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ORIGINAL ARTICLE

A novel dual-covering method in video-assisted thoracic surgery for pediatric primary spontaneous pneumothorax

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Abstract

Background Primary spontaneous pneumothorax (PSP) generally occurs in young adults, whereas pediatric PSP is uncommon. It is difficult to source reliable data on pediatric PSP, the management of which is based on guidelines for adult PSP; however, the rate of recurrence after video-assisted thoracoscopic surgery (VATS) for pediatric PSP is reported to be higher.

Methods We reviewed retrospectively a collective total of 66 surgical cases of a first pneumothorax episode in 46 children under 16 years of age, who were treated at our hospital between February, 2005 and November, 2017.

Results The surgical cases were divided into two groups, depending on how the treated lesions were covered. In the dual-covering (DC) group, the PSP was covered by oxidized regenerated cellulose and polyglycolic acid (8 patients; 13 cases) and in the single-covering (SC) group, the PSP was covered by oxidized regenerated cellulose (38 patients; 53 cases). There was no incidence of recurrence after surgery in the DC group, but 17 cases (32.1%) of recurrence after surgery in the SC group. This difference was significant.

Conclusion The DC method prevented the recurrence of PSP more effectively than the SC method after VATS in pediatric patients. Long-term follow-up after VATS for pediatric PSP is also important because of the risk of delayed recurrence.

Keywords Primary spontaneous pneumothorax · Pediatric · Video-assisted thoracoscopic surgery · Oxidized regenerated cellulose · Polyglycolic acid

Introduction

Primary spontaneous pneumothorax (PSP) is much less common in children than adults [1] and its precise incidence is still unclear [2]. Moreover, the management of pediatric PSP is controversial and its recurrence rate after video-assisted thoracoscopic surgery (VATS) is reported to be higher than that of adult PSP [2].

Referral to a thoracic surgeon should be considered for PSP complicated by a second ipsilateral pneumothorax, synchronous bilateral pneumothoraces, persistent air leak, and other sequelae [3]. However, the recurrence rate of pediatric PSP after VATS tends to be high [4–6]. There are few in depth studies about the most effective surgical approach for pediatric PSP because of its low prevalence. Several surgical methods for pediatric PSP have been reported, including pleurectomy, mechanical pleurodesis, and pleural abrasion [1, 5, 7, 8]. Although these methods may improve outcomes, the recurrence rate after VATS for pediatric PSP has been reported to be higher than 10% [1, 5, 7, 9].

VATS with staple-line coverage was recently found to be non-inferior to VATS with mechanical pleurodesis for adult PSP [10]. Moreover, the results of several studies have shown promising outcomes of using the covering method with oxidized regenerated cellulose (ORC) for intractable secondary spontaneous pneumothorax [11, 12]. However, the outcomes of VATS with staple-line coverage for pediatric PSP have not been reported. We conducted this study to examine the effectiveness of the covering methods for pediatric PSP. The covering methods we examined used two kinds of pleural covering materials: ORC and polyglycolic acid (PGA).

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Patients and methods

Study design

We performed an in vivo experiment, aimed to establish the effectiveness of the dual-covering method, prior to its clinical application. Then, we conducted the retrospective clinical trial. Between February 2005 and November 2017, a total of 3247 patients underwent VATS for pneumothorax in the Tamagawa and Ebara hospitals. We also examined the age-categorized distribution data between July 2012 and June 2017, which revealed that under-16-year-olds accounted for only 3.6% according to age bracket as for hospitalization, whereas the same group occupied approximately 20% of the group that needed reoperation after VATS (Fig. 1). Therefore, 66 surgical cases (46 patients) of the first pneumothorax episode occurring in patients younger than 16 years of age were defined as pediatric PSP in this retrospective study. Eligibility for surgery included ipsilateral or bilateral recurrent PSP after the first pneumothorax episode. Cases of secondary spontaneous pneumothorax were excluded. The surgical cases were divided into two groups: a dual-covering (DC) group, in which the lesions were covered by oxidized regenerated cellulose and polyglycolic acid; and a single-covering (SC) group, in which the lesions were covered by oxidized regenerated cellulose.

Recurrent PSP was diagnosed by chest X-ray findings in all the study patients. Before surgery, the culprit lesions were also evaluated on chest computed tomography (CT) scans. All patients underwent outpatient follow-up by chest X-ray 2 weeks, 3 months, and 6 months after surgery. Recurrence after surgery was generally identified by chest X-ray. Patients could also visit our clinic if they had chest pain or respiratory discomfort after the 6-month follow-up period.

Surgical procedure

All procedures were performed with the patients in the lateral decubitus position, under general anesthesia with differential lung ventilation. The standard procedure was performed as follows:

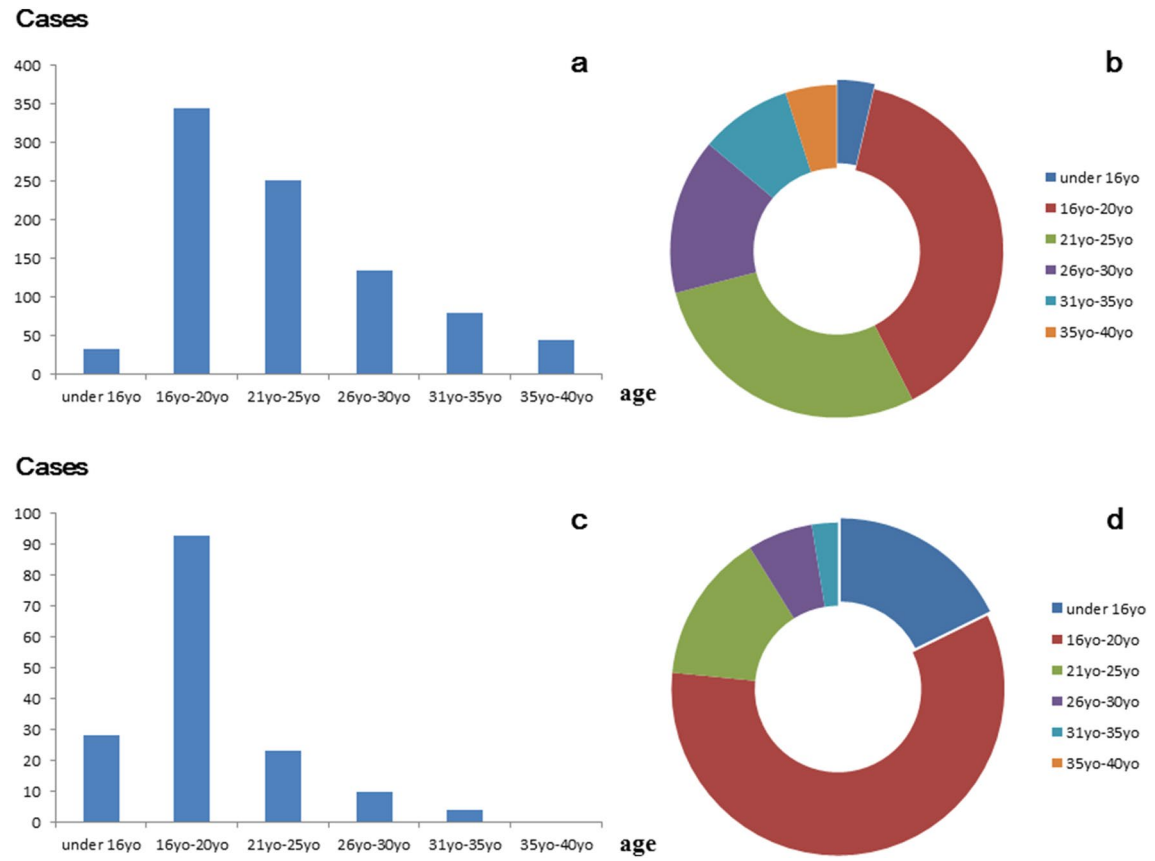

Fig. 1 Age-categorized distribution data between July, 2012 and June, 2017. The upper graphs show the number (**a**) and proportion (**b**) of hospitalizations for pediatric spontaneous pneumothorax. The lower graphs show the number (**c**) and proportion (**d**) of reoperations after video-assisted thoracoscopic surgery, including cases in which the first operation was performed in another hospital

1. Three ports were inserted in the second intercostal space at the middle axillary line, in the fourth intercostal space at the middle axillary line, and in the fifth intercostal space at the posterior axillary line, respectively.
2. The visceral pleura was examined thoroughly for lesions, using a 10-mm flexible thoracoscope (Olympus Optical Tokyo, Japan).
3. Bullae/blebs were resected using endoscopic devices (GIA Universal; Covidien, Mansfield, MA or Echelon; Ethicon, Cincinnati, OH), or by ligation with absorbable threads (Endoloop, Ethicon), or with abrasion by a low-thermal coagulation device (Floating Ball, Covidien), depending on the situation.
4. The absence of air leakage was confirmed.

In the SC group, the treated lesions and more than 3 cm around the treated lesions were covered by ORC mesh alone (Surgicel, Ethicon). In the DC group, the treated lesions were covered with a PGA sheet (Neoveil; Gunze, Kyoto, Japan), followed by 2–3 sheets of ORC mesh which were overlaid to completely cover the PGA sheet with 5 ml of fibrin glue (FG) (Beriplast P; CSL Behring, Marburg, Germany; Bolheal; Kaketsuken, Kumamoto, Japan) (Fig. 2). Patients were discharged the day after removal of the chest tube.

In vivo experiment

The procedure for the in vivo experiment was described in a previous report, which investigated the effectiveness of SC methods using ORC mesh, PGA, and FG [11]. Briefly, beagle dogs weighing more than 8 kg were anesthetized with an intramuscular injection and then a continuous intravenous injection of anesthetic agents. Once deep anesthesia was achieved, the dogs were secured on the operation table in a left lateral decubitus position. After intratracheal intubation, mechanical ventilation was initiated. Standard thoracotomy was performed via the third intercostal space. We created four complete defects, each 0.5 cm × 2.0 cm, in the visceral pleura over the anterior lobe and posterior lobes. We rubbed over the lesions with FG, and then covered each with a PGA sheet. FG was applied again and we overlaid the lesions with ORC mesh. Following the DC procedure, we rubbed the lesions again with FG, and anchored each corner of the PGA sheet and ORC mesh with absorbable threads. After confirming the absence of air leakage, we closed the chest wound. Thoracotomy was performed again 2 weeks, 1 month, and 3 months after the initial procedure to inspect the area and obtain pathological specimens.

Ethical statement

The study protocol was approved by the institutional review boards of Tamagawa Hospital and Ebara Hospital, with participant consents implied by the return of the questionnaires or by the method of opt-out. The animal experiment was carried out in strict accordance with the guidelines for the care and use of laboratory animals, and all efforts were made to minimize suffering.

Statistical analysis

Continuous variables were expressed as means ± the standard deviation and analyzed by the Student *t* test. Categorical variables were expressed by frequency and analyzed by the Fisher's exact test. Probability of non-recurrence was estimated by the Kaplan–Meier method, with comparisons performed by the log-rank test. The threshold for significance was $p < 0.05$. Statistical analysis was conducted using EZR software [13].

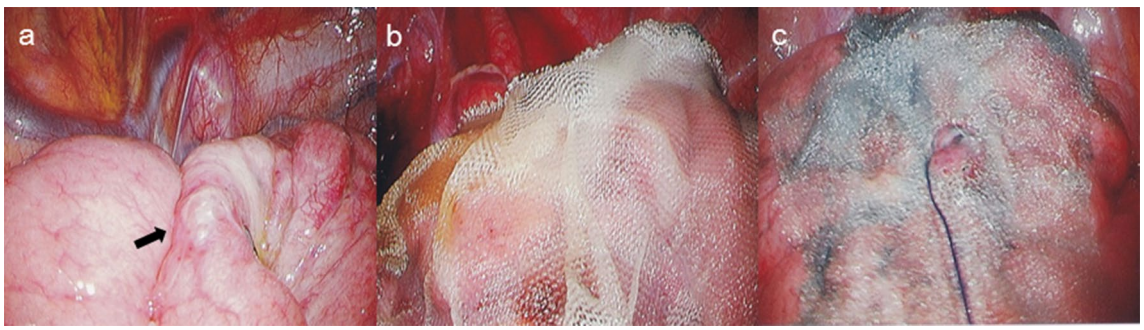

Fig. 2 The techniques of the single-covering method and the dual-covering method. **a** Identification and treatment of the culprit lesions. **b** The lesions and more than 3 cm surrounding them were covered by ORC mesh. **c** The treated lesions were covered by a PGA sheet. The single-covering method consists of **b**, following **a**. The dual-covering method consists of **b**, following **a, c**. The arrow indicates the bullae

Results

Patients

The DC group is comprised of 8 patients (13 cases), and the SC group is comprised of 38 patients (53 cases). The median age of the patient at the first pneumothorax episode was 14.0 years old for the DC group and 14.7 years old for the SC group. The DC included 7 male patients (87.5%), and the SC included 29 male patients (76.3%). There were no significant differences in gender frequencies or age at the first pneumothorax episode between the groups (Table 1).

Procedures

There were 8 operations (61.5%) for right pneumothorax in the DC group and 20 (37.7%) in the SC group. Partial resection of lung was performed in 8 (61.5%) of the DC operations and 41 of the SC operations (77.4%). There were no significant differences between the groups in the selection of treating methods for bullae/blebs (Table 1). Pathological examinations proved that all the resected lesions contained bullae/blebs, not including pleural tumors or thoracic endometriosis.

Perioperative management

The chest drainage tube was removed after an average of 4.2 days in the DC group and 4.8 days in the SC group (Table 1). The average hospital stay postoperatively was 5.9 days in the DC group and 6.2 days in the SC group (Table 1). There was no mortality or any case of massive blood loss requiring blood transfusion or conversion to open thoracotomy in either group. Postoperative complications included five cases of persistent air leakage for more than 1 week in the SC group, one case of fever of unknown origin in the DC group, and one case of reoperation being needed in the SC group (Table 1). All patients returned to their social activities after discharge without compromise of their quality of life. There were no significant differences between the groups in any of these factors.

Recurrence

The mean follow-up was 12.0 months for the DC group and 13.4 months for the SC group. There was no case of recurrence after VATS in the DC group, but 17 cases (32.1%) in the SC group. Reoperations were needed in 12 cases (70.6%) and 5 (29.4%) resolved with follow-up observations. There was a significant difference in recurrence rates between the groups by the Fisher's exact test ($p=0.02$) and the log-rank test ($p=0.03$) (Table 1; Fig. 3).

In vivo experiment

We performed thoracotomy again 2 weeks, 1 month, and 3 months after the initial thoracotomy. By 2 weeks after the initial procedure, the pleural adhesions were observed macroscopically to have peeled off and inflammation of the visceral pleura was seen microscopically. By 1 month, the pleural adhesions were weak macroscopically and microscopically, the inflammation of the visceral pleura had improved and there was pleural thickening. The ORC mesh was no longer observed, but the PGA sheet was still observed. By 3 months, the pleural adhesions were weak macroscopically, except around the anchoring sutures with absorbable threads. The inflammatory reaction of the

Table 1 Patient characteristics

	Dual-covering group (13 cases/8 patients)	Single-covering group (53 cases/38 patients)	*P*
Age at first pneumothorax episode (year),mean (SD)	14.0 (0.6)	14.7 (1.9)	0.15[1]
Sex (male), *n* (%)	7 (87.5)	29 (76.3)	0.66[2]
Operation side (right), *n* (%)	8 (61.5)	20 (37.7)	0.21[2]
Partial resection of lung (done), *n* (%)	8 (61.5)	41 (77.4)	0.29[2]
Follow-up period after VATS (months), mean (SD)	12.0 (14.3)	13.4 (11.5)	0.36[1]
Median observation period (months), mean (range)	7 (2–38)	7 (1–60)	0.42[1]
Recurrence after operation (confirmed), *n* (%)	0 (0)	17 (32.1)	0.02[2]
Thoracic drainage after operation (days), mean (SD)	4.2 (2.3)	4.8 (4.1)	0.14[2]
Length of hospitalization after operation (days), mean (SD)	5.9 (2.5)	6.2 (4.1)	0.28[2]
Air leak for more than 1 week after operation (confirmed), *n* (%)	0 (0)	5 (9.4)	0.32[1]

[1] *t* test

[2] Fisher's exact test

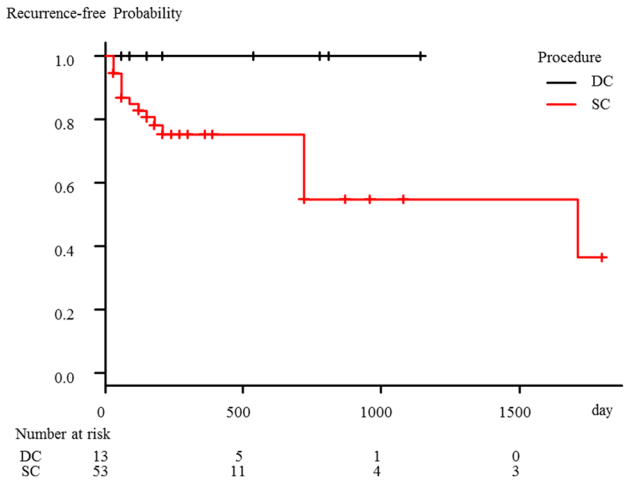

Fig. 3 Recurrence-free rate after video-assisted surgery for pPSP. Kaplan–Meier estimation of the probability of remaining free of recurrence showed a significant difference between the dual-covering and single-covering methods over a mean follow-up period of 12.0 months and 13.4 months, respectively ($p = 0.03$)

visceral pleura had resolved microscopically and the pleural thickening remained. The PGA sheet was barely observed (Fig. 4).

Discussion

Figure 1 shows why we selected the population of under-16-year-old children for this study. The group of under-16-year-olds was the minimum according to age bracket for hospitalization to treat PSP, whereas the same group was the second highest group for reoperation after VATS. We hypothesized that this specific group required different surgical treatment to other groups.

We generally use two materials in thoracic surgery in Japan, namely PGA and ORC, because of their feasibility and usability. The efficacy of PGA sheets for bullectomy has been reported [14]. The findings indicated that PGA was effective for preventing prolonged postoperative air leaks and reducing the recurrence rate of PSP after VATS [14]. The effectiveness of ORC mesh has also been described [10]. A randomized trial showed that the results of placing a visceral pleural covering after bullectomy were not inferior to those of mechanical pleurodesis [10]. ORC mesh covering of the visceral pleura was also found to be effective for secondary pneumothorax caused by lymphangioleiomyomatosis [11] and Birt–Hogg–Dubé syndrome [12]. A meta-analysis also showed that ORC mesh could reduce complications associated with adhesions in abdominal surgery [15].

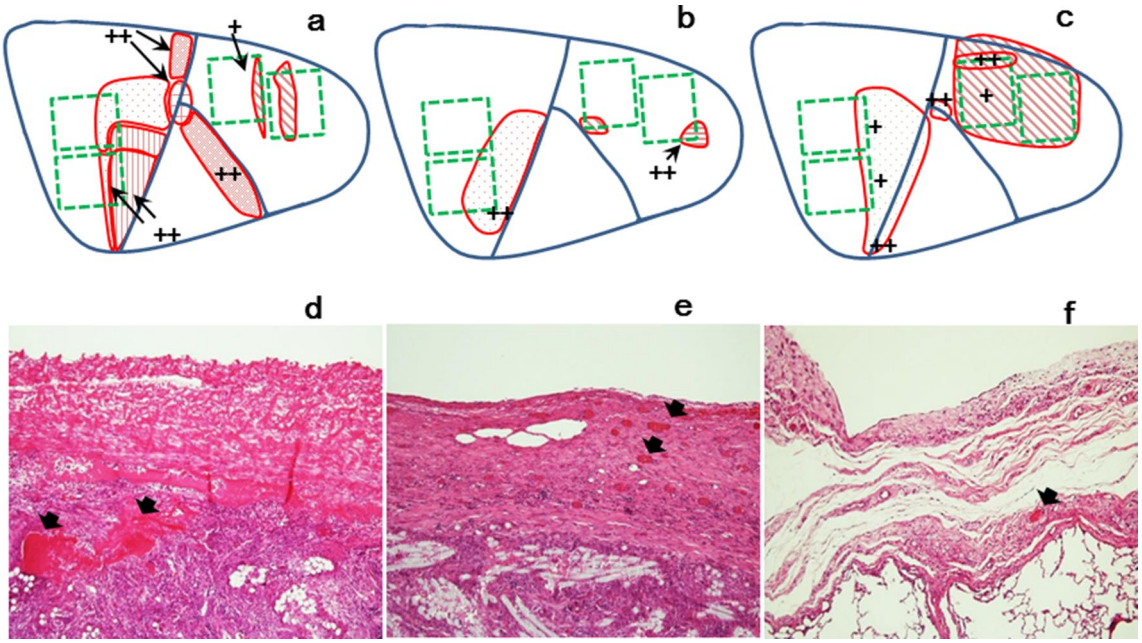

Fig. 4 In vivo experiment. Macroscopic examination revealed no evidence of strong pleural symphysis, except in the corner of the created pleural defects that had been repaired and sutured with absorbable material. Microscopic examination revealed thickening of the visceral pleura and decreasing inflammation over time. **a**–**c** Macroscopic findings. **d**–**f** Microscopic findings (hematoxylin and eosin staining, low-magnification view). **a, d** 2 weeks after thoracotomy. **b, e** 1 month after thoracotomy. **c, f** 3 months after thoracotomy. Rectangles with dashed lines indicate lesions with pleural defects. Plus symbol indicates strong pleural adhesions. The regions enclosed by curved lines show weak adhesions. Arrows indicate the fragments of PGA

This study yielded three notable observations. First, the recurrence rate after VATS for pediatric PSP was high, even though the ORC mesh covering was added after bullectomy. Second, no recurrence developed after VATS using the DC method. Third, recurrence of pediatric PSP was observed after the 6-month follow-up period. These results might account for why the DC method could have influenced the development of pleural thickening and simultaneously protected against pleural symphysis with the chest wall. Our in vivo experiment results supported that the DC method seemed to lead to these results. The pleural thickening helped prevent rupture of the visceral pleura in the study patients, even if there was new bulla formation or if the initial bullae had been incompletely resected. Regarding the prevention of pleural adhesions, a previous report also concluded that pleural reinforcement was better than replacement of pleural symphysis [10]. We hypothesized that neogenesis of bullae might develop in a lesion treated by incomplete pleurodesis, in which a continuous high tensional force could be exerted, such as would occur in the peripheral zone of the region of pleural symphysis or in the staple line. This was reflected by the anchoring sutures in our animal experiment. The effect would result in repeated extension of the visceral pleura with inflation and deflation of the affected lung. Therefore, ORC covering seems reasonable for reinforcing the visceral pleura and preventing pleural symphysis. However, as ORC mesh resolves over several days [11], ORC covering over the PGA sheet, which remained in place for several months in our in vivo experiment and a previous study [11], seems ideal for the treatment of pediatric PSP, in which delayed neogenesis of bullae may occur in association with a young patient's continued physical growth.

Because the use of chemical pleurodesis, such as graded talc, has declined with the advent of VATS for PSP [3] and the long-term risks of graded talc have not been sufficiently studied in pediatric patients, we did not investigate chemical pleurodesis in this study. For the same reason, SC by PGA, which can generate pleural symphysis was not used in this study [11]. The delayed recurrence 6 months after VATS in our patients (Fig. 2) suggests that neogenesis of bullae could occur in association with physical growth. Thus, long-term follow-up and further investigation of this phenomenon are important for the management of pediatric PSP.

This study was limited by its retrospective and nonrandomized design; however, because the prevalence of pediatric PSP is low, we performed a retrospective study. The DC method is feasible and easy to use for other conditions leading to intractable pneumothorax and cystic lung diseases.

In conclusion, this study yielded three important results. First, the recurrence rate of surgery for pediatric PSP was high, even with ORC mesh coverage. Second, the DC methods prevented the recurrence of pediatric PSP after VATS, effectively. Third, long-term follow-up is needed for pediatric PSP after VATS. Recurring pediatric PSP after surgery has negative psychological, developmental, and financial effects on patients and their families. Thus, we must continue to investigate and improve the treatments for pediatric PSP.

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