothorax				
JSPCLD: Japan Society for Pneumothorax and Cystic Lung Disease				
ACCP: American College of Chest Physician				

Table 2
Results of univariate and multivariate analyses of persistent air leak after the initial treatment

	Univariate analysis		Multivariate analysis	
	OR* (95% CI)	**p-value**	**OR* (95% CI)**	**p-value**
Age (≥ 50 years)	2.1 (1.5–2.9)	< .0001	1.2 (0.6–2.5)	0.54
Sex		0.049		0.85
Male	1.6 (1.0-2.5)		1.1 (0.6–1.9)	
Female	1 (reference)		1 (reference)	
Smoking history (≥ 10 packs-year)	2.4 (1.6–3.4)	< .0001	1.2 (0.7–2.2)	0.48
First or repeated episode of ipsilateral pneumothorax		< .0001		0.0022
First	1 (reference)		1 (reference)	
Repeated	2.3 (1.6–3.2)		1.9 (1.3–2.9)	
Side		0.093		0.33
Right	1 (reference)		1 (reference)	
Left	0.7 (0.5–1.1)		0.8(0.6–1.2)	
Type of spontaneous pneumothorax		< .0001		0.20
PSP	1 (reference)		1 (reference)	
SSP	2.1 (1.5-3.0)		1.6 (0.8–3.3)	
Degree of lung collapse defined by JSPCLD		< .0001		0.082
High	3.5 (2.1–5.7)	< .0001	2.1 (1.1–4.2)	0.032

OR: odds ratio, CI: confidence interval, SSP: secondary spontaneous pneumothorax, PSP: primary spontaneous pneumothorax, JSPCLD: Japan Society for Pneumothorax and Cystic Lung Disease

* >1 indicates risk factor and; <1 indicates preventive factor

	Univariate analysis		Multivariate analysis	
Middle	2.2 (1.4–3.5)	0.0009	1.5 (0.8–2.7)	0.21
Low	1 (reference)		1 (reference)	
Radiological finding				
Bulla formation	3.1 (2.1–4.6)	< .0001	2.6 (1.7–4.1)	< .0001
Pulmonary fibrosis	0.9 (0.4-2.0)	0.78		
Initial treatments		< .0001		0.18
Observation	1 (reference)		1 (reference)	
Aspiration	1.3 (0.4–4.3)	0.61	0.7 (0.2–2.5)	0.62
Drainage	3.3 (2.1–5.2)	< .0001	1.5 (0.8–2.8)	0.19

OR: odds ratio, CI: confidence interval, SSP: secondary spontaneous pneumothorax, PSP: primary spontaneous pneumothorax, JSPCLD: Japan Society for Pneumothorax and Cystic Lung Disease

* >1 indicates risk factor and; <1 indicates preventive factor

Table 3
Recurrence of ipsilateral pneumothorax after the last treatment

Treatment	Number of treatments, n (%)	Number of recurrences, n (recurrence rate, %)
Total	666* (100)	126 (18.9)
Observation	153 (23.0)	18 (11.8)
Aspiration	18 (2.7)	3 (16.7)
Drainage	262 (38.3)	67 (25.6)
Pleurodesis	63 (9.5)	15 (23.8)
Surgery	170 (25.5)	23 (13.5)

* Two patients died before cessation of air leak were excluded.

Table 4
Results of univariate and multivariate analyses of recurrence after the last treatment

	Univariate analysis		Multivariate analysis	
	HR* (95% CI)	**p-value**	**HR* (95% CI)**	**p-value**
Age (≥ 50 years)	0.9 (0.6–1.3)	0.55		
Sex		0.26		
Male	0.8 (0.5–1.2)			
Female	1 (reference)			
Smoking history (≥ 10 packs-year)	0.9 (0.6–1.3)	0.59		
First or repeated episode of ipsilateral pneumothorax		0.047		0.0032
First	1 (reference)		1 (reference)	
Repeated	1.4 (1.0–2.0)		1.8 (1.2–2.5)	
Side		1.0		
Right	1 (reference)			
Left	1.0 (0.7–1.4)			
Type of spontaneous pneumothorax		0.14		0.45
PSP	1 (reference)			
SSP	1.3 (0.9–1.9)		1.2 (0.8–1.7)	
Degree of lung collapse defined by JSPCLD		0.17		0.60
High	1.5 (0.9–2.4)	0.13	1.3 (0.7–2.5)	0.33

HR: hazard ratio, CI: confidence interval, PSP: primary spontaneous pneumothorax, SSP: secondary spontaneous pneumothorax, JSPCLD: Japan Society for Pneumothorax and Cystic Lung Disease

* >1 indicates risk factor; <1 indicates preventive factor

	Univariate analysis		Multivariate analysis	
Middle	1.5 (1.0-2.4)	0.072	1.3 (0.7–2.2)	0.36
Low	1 (reference)		1 (reference)	
Radiological finding				
Bulla formation	1.2 (0.9–1.8)	0.27		
Pulmonary fibrosis	0.3 (0.1–1.1)	0.075	0.4 (0.1–1.4)	0.20
Last treatment		0.0003		0.0005
Observation (n = 153)	1 (reference)		1 (reference)	
Aspiration (n = 18)	1.3 (0.4–4.6)	0.65	0.9 (0.3–3.3)	0.92
Drainage (n = 262)	2.1 (1.2–3.6)	0.0029	1.7 (0.9–3.2)	0.10
Pleurodesis (n = 63)	2.0 (1.0-3.9)	0.060	1.4 (0.6-3.0)	0.43
Surgery (n = 170)	0.8 (0.4–1.4)	0.42	0.6 (0.3–1.2)	0.11
HR: hazard ratio, CI: confidence interval, PSP: primary spontaneous pneumothorax, SSP: secondary spontaneous pneumothorax, JSPCLD: Japan Society for Pneumothorax and Cystic Lung Disease				
* >1 indicates risk factor; <1 indicates preventive factor				

Figures

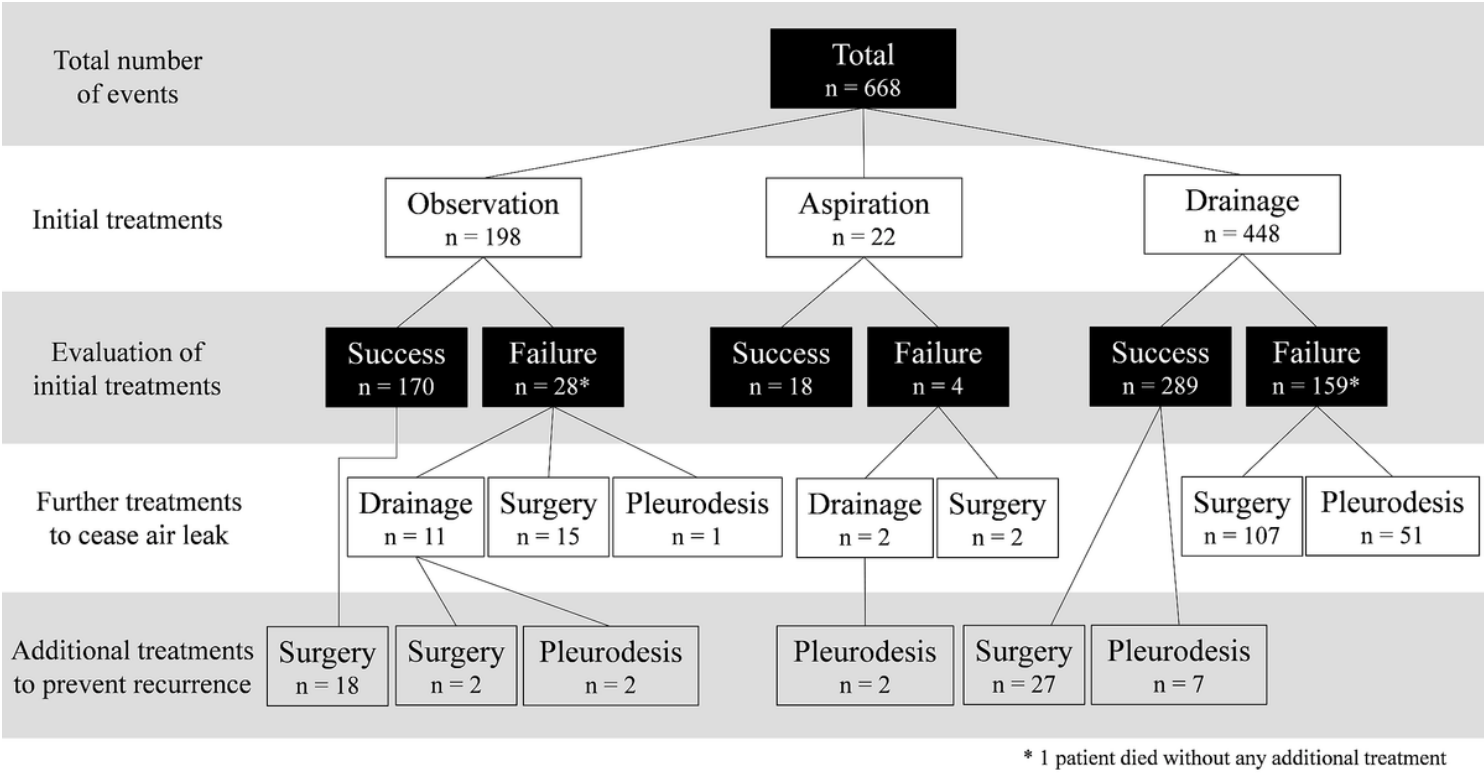
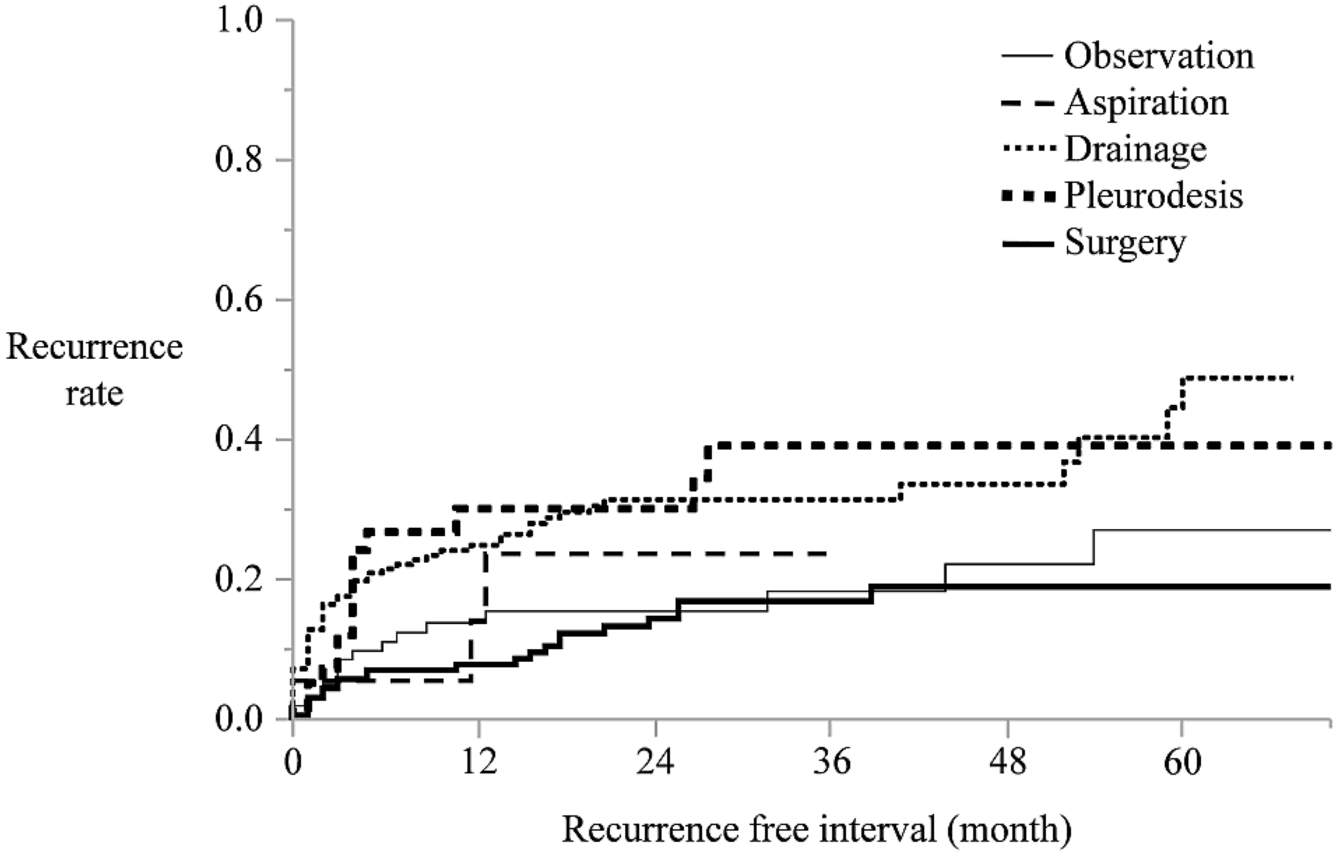


Figure 1

Flow chart of initial, further, and additional treatments * One patient died without any additional treatment.



Number at risk						
Observation	153	55	38	26	18	14
Aspiration	18	11	4	1	0	
Drainage	262	103	65	39	23	13
Pleurodesis	63	21	16	8	6	3
Surgery	170	118	82	45	30	17

Figure 2

Kaplan-Meier curve of the cumulative recurrence of ipsilateral pneumothorax after the last treatment