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Original Article

Surgery for Secondary Spontaneous Pneumothorax with Chronic Lung Diseases

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Purposes: Secondary spontaneous pneumothorax (SSP) is occasionally observed in elderly patients suffering from diffuse lung diseases. The purpose of this study was to analyze the outcomes of surgical treatment of SSP patients with chronic lung diseases.
Methods: In total, 242 patients who underwent surgery for spontaneous pneumothorax at Chiba University Hospital from January 2006 to October 2016 were included in this study. The patients' records were reviewed retrospectively for data on their background, surgical treatment, morbidity, mortality, and recurrence.
Results: Of the spontaneous pneumothorax cohort, primary spontaneous pneumothorax (PSP) accounted for 144 patients. Among the 98 patients with SSP, 57 cases were caused by chronic obstructive pulmonary disease (COPD) and 21 were caused by interstitial pneumonia (IP). The postoperative complication rate was 19.3% in the COPD group, 42.9% in the IP group, and 11.1% in the PSP group. The recurrence rate was 5.3% in the COPD group, 28.6% in the IP group, and 21.5% in the PSP group.
Conclusions: The morbidity and recurrence were comparable between PSP and SSP cases with COPD, whereas these values were unfavorable in SSP cases with IP compared with PSP ones. Surgical intervention should be carefully considered in SSP patients with IP.

Keywords: secondary spontaneous pneumothorax, surgery, chronic obstructive pulmonary diseases, interstitial pneumonia

Introduction

Secondary spontaneous pneumothorax (SSP) is defined as pneumothorax that develops secondary to an underlying pulmonary disease. Many diffuse lung diseases can be involved in SSP. The most common diseases associated with SSP are chronic obstructive pulmonary disease (COPD) and interstitial pneumonia (IP). SSP differs from primary spontaneous pneumothorax (PSP) in many aspects, such as the varied locations of bullae in SSP and the high morbidity and mortality rates, even if surgery is performed.[1–4] However, few studies have explored the surgical treatment of SSP, and the complications and recurrence rate have not been evaluated in a large population.

Therefore, we investigated patients with SSP caused by COPD or IP and compared the outcomes of surgical treatment with those in patients with PSP.

Materials and Methods

We retrospectively reviewed 242 patients who underwent surgery for spontaneous pneumothorax at our hospital from January 2006 to October 2016. The patients'

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Table 1 Patient characteristics

	PSP (n = 144)	COPD (n = 57)	IP (n = 21)
Ages	23 (13–56)	63 (37–82) (p <0.01)	63 (31–77) (p <0.01)
Sex (male/female)	124/20	53/4	17/4
Smoking history	43 (29.9%)	57 (100%) (p <0.01)	16 (76.2%) (p <0.01)
Immunosuppressive therapy	0	0	12 (57.1%) (p <0.01)
Surgical approach			
Thoracoscopic surgery	124 (86.1%)	31 (54.4%) (p <0.01)	15 (71.4%) (p = 0.01)
Open thoracotomy	20 (13.9%)	26 (45.6%) (p <0.01)	6 (28.6%) (p = 0.01)
Surgical time (minutes)	106 (34–309)	127 (48–291) (p <0.01)	122 (60–323) (p = 0.17)
Surgical procedure			
Partial lung resection	118 (81.9%)	35 (54.4%) (p <0.01)	7 (33.3%) (p <0.01)
Ligation of bullae	25 (17.4%)	17 (29.8%) (p = 0.02)	7 (33.3%) (p = 0.04)
Pulmorrhaphy	0	5 (8.8%) (p <0.01)	3 (14.3%) (p <0.01)
Others	1 (0.8%)	0	4 (19.0%)
Pleural reinforcement (+)	135 (93.8%)	51 (89.5%)	19 (90.5%)
Preoperative treatment (+)	27 (18.8%)	11 (19.3%)	10 (47.6%) (p <0.01)

PSP: primary spontaneous pneumothorax; COPD: chronic obstructive pulmonary disease; IP: interstitial pneumonia

records were reviewed retrospectively for data on their clinical background, surgical treatment, morbidity, mortality, recurrence, and treatment for recurrence. We investigated patients with SSP caused by COPD or IP and compared the outcomes of surgical treatment with those in patients with PSP. The definition of the classifications (PSP and SSP) in this study is established based on the observations derived from computed tomography (CT) scans and patient background information. The chest CT scans were reviewed by three highly skilled thoracic surgeons (K.T., H.S., and T.I.), each possessing extensive experience of 17, 23, and 16 years, respectively. We categorized SSP based on the presence of emphysema and IP as observed in the scans. Because the patient was classified as PSP regardless of age, a 56-year-old case without the CT findings of emphysema and IP, he was classified as PSP even at age 56. During the period of 11 years employed for this study, 30 surgeons performed the operation for pneumothorax.

The study protocol was approved by the ethics committee of Chiba University Medical Faculty (approval number 3004). All patient's data were fully anonymized before we accessed them, and the ethics committee of Chiba University waived the requirement for informed consent.

All statistical analyses were performed with the JMP software program, ver. 13.0 (SAS Institute Inc, Cary, NC, USA). Comparisons between two groups were performed by the Fisher's exact test. Significance was set at $p < 0.05$.

Results

There were 144 patients with PSP and 98 with SSP. SSP with COPD was noted in 57 patients and SSP with IP in 21. Other causes of SSP were Birt–Hogg–Dubé syndrome (n = 7), catamenial pneumothorax (n = 5), lymphangioleiomyomatosis (n = 2), and unclassified (n = 6). The patients' background characteristics are summarized in **Table 1**. The mean age was 23 years in the PSP patients and 63 years in the SSP patients with COPD or IP ($p < 0.01$). Smoking history was higher in COPD and IP patients than in PSP patients ($p < 0.01$).

Table 2 Preoperative treatment

	PSP (n = 10)	COPD (n = 11)	IP (n = 6)
Pleurodesis	9 (90.0%)	10 (90.9%)	0
Use of the XIII coagulation factor	0	1 (9.1%)	1 (16.7%)
Bronchial embolization using silicone	0	0	1 (16.7%)
TGF method	1 (10.0%)	0	4 (66.6%)

PSP: primary spontaneous pneumothorax; COPD: chronic obstructive pulmonary disease; IP: interstitial pneumonia; TGF: thoracographic fibrin glue sealing

Table 3 Postoperative results

	PSP (n = 144)	COPD (n = 57)	IP (n = 21)
Additional treatment	10 (6.9%)	9 (15.8%) ($p < 0.05$)	8 (38.1%) ($p < 0.01$)
Complication	16 (11.1%)	11 (19.3%) ($p < 0.01$)	9 (42.9%) ($p < 0.01$)
Recurrence	31 (21.5%)	3 (5.3%) ($p < 0.01$)	6 (28.6%)
Death	0	0	1 (4.8%) ($p < 0.01$)
Average observation period (days)	470 (7–3420)	597 (9–3630)	567 (6–2075)

PSP: primary spontaneous pneumothorax; COPD: chronic obstructive pulmonary disease; IP: interstitial pneumonia

Immunosuppressive therapy was used only in IP patients ($p < 0.01$). The surgical approaches used were videothoracoscopy or open thoracotomy, with the latter more commonly performed in the SSP group ($p < 0.01$). The mean surgical duration was 106 minutes in the PSP group and 126 minutes in the SSP group ($p < 0.01$). The surgical procedure varied, and partial lung resection was more frequently performed in the PSP group than in the SSP group ($p < 0.01$). Pulmorrhaphy was more frequently performed in the SSP group than in the PSP group ($p < 0.01$).

The preoperative treatments performed are listed in **Table 2**. Indications for operation are not different among the three groups. We have considered surgical intervention when the duration of drain retention exceeds 1 week. The criteria for preoperative treatment vary across different diseases. Within the IP group, patients typically exhibit compromised health status and a heightened surgical risk. Consequently, preoperative treatments were administered with greater frequency in the IP group compared to those in the PSP and COPD groups ($p < 0.01$). Pleurodesis was frequently performed in the PSP and COPD groups, whereas it was not performed at all in the IP group. The thoracographic fibrin glue sealing (TGF) method was frequently performed in the IP group. TGF stops the air leak of intractable pneumothorax by interventional radiology.[5)]

Regarding the surgical procedures, pleural covering with absorbable sheet materials was often performed to prevent recurrence. In the SSP group, polyglycolic acid or oxidized cellulose sheets with fibrin glue were more often used for reinforcement of the pleura than in the PSP group.

The mean duration of postoperative drainage tube placement was longer in the IP group than in the COPD group (3.5 ± 4.9 days in the COPD group and 8.5 ± 11.7 days in the IP group, $p < 0.05$). More patients required additional treatment in the IP group than in the COPD or PSP group (10 cases [6.9%] in the PSP group, 9 cases [15.8%] in the COPD group, and 8 cases [38.1%] in the IP group) (**Table 3**).

The postoperative additional treatments performed are listed in **Table 4**. Further elucidation regarding the indications and methodologies employed for additional postoperative treatment in each respective disease is as follows. Prolonged pulmonary fistula serves as the primary indication necessitating such interventions. However, the specific approach employed varies across different diseases. Notably, in the case of IP, pleurodesis presents a heightened risk of acute exacerbation. Therefore, we have strived

Table 4 Postoperative additional treatment

	PSP (n = 10)	COPD (n = 9)	IP (n = 8)
Pleurodesis	8 (80.0%)	8 (88.9%)	3 (37.5%)
Use of the XIII coagulation factor	0	0	1 (12.5%)
Bronchial embolization using silicone	0	0	1 (12.5%)
TGF method	0	0	1 (12.5%)
Reoperation	0	0	4 (50.0%)
Redrainage	2 (20.0%)	1 (11.1%)	1 (12.5%)

PSP: primary spontaneous pneumothorax; COPD: chronic obstructive pulmonary disease; IP: interstitial pneumonia; TGF: thoracographic fibrin glue sealing

Table 5 Morbidity, mortality, and recurrence rates of SSP patients after surgery

Author (year)	Cases	Morbidity	Mortality	Recurrence
Waller (1999)[13]	55	N.E.	2 (3.6%)	4 (7.3%)
Onuki et al. (2002)[14]	59	N.E.	0	3 (5.0%)
Nakajima et al. (2009)[7]	87	22 (25.3%)	4 (4.6%)	N.E.
Zhang et al. (2009)[15]	107	27 (25.2%)	5 (4.7%)	3 (2.8%)
Isaka et al. (2013)[3]	97	20 (20.6%)	4 (4.1%)	9 (9.3%)
Ichinose et al. (2016)[16]	183	23 (13.0%)	6 (3.0%)	30 (16%)
This series (COPD)	57	11 (19.3%)	0	3 (5.3%)
This series (IP)	21	9 (42.9%)	1 (4.8%)	6 (28.8%)

SSP: secondary spontaneous pneumothorax; COPD: chronic obstructive pulmonary disease; IP: interstitial pneumonia; N.E.: not expressed

to avoid pleurodesis in the IP group, opting instead for alternative treatments including the utilization of the XIII coagulation factor, bronchial embolization using silicone, the TGF method, and the possibility of reoperation. Pleurodesis using OK432 was frequently performed in the PSP and COPD groups. Postoperative complications were more frequent in the SSP group than in the PSP group (11.1% in the PSP group, 19.3% in the COPD group, and 42.9% in the IP group) ($p < 0.01$) (**Table 3**).

The postoperative recurrence rate was lower in the COPD group than that in the IP or PSP group (21.5% in the PSP group, 5.3% in the COPD group, and 28.6% in the IP group) (**Table 3**). The mean time to recurrence from surgery was 443, 1660, and 28.3 days in the PSP, COPD, and IP groups, respectively. Of note, 80.4% of cases of recurrence occurred within 2 years from surgery in the PSP group and 100% occurred within 1 year from surgery in the IP group; in contrast, all cases of recurrence in the COPD group occurred ≥2 years from surgery. There was one mortality in the IP group due to acute exacerbation.

Following the univariate analysis, immunosuppressive therapy and IP demonstrated significant differences with risk factors of pneumothorax recurrence ($p < 0.01$). However, the multivariate analysis did not reveal any significant differences.

Discussion

SSP is caused by various underlying pulmonary diseases, typically COPD or IP. The treatment strategy for SSP with COPD and IP should be distinguished from that for PSP because of the increased risk of mortality and morbidity in elevated rate of recurrence after chest tube drainage.[1–8] Surgery for pneumothorax of elderly patients has been reported to have high morbidity and mortality because of the unfavorable general condition of such patients and the presence of underlying pulmonary diseases,[7–9] and most patients are categorized as having SSP.

Matsuoka et al. reported that thoracoscopic surgery is a safe and effective procedure for SSP in elderly patients and that IP, pulmonary infection, and a low preoperative nutrition state were risk factors for a longer hospitalization.[8] In SSP patients, persistent air leakage has been shown to be a major surgical indication, and surgery is reportedly required in 34% of SSP patients.[10] Prolonged air leakage is more likely to occur as the COPD condition progresses.[9] Early surgical treatment reduces the risk of postoperative complications for SSP.[11] Surgery for SSP contributed to early chest tube removal and favorable outcomes. However, the patient performance status was a risk factor for postoperative complications.

A careful evaluation of each patient's performance status is needed to determine the need for surgical intervention for SSP.[12)]

In SSP patients with IP in the present study, the preoperative treatment and additional postoperative treatment varied. In our department, several options are available as nonsurgical procedures, such as pleurodesis, systemic administration of XIII coagulation factor, bronchial embolization using silicone, and the TGF method for a ruptured lung.

In PSP patients and SSP patients with COPD in the present study, the preoperative treatment and additional postoperative treatment were often pleurodesis. However, we should avoid performing pleurodesis using OK432 in IP patients because pleurodesis can be a risk factor for acute exacerbation. Indeed, among our cases, there was one mortality in the IP group due to acute exacerbation. This patient suffered from empyema because of prolonged air leakage.

The recurrence rates of SSP after surgical treatment reportedly range from 2.8% to 16% (**Table 5**).[3,7,13–16)] In the present study, the recurrence rate was 21.5% in the PSP group, 5.3% in the COPD group, and 28.6% in the IP group. The recurrence rate in the PSP group in this study was high because the ratio of teenaged patients in the PSP group was high (36.8%). The recurrence rate of PSP in teenaged patients is higher than that in older patients because the generation of bullae tends to continue even after surgery.[5)] Moreover, although our hospital is a university hospital, which is an educational institution, various surgeons perform surgery in different ways. Younger surgeons tend to perform surgery for PSP, especially for young patients compared to surgery for SSP. Moreover, we frequently perform thoracoscopic surgery for PSP and thoracotomy for SSP. As reported in literature, the postoperative recurrence rate of pneumothorax after thoracoscopic surgery is higher than that after thoracotomy.[5)] These factors may have been the cause for the higher recurrence rate observed in the PSP group. The time to recurrence from surgery was longer in the COPD group than that in the IP or PSP group. Regarding the mortality and morbidity, the values in the COPD group were comparable to those in the PSP group, whereas the IP group showed markedly poor values. The results of this study suggest that PSP and COPD-associated SSP may have similar treatment plans with the same indications.

There are some limitations to this study. First, this is a single-institution, retrospective study. Second, this study included only patients undergoing surgical management of PSP or SSP, so there is potential bias in the selection of operative vs nonoperative therapy. Third, the treatment modalities, including pleural reinforcement techniques and medications for pleural adhesion, vary based on the underlying disease (PSP, COPD, IP). Consequently, it would be inappropriate to assert that the disparity in recurrence risk is directly attributable to the background disease. Finally, the number of patients in this study cohort is small. Thus, a larger cohort study or a prospective observational study is necessary to verify the outcomes of surgical treatment of SSP patients with chronic lung diseases.

Conclusion

The morbidity and recurrence were comparable between PSP and SSP cases with COPD, whereas these values were unfavorable in SSP cases with IP compared with PSP ones. Surgery for SSP with IP showed high complication and recurrence rates, so we should assess the surgical indication in these patients more carefully.

Author Contribution

Kazuhisa Tanaka, Hidemi Suzuki, Terunaga Inage, Takamasa Ito, Yuichi Sakairi, and Ichiro Yoshino were involved in the study design and data interpretation. Kazuhisa Tanaka, Hidemi Suzuki, and Ichiro Yoshino were involved in the data analysis. All authors critically revised the report, commented on drafts of the manuscript, and approved the final report.

Ethics Approval

The study protocol was approved by the ethics committee of Chiba University Medical Faculty (approval number 3004).

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Disclosure Statement

None declared

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