Original Article

Risk factors for the recurrence of primary spontaneous pneumothorax after video-assisted thoracoscopic surgery in patients younger than 40 years

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Background: Video-assisted thoracoscopic surgery (VATS) is a standard primary spontaneous pneumothorax (PSP) procedure. However, its high recurrence rate compared to open thoracotomy is a problem. Therefore, various methods to prevent recurrence have been developed. The present study investigated the risk factors for postoperative recurrence of PSP after VATS.

Methods: From January 2008 to November 2022, 207 patients younger than 40 years of age without underlying pulmonary disease underwent thoracoscopic bullectomy for PSP. Among them, 96 underwent staple line reinforcement with a polyglycolic acid (PGA) sheet and autologous blood spraying. Patient characteristics and surgical outcomes were analyzed to determine the prognostic factors for postoperative recurrence.

Results: Twenty-seven patients (13.0%) experienced recurrences. A multivariate analysis using Cox regression analysis revealed that age younger than 20 years [P=0.039; hazard ratio (HR) =2.337; 95% confidence interval (CI): 3.283–17.287], history of contralateral pneumothorax (P<0.001; HR =7.533; 95% CI, 1.486–12.336), and no staple line reinforcement (P=0.007; HR =4.282; 95% CI, 1.043–5.236) were risk factors for recurrence after pneumothorax surgery.

Conclusions: Age younger than 20 years and history of contralateral pneumothorax were risk factors for postoperative recurrence of pneumothorax. Staple line reinforcement with a PGA sheet and spraying of autologous blood reduced the postoperative recurrence rate of PSP.

Keywords: Autologous blood; primary spontaneous pneumothorax (PSP); polyglycolic acid sheet (PGA sheet); recurrence; video-assisted thoracoscopic surgery (VATS)

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Introduction

Primary spontaneous pneumothorax (PSP) is common in general hospitals. It is more common in young, tall, thin male individuals without underlying lung disease, and it rare occurs in persons older than 40 years (1). Surgical treatment was performed for recurrent pneumothorax or prolonged air leakage. In recent years, bullectomy using video-assisted thoracoscopic surgery (VATS) has become

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the standard procedure for pneumothorax surgery because it is less invasive and more cosmetically effective than open thoracotomy (2,3). However, its recurrence rate is approximately 4–11%, which is higher than that of open thoracotomy, and the recurrence rate after bullectomy under open thoracotomy is approximately 1% (4,5). Pleurectomy, mechanical or chemical pleurodesis, and staple line reinforcement prevent postoperative recurrence after VATS bullectomy for PSP (6). As a guideline, staple line coverage with an absorbable mesh was introduced in the European Respiratory Society statement about PSP (7), which described that the covering technique appears to be effective for reducing recurrent PSP; however, it suggested that this should be confirmed by further studies. Polyglycolic acid (PGA) sheets are often used as a reinforcing material against staple lines, and the following methods of use have been reported: (I) PGA sheets alone; (II) PGA sheets with fibrin glue; and (III) PGA sheets with autologous blood (8). Since 2014, PGA sheets have been applied as reinforcement against staple lines by spraying 10 mL of autologous blood to fix the sheets at our institution. In the present study, we investigated the outcomes of patients who underwent VATS bullectomy for PSP to evaluate the effectiveness of surgery for preventing PSP recurrence. Furthermore, we reviewed the clinical features to identify the prognostic factors related to recurrence after surgery. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-257/rc) (9).

Highlight box

Key findings

- Among patients with primary spontaneous pneumothorax who underwent video-assisted thoracoscopic bullectomy, age younger than 20 years at surgery, history of contralateral pneumothorax, and no staple line reinforcement were significant prognostic factors for postoperative recurrence.

What is known and what is new?

- Young age and a history of ipsilateral pneumothorax are risk factors for postoperative recurrence. Reinforcing the staple line with a polyglycolic acid sheet and fibrin glue effectively prevents recurrence.
- A history of contralateral pneumothorax may also be a prognostic factor, and using autologous blood instead of fibrin glue may effectively prevent postoperative recurrence.

What is the implication, and what should change now?

- Patient explanations and postoperative observations should be carefully performed. It should be recognized that recurrence rates may be higher for younger patients and those with a history of pneumothorax. Autologous blood may enhance staple line reinforcement and prevent recurrence.

Methods

This study was conducted in accordance with the Declaration of Helsinki (revised in 2013). This retrospective study was approved by the Institutional Review Board of Yokohama Municipal Citizen's Hospital (No. 23-02-01), and the requirement for individual consent for this retrospective analysis was waived. Patients 40 years of age or younger without underlying pulmonary disease who underwent surgery for PSP for the first time at Yokohama Municipal Citizen's Hospital between January 2008 and November 2022 were included in this study. The following clinical features were retrospectively collected from medical records: age at surgery; sex; smoking history; body mass index (BMI); history of both ipsilateral and contralateral PSP; surgical procedure; and follow-up period. During surgery, the bullae and blebs were resected using a stapling device. In some patients, staple line coverage was performed with a PGA sheet, and 10 mL of autologous blood taken from a radial arterial line was sprayed. Patients typically attended routine follow-up appointments 2 weeks and 4 to 8 weeks after surgery. Recurrence was defined as a diagnosis of ipsilateral pneumothorax at a medical institution after the initial appointment. Further additional follow-up was conducted by phone or mail for all patients.

Statistical analysis

All statistical analyses were performed using SPSS software (version 26.0; IBM Corporation, Armonk, NY, USA). Categorical variables of the two groups were evaluated using the chi-square test. Recurrence-free survival (RFS) was estimated using the Kaplan-Meier method, and differences between survival curves were analyzed using the log-rank test. The Cox proportional hazards regression model was used to evaluate the potential prognostic factors for recurrence after VATS bullectomy and to calculate hazard ratios. Statistical significance was set at $P<0.05$.

Results

During this study, VATS bullectomy for pneumothorax was performed for 249 patients. The study cohort included

207 patients who underwent VATS bullectomy for PSP. Twenty-seven patients with postoperative recurrence, six patients with emphysema, four patients with Marfan syndrome, three patients with catamenial pneumothorax, one patient with aspergillus infection, and one patient with pneumocystis infection were excluded. The median follow-up period was 31.3 months (range, 1.0–143.2). Among 207 patients, 27 (13.0%) experienced postoperative recurrence of ipsilateral PSP. The median time between surgery and recurrence was 14.2 months (range, 0.7–104.2). The clinical features and differences between the recurrent and nonrecurrent groups are shown in *Table 1*. There were no significant differences in sex, smoking history, BMI, history of ipsilateral pneumothorax, laterality, hemothorax, bullae or blebs at the apex of the lung, and number of bulla or bleb resections. Compared with the nonrecurrence group, more patients in the recurrence group were younger than 20 years, had a history of contralateral pneumothorax, and had no staple line reinforcement with a PGA sheet and autologous blood. The univariate analysis indicated that age younger than 20 years, history of contralateral pneumothorax, and no staple line reinforcement were significant prognostic factors for poor RFS (*Table 2*). The Kaplan-Meier curves of RFS after VATS bullectomy for these factors are shown in *Figure 1*. The results of the multivariate analysis of RFS after VATS bullectomy are shown in *Table 3*. The multivariate analysis using the Cox regression analysis revealed that age younger than 20 years [P=0.039; hazard ratio (HR) =2.337; 95% confidence interval (CI), 3.283–17.287), history of contralateral pneumothorax (P<0.001; HR =7.533; 95% CI, 1.486–12.336), and no staple line reinforcement (P=0.007; HR =4.282; 95% CI, 1.043–5.236) were risk factors for recurrence after VATS bullectomy for PSP.

Discussion

The postoperative recurrence rate of VATS bullectomy for PSP at our institution was 13.0%, which is somewhat higher than the recurrence rates reported by previous publications (4,5). However, the recurrence rate of cases with staple line reinforcement was 5.2%, which is comparable to the recurrence rate after thoracoscopic surgery with staple line reinforcement with a PGA sheet reported by previous works (2.6–13.8%) (10-14). Furthermore, we demonstrated that age younger than 20 years, a history of contralateral pneumothorax, and no staple line reinforcement with a PGA sheet and autologous blood were significant prognostic factors for unfavorable outcomes.

Although age younger than 20 years is considered a risk factor for postoperative recurrence of PSP, it has been reported that postoperative recurrence may be more common in younger patients. Risk factors have been reported as 17, 20, and 23 years of age and younger (13,15,16). It has been shown that patients with PSP at a young age, when physical development is rapid, gain weight normally but grow taller quickly, resulting in an elongated body shape (17). The rapid increase in the vertical dimensions of the thorax compared to the horizontal dimensions during this period is thought to have some effect on the intrathoracic pressure at the apex of the lungs and promote bulla formation (18), which may be a cause of postoperative PSP recurrence in young patients.

We also showed that a preoperative history of contralateral pneumothorax might be a risk factor for recurrence after VATS bullectomy. A history of ipsilateral pneumothorax is a possible risk factor (13,16); however, there are no reports of a history of contralateral pneumothorax as a risk factor. Although there is no clear reason for this, we know empirically that patients with PSP often have bilaterally symmetrical lung bulla on computed tomography. A history of pneumothorax may reflect body type or pleural fragility that predisposes the bulla to form or fail.

Pleurectomy and mechanical or chemical pleurodesis are simple and effective methods that have been performed to prevent postoperative PSP recurrence after VATS bullectomy for PSP (6). However, postoperative pain, postoperative bleeding, disruption of normal pleural physiology, and the potential for severe intrapleural adhesions may be disadvantages for younger patients (6,19,20). As an alternative to these preventive methods, staple line coverage has been performed to reinforce the visceral pleura. The use of staple line reinforcement with a PGA sheet for preventing the postoperative recurrence of PSP has been reviewed by many studies performed in Asian countries, and it has been found to be effective (8,10,12-14). According to the 2014 annual report of the Japanese Association for Thoracic Surgery, of 12,673 patients who underwent VATS bullectomy, the visceral pleura was reinforced with absorbable sheets in 6,432 (50.7%) (5). Due to its softness, the PGA sheet is associated with difficulties during thoracoscopic surgery when applying it to fit the staple line after bullectomy properly. Therefore, many centers use fibrin glue when the PGA sheets are fitted to the staple line. However, it is difficult to

Table 1 Comparison of patient characteristics between the postoperative pneumothorax recurrence and non-recurrence groups

Variables	Recurrence (n=27)	Non-recurrence (n=180)	P value
Age at operation (years)			0.005
<20	17	63	
≥20	10	117	
Sex			0.560
Male	25	160	
Female	2	20	
Smoking history			0.224
Yes	4	46	
No	23	134	
Body mass index (kg/m^2)			0.683
<18.5	11	66	
≥18.5	16	114	
History of ipsilateral pneumothorax			0.176
Yes	18	95	
No	9	85	
History of contralateral pneumothorax			0.001
Yes	10	23	
No	17	157	
Operation side			0.610
Right	10	76	
Left	17	104	
Hemopneumothorax			0.497
Yes	1	13	
No	26	167	
Bulla or bleb location			0.570
Apical area	25	168	
Other area	2	12	
Number of resections			0.630
1	21	147	
≥2	6	33	
Stapling line reinforcement			0.002
Yes	5	91	
No	22	89	

Table 2 Univariate analyses for recurrence-free survival

Variables	1-year RFS (%)	3-year RFS (%)	P value
Age at operation (years)			0.014
<20	90.4	82.5	
≥20	95.6	88.9	
Sex			0.537
Male	86.8	56.7	
Female	100.0	91.7	
Smoking history			0.214
Yes	93.3	90.2	
No	93.5	84.8	
Body mass index (kg/m^2)			0.894
<18.5	94.2	88.5	
≥18.5	93.0	84.8	
History of ipsilateral pneumothorax			0.122
Yes	91.9	81.4	
No	95.3	91.6	
History of contralateral pneumothorax			<0.001
Yes	86.8	56.7	
No	94.7	91.1	
Operation side			0.666
Right	93.5	85.9	
Left	93.4	86.6	
Hemopneumothorax			0.439
Yes	100.0	92.9	
No	93.5	85.7	
Bulla or bleb location			0.933
Apical area	93.5	85.8	
Other area	92.9	79.6	
Number of resections			0.792
1	94.6	87.3	
≥2	88.6	81.7	
Staple line reinforcement			0.034
Yes	96.6	92.8	
No	90.6	82.1	

RFS, recurrence-free survival.

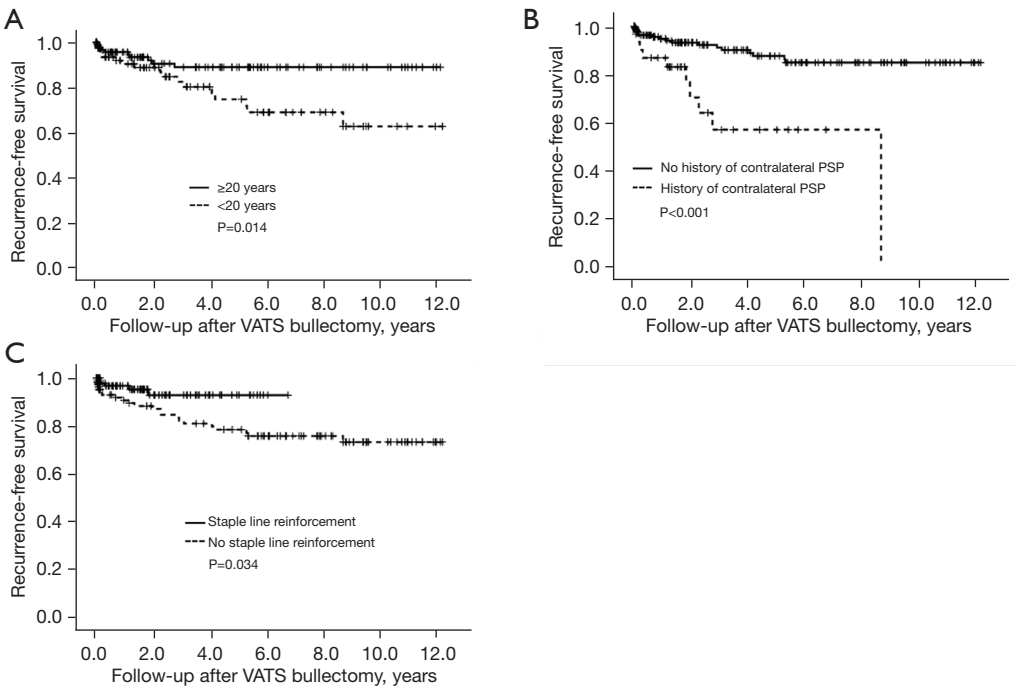

Figure 1 Kaplan-Meier curves for recurrence-free survival after VATS for patients with primary spontaneous pneumothorax according to (A) age younger than 20 years or age 20 years or older; (B) history of contralateral pneumothorax; and (C) staple line reinforcement with a polyglycolic acid sheet and autologous blood. VATS, video-assisted thoracoscopic surgery; PSP, primary spontaneous pneumothorax.

Table 3 Multivariate analysis for recurrence-free survival

Variables	HR	95% CI	P value
Age at operation (years)			
≥20			
<20	2.337	3.283–17.287	0.039
History of contralateral pneumothorax			
No			
Yes	7.533	1.486–12.336	<0.001
Staple line reinforcement			
Yes			
No	4.282	1.043–5.236	0.007

HR, hazard ratio; CI, confidence interval.

completely inactivate and remove viruses, such as human parvovirus B19, during the current manufacturing process for fractionated plasma products, and there is a risk of infection (21). Therefore, we used autologous blood instead of fibrin glue to fix PGA sheets. The effectiveness of staple line reinforcement using PGA sheets with autologous blood for preventing the postoperative recurrence of PSP has been demonstrated only by studies performed in Japan, and the study populations were limited (22,23). In this study, the method using PGA sheets with autologous blood had a recurrence rate comparable to that of prophylaxis using PGA sheets and fibrin glue (10-14). Autologous blood may be superior to fibrin glue in terms of simplicity, infection, and cost-effectiveness. However, as shown by using autologous blood during pleurodesis for prolonged pneumothorax and postoperative air leaks (24,25), spraying as little as 10 mL of autologous blood may cause pleurodesis via pleural irritation and inflammation due to clot formation and subsequent blood fibrinogen activity. In addition, PGA sheets induce severe inflammation and adhesions between the parietal and visceral pleura, which may adversely affect future thoracic surgery (26). In this study, five patients in the group with staple line reinforcement using a PGA sheet and autologous blood experienced recurrence; however, because all were minor pneumothorax occurrences that did not require surgery, it was not possible to determine the actual extent of adhesions that had occurred.

This study had several limitations. It was conducted at a single institution and retrospective. Although this

study excluded patients with secondary spontaneous pneumothorax other than PSP based on the medical records and CT images, the bulla was not located at the apical area in 14 patients; therefore, spontaneous pneumothorax caused by genetic predisposition may not have been completely excluded (27). Furthermore, the study population was relatively small, and only 27 patients experienced recurrence. Therefore, selection and information bias may have existed, and the study might have been underpowered to perform statistical analyses. A multicenter prospective study is needed to confirm the results of this study.

Conclusions

Among patients with PSP younger than 40 years of age who underwent VATS bullectomy, age younger than 20 years at surgery and a history of contralateral pneumothorax were considered risk factors for postoperative recurrence. In addition, reinforcing the staple line with a PGA sheet and spraying of autologous blood may effectively prevent postoperative recurrence.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-257/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-257/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-257/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (revised in 2013). This study was approved by the Institutional Review Board of Yokohama Municipal Citizen's Hospital (No. 23-02-01), and the requirement for individual consent for this retrospective analysis was waived.

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