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

Mitsuhiro Isaka*, Katsuyuki Asai and Norikazu Urabe

Division of Thoracic Surgery, Numazu City Hospital, Numazu, Shizuoka, Japan

* Corresponding author. Division of Thoracic Surgery, Numazu City Hospital, Harunoki 550, Higashi-shiiji, Numazu, Shizuoka 410-0302, Japan. Tel: +81-55-9245100; fax: +81-55-9245133; e-mail: mi.isaka@scchr.jp (M. Isaka).

Received 30 January 2013; received in revised form 8 April 2013; accepted 17 April 2013

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 SSP 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
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 cmH2O 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 PaO2 was 85.8 ± 18.8 mmHg (range 60.2–165 mmHg, some patients were treated with oxygen therapy), and mean PaCO2 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.
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. 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).

**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).

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

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

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).
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

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hazard ratio</th>
<th>95% confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goddard score ≥ 7</td>
<td>7.79</td>
<td>1.28–149.31</td>
<td>0.023</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>4.21</td>
<td>0.99–17.21</td>
<td>0.051</td>
</tr>
<tr>
<td>Treatment of bulla without the use of staplers</td>
<td>2.90</td>
<td>0.58–12.14</td>
<td>0.18</td>
</tr>
</tbody>
</table>

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

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

*aInitial open thoracotomy.*
sclerosing agents, for example OK-432, resulted in cluminosity 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 pre-operative 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.

REFERENCES