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Surgery for secondary spontaneous pneumothorax: risk factors for recurrence and morbidity

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Abstract

OBJECTIVES: Secondary spontaneous pneumothorax (SSP) is more common in elderly patients; it has high rates of recurrence and mortality, even if surgery is performed. There has been little study on the surgical treatment of SSP. Therefore, we analysed the outcomes of surgical treatment of SSP patients, and investigated the risk factors of recurrence and morbidity.

METHODS: We studied 97 consecutive surgical treatments on 94 patients with SSP who had emphysematous changes of lung retrospectively. Emphysematous changes on preoperative computed tomography image were evaluated by the Goddard score, which is a visual scoring system. First, video-assisted thoracoscopic surgery was performed, followed by bullectomy for the responsible lesions.

RESULTS: The rate of morbidity was 20.6% and that of mortality was 4.1%. Recurrence rate was 9.3%. By multivariate analysis, a Goddard score ≥7 (odds ratio: 8.93, $P = 0.033$) and treatment of bulla without the use of staplers (odds ratio: 11.57, $P = 0.019$) were significant risk factors for morbidity, while pulmonary fibrosis tended to increase the risk of recurrence (hazard ratio: 4.21, $P = 0.051$), and a Goddard score ≥7 (hazard ratio: 7.79, $P = 0.023$) was a significant risk factor for recurrence.

CONCLUSIONS: Surgical treatment in patients with SSP had favourable results. Treatment in which the base of the bulla cannot be definitely shut off with staplers is associated with increased morbidity. Significant emphysematous change on preoperative computed tomography image and pulmonary fibrosis are predictors of recurrence. Patients with these findings should be investigated in terms of the indications of surgery and additional treatment, not only bullectomy.

Keywords: Secondary spontaneous pneumothorax • Video-assisted thoracoscopic surgery • Chronic obstructive pulmonary disease • Recurrence • risk factor

INTRODUCTION

Spontaneous pneumothorax is classified into primary spontaneous pneumothorax (PSP) and secondary spontaneous pneumothorax (SSP). SSP affects patients with underlying pulmonary disease, most of which is chronic obstructive pulmonary disease (COPD). SSP is considered to differ from PSP because of the life-threatening symptoms, the various locations of ruptured bullae and the high recurrence rate and mortality, even if surgery is performed [1, 2]. However, data and treatment of patients with PSP and SPP were mixed together in most studies and reviews, and the number of SSP cases in each study was small. There have been a few studies to investigate the risk factors related to recurrence of spontaneous pneumothorax [3, 4]; however, there has been little study on the surgical treatment of SSP in the elderly, and the independent risk factors of recurrence after surgery for only SSP have not been evaluated yet. Therefore, we investigated only patients with SSP who had emphysematous change of lung in a single institution, and aimed to identify the specific risk factors for recurrence and morbidity of SSP.

MATERIALS AND METHODS

We retrospectively reviewed the patients with SSP who had emphysematous change of the lung who had undergone surgical treatment in our institution from January 2005 to January 2011. All patients were enrolled in accordance with the regulations of the institutional review board.

We reviewed age, sex, Eastern Cooperative Oncology Group (ECOG) performance status, smoking status, preoperative computed tomography (CT) image, surgery and the postoperative follow-up to investigate the risk factors for postoperative morbidity, mortality and recurrence. Smoking status was expressed using the Brinkman index, which was calculated as the number of cigarettes smoked per day multiplied by the number of years of smoking.

For evaluation of emphysematous change on preoperative CT image, the visual scoring system described by Goddard *et al.* [5] was used because it enables easy checking of the area of low attenuation. This system uses a four-point scale for emphysematous destruction identified as areas of low attenuation in the lung in

order to grade disease severity. A score of 1 represents destruction up to 25%, 2 is given for up to 50%, 3 for up to 75% and 4 for up to total absence of normal lung tissue. Hunsaker *et al.* [6] used a modified scoring system, in which the two lungs were each divided into upper and lower zones, and the maximum score, representing marked diffuse emphysema, was 16. The CT findings were evaluated by thoracic surgeons and the division of Diagnostic Radiology in our institution. We were blinded to the clinical data when we evaluated preoperative CT images using this modified scoring system.

In preoperative comorbidities, cardiovascular and cerebrovascular disease was defined as treatment history of angina pectoris, myocardial infarction and cerebral stroke. The diagnosis of pulmonary fibrosis was based on abnormalities such as fibrosis, peripheral reticular opacity or honeycombing on preoperative chest CT. Major postoperative complications were defined as respiratory failure requiring home oxygen therapy or temporary ventilatory support, pneumonia, prolonged air leak for >5 days after surgery and drainage due to bleeding. Recurrence was defined as a further ipsilateral pneumothorax after removal of the chest tube, including cases of recurrence before discharge. The patients who underwent surgery for SSP and developed contralateral SSP were considered as new cases.

Surgical treatment

Surgery for SSP was the treatment of choice for pneumothorax with persistent air leak or recurrent pneumothorax in a short period. Surgical treatment was started through thoracoscopy under general anaesthesia and single-lung ventilation. First, video-assisted thoracoscopic surgery (VATS) was performed. Three or four access ports were used for VATS. Conversion to open thoracotomy (muscle-sparing axillary thoracotomy) was indicated in patients with diffuse bullae, giant bullae, serious pleural adhesions or no lung collapse. We did not repair all of the bullae, but concentrated on repairing only bullae with air leak and ultrathin-walled bullae (bullectomy if possible). When we selected bullectomy as the treatment for stopping air leak, buttress staple with polyglycolic acid felt (Neoveil tube type, Gunze Co., Kyoto, Japan) was used to prevent a second injury for fragile lung tissue around the staple lines and recurrence. Pleurodesis was performed only when the surgeon required it. The sclerosing agents were OK-432 and tetracycline at first, and were changed to talc poudrage from 2008. At the end of the surgery, one chest tube was inserted and connected to 8 cmH_2O of wall suction.

Postoperative care

Postoperative pain was managed by using mainly oral medication such as non-steroidal anti-inflammatory drugs and sometimes epidural anaesthesia. Chest tubes were removed postoperatively, by which time, the lungs were fully expanded and no air leakage was present. If the patient had prolonged postoperative air leak for >5 days, pleurodesis was performed with OK-432 or talc slurry. If conservative treatment failed, reoperation was taken into consideration.

Follow-up

The follow-up after discharge continued for 1–2 months, and patients were then referred back to their primary care setting unless problems were detected at the initial follow-up. Long-term data about pneumothorax recurrence and current status were obtained by telephone interviews.

Statistical analysis

The best discriminative cut-off values for Brinkman index and Goddard score were assessed by receiver operating curve analysis. Comparisons between two groups were performed by Fisher's exact test and Mann–Whitney's *U*-test. Logistic regression analysis was used to identify the risk factors for postoperative morbidity. The cumulative postoperative recurrence rate was estimated by the Kaplan–Meier method, and differences in variables were calculated by the log-rank test. Multivariate analyses for the postoperative recurrence rate were performed using Cox's proportional hazard model. Differences were considered statistically significant when $P < 0.05$. The variables that were found to be significantly different by univariate analyses were subjected to multivariate logistic regression analysis and Cox's proportional hazard model.

RESULTS

From January 2005 to January 2011, 410 surgical treatments on 388 patients were performed for spontaneous pneumothorax in our institution (22 surgical treatments for contralateral pneumothorax development). Among these patients, we investigated 97 consecutive surgical treatments (23.7% of all surgical treatments for spontaneous pneumothorax) on 94 patients with SSP in this study. Three patients with SSP had undergone bilateral thoracoscopies metachronously because of contralateral pneumothorax development.

The median age of the patients at the time of surgery was 69 years (range 51–93 years). Eighty-nine patients (91%) with SSP were male. In the data of preoperative arterial blood-gases, mean PaO_2 was 85.8 ± 18.8 mmHg (range 60.2–165 mmHg, some patients were treated with oxygen therapy), and mean $PaCO_2$ was 40.5 ± 6.1 mmHg (range 29.1–58.9 mmHg). The mean operation time was 74 min (range 28–260 min), and the mean volume of bleeding during operation was 12 ml (range 5–180 ml). The mean preoperative and postoperative chest tube drainage times were 5.8 ± 5.2 and 2.2 ± 5.6 days, respectively. The mean postoperative hospitalization lasted 8.1 ± 10.3 days. The median follow-up time after surgery was 24 months.

VATS was performed in 54 cases (55.7%) and conversion to thoracotomy in 43 (44.3%). The resection of bullae (or closure of the base of bullae) with endoscopic staplers was performed in 86 (88.7%), endoscopic loop ligation in only 1, pleurectomy in 2, closure of the air leak point with direct suture or a fibrinogen/thrombin-coated collagen patch (TachoComb; Nycomed, Zurich, Switzerland) in 5 cases. Pleurodesis was performed in 16 cases (16.5%) as follows: 11 cases with talc insufflation, 3 cases with OK-432 and minocycline, 1 with only minocycline, and 1 case with autologous blood.

Mortality

The rate of mortality defined as in-hospital death after surgery was 4.1% (4/97), and all of the deaths were due to pneumonia

Table 1: Results of univariate analyses for postoperative mortality of second spontaneous pneumothorax

Variables	Death ($n = 4$)	Alive ($n = 93$)	*P*-value
Age	80 ± 7	69 ± 10	0.040
ECOG performance status (3–4)	4 (100%)	15 (16%)	0.0011
Brinkman index	916 ± 144	955 ± 633	0.77
Goddard score	9.7 ± 3.8	6.4 ± 4.1	0.16
Pulmonary fibrosis	1 (25%)	10 (11%)	0.33
Preoperative pneumonia	3 (75%)	1 (1%)	0.0001
Preoperative home oxygen therapy	1 (25%)	3 (3%)	0.16
Cardiovascular and cerebrovascular disease	1 (25%)	10 (11%)	0.39
Diabetes mellitus	0	10 (11%)	1.00
Thoracotomy	3 (75%)	40 (43%)	0.32
No treatment of bulla	1 (25%)	23 (25%)	1.00
Pleurodesis	1 (25%)	13 (14%)	0.52

ECOG: Eastern Cooperative Oncology Group.

(range of the period from surgery until death, 8–35 days). Elderly age, ECOG performance status ≥3 and preoperative pneumonia were identified as risk factors for the increased mortality observed in the early postoperative period (Table 1).

The 2-year overall survival rate after surgery was 71.8% (Fig. 1A). During the follow-up period, there were 26 deaths excluding those related to surgery for SSP. The deaths were due to respiratory factors in 8 patients and extrapulmonary factors in 18 (neoplasm in 11 patients, cardiovascular disorders 3, septic shock 1 and unknown 3).

Morbidity

There were no major complications during surgery. The rate of postoperative major morbidity was 20.6%, and respiratory complications comprised 95% of all complications. Respiratory complications were pneumonia (7 patients; 7.2%), respiratory failure (10 patients; 10.3%) and prolonged air leak (3 patients; 3.1%). A non-respiratory complication occurred in only 1 patient, which was bleeding (1%). Risk factors for postoperative major complications were evaluated with univariate and multivariate analyses. The optimal cut-off values of Brinkman index and Goddard score for morbidity were identified as 800 and 7, respectively, by receiver operating characteristic curves. The results of the univariate analysis to identify risk factors of postoperative major complications are given in Table 2. In particular, performance status ≥3 ($P = 0.0005$), Goddard score ≥7 ($P = 0.0001$) and treatment of bullae without the use of staplers ($P = 0.0012$) were significantly associated with morbidity. By multivariate analysis, Goddard score ≥7 (odds ratio: 8.93, $P = 0.033$) and treatment of bullae without the use of staplers (odds ratio: 11.57, $P = 0.019$) were significant risk factors for morbidity (Table 3).

Recurrence

A total of nine patients experienced pneumothorax recurrence after surgery. The recurrence rate was 9.3%. The time to recurrence ranged from 2 days to 39 months. Of note, 89% (8/9) of the recurrences occurred within the first year (Fig. 1B). The optimal cut-off values of the Brinkman index and Goddard score for recurrence were identified as 800 and 7, respectively, by receiver operating characteristic curves. By univariate analysis, the factors that were associated with an increase risk of recurrence were a Goddard score ≥7, pulmonary fibrosis and treatment of bullae without the use of staplers (Table 4). By multivariate analysis, pulmonary fibrosis tended to increase the risk of recurrence (hazard ratio: 4.21, $P = 0.051$), and the independent risk factor for recurrence was a Goddard score ≥7 (hazard ratio: 7.79, $P = 0.023$) (Table 5).

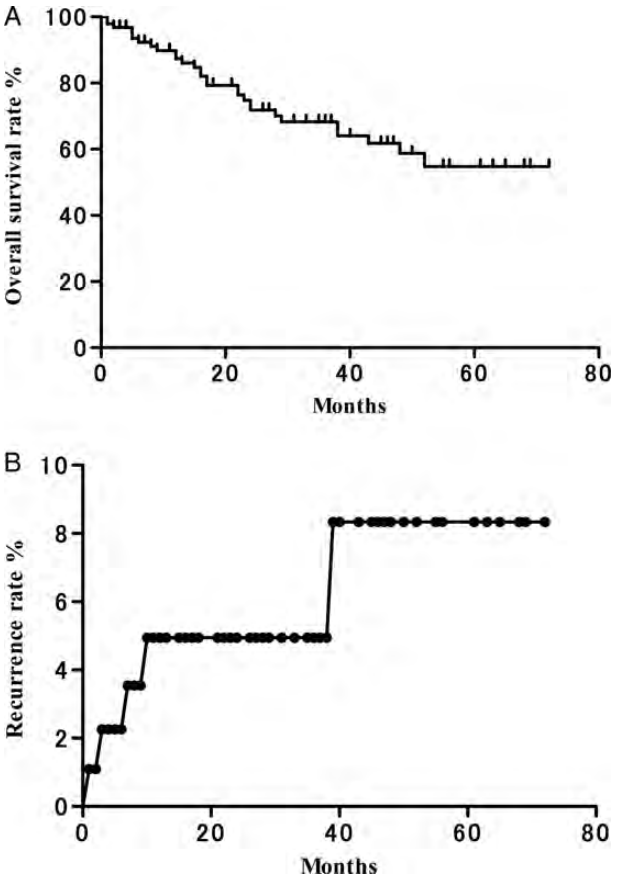

Figure 1: Overall survival curve (**A**) and recurrence curve (**B**) for SSP after surgical treatment. The 2-year overall survival rate and recurrence rate of the patients was 71.8 and 4.9%, respectively.

DISCUSSION

SSP occur in those individuals who have underlying pulmonary disease, which most often is COPD. The treatment strategy for SSP with COPD should be distinguished from that for PSP because of the higher mortality and morbidity, lower healing rate and higher recurrence rate after chest tube drainage [7–9]. Elderly patients with SSP and emphysematous change of lung have marginal pulmonary function and often limited cardiopulmonary reserve. However, a much more aggressive approach is sometimes warranted with appropriate evaluation of the risk and benefit of surgical treatment because the occurrence of pneumothorax in a patient who has severe emphysema can be life-threatening. The

Table 2: Results of univariate analyses for postoperative morbidity of second spontaneous pneumothorax

Factors	*n*	Morbidity (%)	*P*-value
Age			
<70 years	48	30.6	0.047
≥70 years	49	12.5	
Sex			
Male	88	21.6	0.68
Female	9	11.1	
ECOG performance status			
0–2	78	12.8	0.0005
3–4	19	52.6	
Brinkman index			
<800	38	18.4	1.0
≥800	52	17.3	
Goddard score			
<7	48	6.3	0.0001
≥7	38	42.1	
Pulmonary fibrosis			
Yes	9	55.6	0.017
No	88	17.0	
Preoperative pneumonia			
Yes	4	75.0	0.027
No	93	18.3	
Preoperative home oxygen therapy			
Yes	4	75.0	0.027
No	93	18.3	
Cardiovascular and cerebrovascular disease			
Yes	11	36.4	0.23
No	86	18.6	
Diabetes mellitus			
Yes	10	20.0	1.0
No	87	20.7	
Operation type			
VATS	54	9.3	0.0025
Thoracotomy	43	34.9	
Place of bulla with air leak			
Upper and middle lobe	65	16.9	0.43
Lower lobe	31	29.0	
Adhesion between bulla with air leak and chest wall			
Yes	61	16.4	0.20
No	36	27.8	
Treatment of bulla with air leak using staplers			
Yes	86	15.1	0.0012
No	11	63.6	
Pleurodesis			
Yes	16	50.0	0.0039
No	81	14.8	

ECOG: Eastern Cooperative Oncology Group.

Table 3: Results of multivariate analyses for postoperative morbidity of second spontaneous pneumothorax

Variables	Odds ratio	95% confidence interval	*P*-value
Age ≥70 years	4.57	0.76–41.37	0.12
ECOG performance status 3–4	2.31	0.39–13.28	0.34
Goddard score ≥7	8.93	1.43–95.64	0.033
Pulmonary fibrosis	2.23	0.29–17.49	0.43
Preoperative pneumonia	2.23	0.065–77.83	0.75
Preoperative home oxygen therapy	3.79	0.29–104.12	0.34
Conversion to thoracotomy	1.48	0.28–8.09	0.64
Treatment of bulla without the use of staplers	11.57	1.66–114.52	0.019
Pleurodesis	4.63	0.60–45.85	0.15

ECOG: Eastern Cooperative Oncology Group.

Table 4: Results of univariate analyses for postoperative recurrence of second spontaneous pneumothorax

Variables	*n*	2 year-recurrence rate	*P*-value
Age			
<70 years	48	2.1	0.094
≥70 years	49	5.3	
Sex			
Male	88	9.8	0.34
Female	9	0	
ECOG performance status			
0–2	78	4.3	0.0011
3–4	19	28.0	
Brinkman index			
<800	38	11.5	0.61
≥800	52	6.2	
Goddard score			
<7	48	2.2	0.028
≥7	38	20.0	
Pulmonary fibrosis			
Yes	9	44.4	<0.0001
No	88	4.9	
Diabetes mellitus			
Yes	10	11.1	0.98
No	87	8.7	
Operation type			
VATS	54	4.0	0.14
Thoracotomy	43	5.8	
Place of bulla with air leak			
Upper and middle lobe	65	8.4	0.42
Lower lobe	31	5.6	
Adhesion between bulla with air leak and chest wall			
Yes	61	5.0	0.089
No	36	12.5	
Treatment of bulla with air leak using staplers			
Yes	86	2.7	0.013
No	11	34.6	
Pleurodesis			
Yes	16	0	0.20
No	81	10.5	

ECOG: Eastern Cooperative Oncology Group.

postoperative morbidity, mortality and recurrence rate in the reports published to date are given in Table 6 [10–18].

In this study, postoperative mortality was 4.1%, and the risk factors that were significantly associated with postoperative mortality were old age and poor performance status. Moreover, surgical treatment for patients with preoperative pneumonia should be avoided because of the particularly high mortality. The 2-year overall survival rate of the patients with SSP after surgery was 71.8% in this study. Among the deaths excluding in-hospital death

after surgery, the rate of those related to extrapulmonary causes, most of which were neoplasm, was 69.2%. These findings suggest that most of the patients with SSP who are elderly and heavy smokers have poor prognoses by nature, and the treatment, particularly surgery for SSP, should be selected accordingly.

Morbidity of SSP after surgical treatment was reported to range from 19.2 to 37.5% [10, 12, 14, 15, 17, 18]. In these previous studies, only one reported independent risk factors of postoperative morbidity, namely, preoperative hypercapnia and no pleurodesis [18]. In this study, the rate of postoperative morbidity was 20.6%, and respiratory complications comprised 95% of all complications. Our statistical analysis showed that treatment of bulla without the use of staplers was one of the independent risk factors of morbidity. In the treatment of bulla, stapling wedge resection was superior to ligation of the bulla and subtotal pleurectomy [19], and the guidelines of the American College of Chest Physicians also recommend staple bullectomy as the preferred procedure for bullectomy [20]. When the base of the bulla with air leak could not be treated with staplers for some technical reasons, for example, strong adhesion between the lung around the bulla and the chest wall, the residual bulla responsible for pneumothorax also induced prolonged air leak and other respiratory complications. Secure and tensionless treatment of the base of the bulla with air leak is very important to prevent complications after the surgery for SSP.

Recurrence rates of SSP after surgical treatment were reported to range from 0 to 15.8% [11–18]. In our institution, the recurrence rate after surgery was 9.3% (9/97) for SSP, in contrast to the value of 4.8% for PSP (15/313) during the same period, and other reports showed similar findings that the independent risk factor for recurrence of spontaneous pneumothorax was SSP [3, 4]. However, in these reports, the patient background was a mixture of PSP and SSP, with and without surgery, and there were no reports showing the independent risk factors for recurrence of only SSP after surgical treatment.

In this study, multivariate analysis showed that pulmonary fibrosis tended to increase the risk of recurrence. Lungs with pulmonary fibrosis are generally rigid and fragile and collapse easily. This is associated with the difficulty of treating bullae and the increased mortality in the patients with SSP [10].

In addition, the independent risk factor of recurrence and morbidity was a higher Goddard score in this study; that is, more prominent emphysematous change on preoperative CT image increased the risk of recurrence and morbidity. Evaluation of the level of severity of emphysema is important for the investigation of SSP; however, it is difficult for patients with SSP to undergo pulmonary function test before surgery, for example, spirometry measurement. In this study, we selected the Goddard score, which is a visual scoring system for evaluation of emphysematous change on preoperative CT image, as the evaluation method of emphysema because it can be easily and objectively estimated in any institution. When the emphysematous change of lung was distinct, the risk of recurrence was high, even if assured bullectomy was performed with a buttress staple, because the fragility of the lung was related to failure of the surface of the lung and development of another thin-walled bulla. Additional treatment, for example, pleurodesis, should be performed when the Goddard score is high on preoperative CT image.

The recurrence rates after surgical treatment were reported to be 5.4% for VATS and 1.1% for open surgery in a systematic review [21]. In this study, there was no significant difference between VATS and thoracotomy in terms of both morbidity and recurrence rates. VATS for the surgery of SSP should be chosen first because of its lower invasiveness; however, there should be no hesitation in converting to thoracotomy to ensure a safe bullectomy.

With regard to pleurodesis, some reports have shown its efficacy against SSP [22, 23]. Thoracoscopic talc poudrage was particularly effective for patients with advanced COPD (success rate: 95%, 30-day mortality: 10%, and no major perioperative complications) [22]. In this study, pleurodesis was not routinely used, because talc was not available commercially in Japan, and the use of other

Table 5: Results of multivariate analyses for postoperative recurrence of second spontaneous pneumothorax

Variables	Hazard ratio	95% confidence interval	*P*-value
Goddard score ≥7	7.79	1.28–149.31	0.023
Pulmonary fibrosis	4.21	0.99–17.21	0.051
Treatment of bulla without the use of staplers	2.90	0.58–12.14	0.18

Table 6: Morbidity, mortality and recurrence rates of patients who underwent surgical treatment for second spontaneous pneumothorax

Author (year)	Number of patients	Morbidity (%)	Mortality (%)	Recurrence rate (%)	Conversion to thoracotomy	Length of the follow-up
Tanaka (1993)	24	37.5	4	12.5	Thoracotomy only	Mean: 4.1 years
Waller (1994)	22	22.7	9	0 (18%[a])	–	Mean: 8.6 months
Passlick (1998)	34	25	0	0	29.4%	Median: 29 months
Waller (1999)	55	–	3.6	7.3	–	At least 12 months
Onuki (2002)	53 (59 operations)	–	0	1.7 (5%[a])	91.5%	Mean: 33 months
Qureshi (2008)	19	–	5.3	15.8	45.1%[b]	6–8 weeks after operation
Nakajima (2009)	86 (87 operations)	24.3	5.5	–	6%	–
Zhang (2009)	107	25.2	4.7	2.8	55.1%[b]	–
Shaikhrezai (2010)	89 (94 operations)	19.2	2.1	3.9	1.1%	Median: 73 months
Current study	95 (97 operations)	20.6	4.1	9.3	44.3%	Median: 24 months

[a]Early revisional thoracotomy for postoperative persistent air leak.
[b]Initial open thoracotomy.

sclerosing agents, for example OK-432, resulted in clumsiness during surgery due to being liquid solutions. Moreover mechanical pleurodesis, for example pleurectomy, is not often performed because of the possibility that mechanical pleurodesis results in postoperative complications such as bleeding. There was no significant difference in recurrence rates, whether chemical pleurodesis was used or not; however, no recurrence was seen in the patients who underwent chemical pleurodesis. Although the usage of pleurodesis in combination with surgery or by itself is the subject of future investigation, the treatment is an important option for patients with SSP, particularly those who are considered to be at risk in surgery.

In conclusion, surgical treatment in patients with SSP had favourable results. This study suggested that, when safe stapling of the bulla is feasible, surgical treatment for SSP should be performed aggressively in terms of pursuing a radical cure. However, patients for whom the base of the bulla is judged as untreatable with staplers, with significant emphysematous change on preoperative CT image and pulmonary fibrosis, should be investigated for the indications for surgery and additional treatments such as pleurodesis because of their high morbidity and recurrence rates.

Conflict of interest: none declared.

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