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ORIGINAL ARTICLE

Control of air leakage during pleurectomy/decortication by the ventilation and anchoring method

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Abstract

Objectives We previously established a novel method of lung repair called the ventilation and anchoring (V/A) method. We evaluated the usefulness of the V/A method for controlling air leakage during pleurectomy/decortication (P/D).

Methods For this study, we enrolled patients with malignant pleural mesothelioma (MPM) who planned to receive P/D. Our lung repair method involves (1) suturing lung parenchyma for an apparent injured lesion and (2) coating the lung parenchyma with fibrin glue (FG) using the V/A method. The tidal volume (TV) was measured under pressure-controlled ventilation in the ipsilateral-affected lung 10 times at the following four points: after thoracotomy, at completion of visceral pleurectomy, after suturing lung parenchyma, and 5 min after coating with FG. The primary endpoint was the mean TV (mTV) change, and the secondary endpoints were the duration of air leakage and incidence of pleurodesis.

Results Between April 2014 and April 2016, 25 patients of the 29 consecutive patients enrolled were eligible. The mTV significantly decreased after completion of visceral pleurectomy but significantly increased after repair of the lung parenchyma, especially after coating with FG. The median duration of postoperative air leakage was 4 days (range: 2–19 days). Postoperative air leakage > 7 days was observed in 11 (44%) patients. Of these 11 patients, 6 received pleurodesis; however, no further revision was needed.

Conclusions Significant increases in TV were observed after coating with FG via the V/A method during P/D. Coating with FG using the V/A method can contribute to a reduction in air leakage during P/D.

Keywords Fibrin glue · Malignant pleural mesothelioma · Pleurectomy/decortication

Abbreviations

EPP	Extrapleural pneumonectomy
FG	Fibrin glue
MPM	Malignant pleural mesothelioma
mTV	Mean tidal volume
P/D	Pleurectomy/decortication
PGA	Polyglycolic acid
TV	Tidal volume
V/A	Ventilation–anchoring

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Introduction

Since it preserves a favourable quality of life [1, 2], pleurectomy/decortication (P/D) is preferred as part of multimodal treatment for malignant pleural mesothelioma (MPM) [3]. Visceral pleurectomy is a challenging part of the surgery, and it is difficult to avoid injuring the lung parenchyma. Overall, the most frequent complication of P/D is prolonged air leakage, which can lead to various other complications [3–10]. To the best of our knowledge, there is no established procedure to control air leakage during P/D.

We have established a novel method of lung repair called the ventilation and anchoring (V/A) method using fibrin glue (FG) [11]. Here, we explore the application of the V/A method to control air leakage during P/D in a clinical setting. In this prospective study, we evaluated the usefulness of the V/A method for controlling air leakage during P/D.

Patients and methods

Patients

We conducted a prospective study to evaluate the efficacy of the V/A method in patients with MPM who underwent P/D. We enrolled consecutive patients with histologically proven MPM who planned P/D following neoadjuvant chemotherapy at the Hyogo College of Medicine Hospital between April 2014 and March 2016. The institutional review board at the Hyogo College of Medicine (number 1689) approved this study on April 9, 2014, and written informed consent was obtained from all the patients. We collected the medical records of all enrolled patients, including operation notes.

Surgical procedure of P/D, including management of intraoperative air leakage

We have previously described our P/D procedure [6]. After completion of visceral pleurectomy, repair of the lung parenchyma was performed to control air leakage. The procedure is explained as follows:

Step 1: Suturing.

Injured lung parenchyma with massive air leakage was sutured using 4-0 polypropylene with a pledget. Then, the area was covered with TachoSil® (Takeda Austria GmbH, Linz, Austria) to provide reinforcement, if required.

Step 2: Coating with FG using the V/A method [11] (supplemental file).

After suturing, 5 ml of fibrinogen solution was spread onto the lung parenchyma using the finger-rubbing method with gentle ventilation (Fig. 1A). Then, fibrinogen and thrombin (5.0 ml) were sprayed over the entire lung parenchyma (Fig. 1B). Two different FG products were used: Bolheal® [The Chemo-Sero-Therapeutic Research Institute, Kumamoto, Japan] was used before October 2015, and Beriplast P® [CSL Behring, King of Prussia, Pennsylvania, USA] was used after November 2015.

Postoperative management of air leakage

Continuous suction with − 5-cm H_2O was performed. In patients with prolonged air leakage (> 7 days), pleurodesis using an automatous blood patch, with or without 50% glucose, was performed, if required. Radiological examinations, including chest X-rays and computed tomography, were routinely performed to evaluate lung expansion. Drainage tubes were removed if visual inspection indicated that air leakage had ceased.

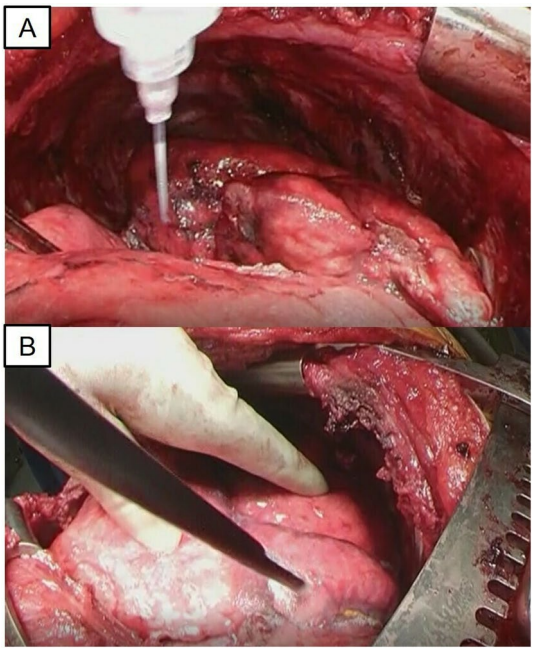

Fig. 1 Ventilation and anchoring method technique. (**A**) Coating of the surface of the lung parenchyma with fibrinogen solution under bilateral ventilation. A bubble is visible where air leakage is occurring. (**B**) Spraying fibrinogen and thrombin onto the surface of the lung parenchyma

Conversion from P/D to EPP was chosen for patients whose intraoperative findings indicated that macroscopic complete resection could only be achieved by EPP because of a diffuse residual tumour on the pulmonary parenchyma.

Outcome measures

We measured the tidal volume (TV) in the ipsilateral-affected lung 10 times at the following four points: (1) after thoracotomy, (2) on completion of visceral pleurectomy, (3) after suturing of the lung parenchyma, and (4) 5 min after FG coating using the V/A method. TV was measured 10 consecutive times by anaesthetists, and we defined the mean value of TV as mTV. At the time of measurement, the ventilator settings were the following: $FiO_2 = 1.0$, respiratory rate = 10 times/minute, peak inspiratory pressure = 15 cm H_2O, and positive end-expiratory pressure = 0 cm H_2O. Bronchial washing was performed prior to measurement to prevent airway obstruction.

The primary endpoint of this study was to evaluate mTV changes at the ipsilateral-affected lung before and after visceral pleurectomy. Secondary endpoints were the duration of, and incidence of pleurodesis for, postoperative air

leakage. Since we used two types of FG, we also compared the clinical courses of the patients treated with each glue.

Statistical analysis

Data are summarised as means ± standard deviations or medians with interquartile ranges. A two-tailed *t* test was used to compare paired continuous data. A non-parametric test (Mann–Whitney *U* test) was used to compare the two groups. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). Two-tailed *P* values < 0.05 indicated statistical significance.

Results

Twenty-nine patients were enrolled in this study. Of the 29 patients, 3 were converted to EPP due to tumour invasion of the lung parenchyma, and 1 patient underwent a completion pneumonectomy 10 days after P/D due to residual ipsilateral lung deficiency. The characteristics of the remaining 25 patients are shown in Table 1. The median age was 64 years (range: 42–77 years), 23 (92%) were male, and 11 (44%) had right-side MPMs.

The mTV measurements of each patient are shown in Fig. 2. The mTV significantly decreased after completion of visceral pleurectomy but significantly increased after lung parenchyma repair, especially after FG coating.

The distribution of postoperative air leakage durations is shown in Fig. 3, and the median duration was 4 days (range: 2–19 days). Postoperative air leakage was > 7 days all 11 (44%) patients with postoperative air leakage. Of these 11 patients, 6 received pleurodesis using an automatous blood patch, but no further revision was needed to control postoperative air leakage.

Bolheal® FG was used in 14 patients, and Beriplast P® FG was used in 11 patients. Changes in mTV before and after using FG were greater for the Bolheal group than the Beriplast P group (168 ml vs. 106 ml, P = 0.37). As shown in Fig. 4, the duration of postoperative air leakage was significantly shorter in the Bolheal group than in the Beriplast group (3 days vs. 9 days, $P < 0.01$), and the incidence of pleurodesis was significantly lower in the Bolheal group than in the Beriplast P group (0% vs. 60%, $P < 0.01$).

Discussion

This prospective study measured changes in mTV during P/D before and after the repair of lung parenchyma using the V/A method. To the best of our knowledge, it is the first report to evaluate the usefulness of FG for control of air leakage during P/D. Significant increases in mTV were

Table 1 Patient characteristics

Age (years)	Mean (range)	64 (42–77)
Sex	Male	23
	Female	2
Side	Right	11
	Left	14
Stage	T1N0M0	14
	T2N0M0	7
	T3N0M0	4
Fibrin glue	Bolheal®	14
	Beriplast P®	11
Duration of postoperative air leakage (days)	Mean (range)	4 (2–19)
Pleurodesis	Yes	6
	No	19

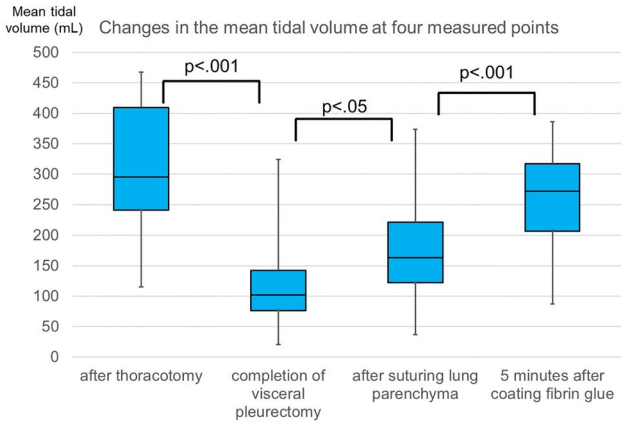

Fig. 2 Changes in mean tidal volume at four measured points

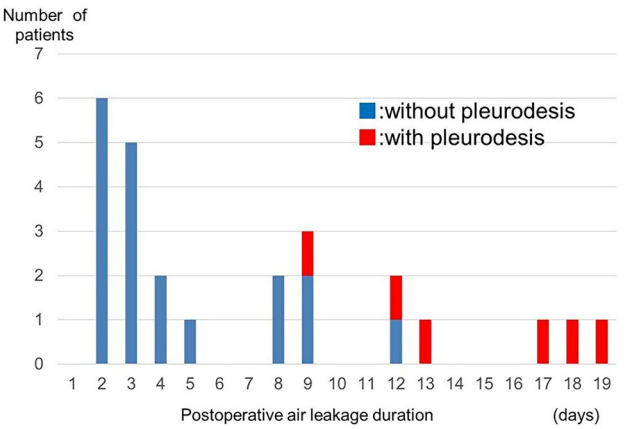

Fig. 3 Distribution of postoperative air leakage durations

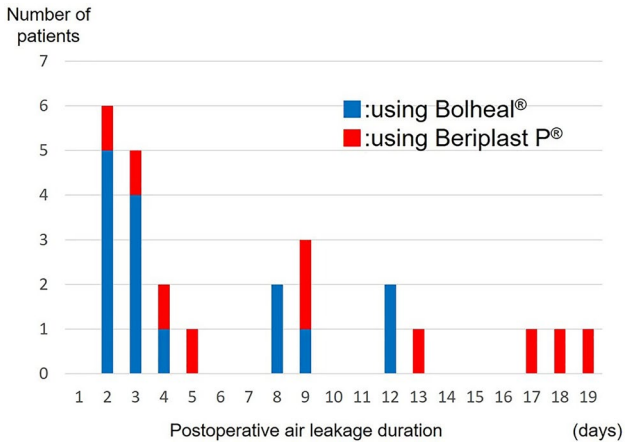

Fig. 4 Distribution of postoperative air leakage durations according to fibrin glue type

observed after coating with FG by the V/A method, and the median duration of postoperative air leakage was 4 days in this study, which suggested that the V/A method contributes to a favourable postoperative period. Due to technical issues of P/D [12], the management of air leakage is essential. In general, prolonged air leakage is the most frequent P/D complication, with an incidence of 18.5%–73% [3–10]. In our study, prolonged air leakage (≥ 7 days) was also observed in 44% of patients; however, no further revisions related to air leakage were needed in this study.

The V/A method was introduced by Kondo et al. [11], who showed that coating with FG under ventilation helped repair air leakage due to pleural defects in an ex vivo pig model. Kondo et al. also found that the application of fibrin solution under ventilation could induce the glue to penetrate deeper into the lung parenchyma compared with conventional methods [13–15]. Kondo et al. also noted that high tolerance of pressure was obtained through use of a stronger anchor with a coated polyglycolic acid (PGA) sheet [11]. However, we did not use the PGA sheet in this study. Since promoting lung expansion and adhesion to the chest wall is essential for controlling air leakage after P/D, we thought using a PGA sheet might interrupt lung expansion. Based on our results, the V/A method should help control air leakage after P/D, even without a PGA sheet.

Since the V/A method is not a complicated procedure, it could be used to repair lung parenchyma in lung resection surgeries other than P/D. Recently, sublobar resection, such as segmentectomy, has been widely attempted for treatment of early-stage lung cancer [16–18]. Segmentectomy often results in postoperative air leakage due to the segmental plane, especially in complicated segmentectomies [16, 17]. Given our favourable results with P/D, we speculate that the V/A method could help control air leakage at the post-segmental plane.

Although several types of FG have been introduced, we used two types in this study. Comparison of the clinical courses between the use of Bolheal® and Beriplast P® indicated that the duration of postoperative air leakage was significantly shorter in the Bolheal group. Previous studies comparing these two FGs have shown that fibrinogen viscosity is lower for Bolheal® than for Beriplast P® [19]. In the V/A method, fibrinogen is delivered to the lung parenchyma through ventilation; thus, we speculate that lower viscosities would make it easier for the glue to penetrate deep into the lung parenchyma, creating a stronger fibrin-like anchor. Therefore, it would be better to use low-viscosity FGs when using the V/A method.

There were several limitations in this study. First, it was a single-arm exploratory study with a small number of patients. Therefore, it could not unequivocally prove the superiority of the V/A method. To reveal the efficacy of the V/A method, a randomised study is required to compare its efficacy. Second, it was difficult to exclude several biases related to surgical technique and tumour status. The degree of lung parenchyma injury could not be standardised due to tumour status or surgical technique, even when the same surgical procedure was attempted.

Despite these limitations, this study is the first to demonstrate the changes in mTV during P/D. We conclude that significant increases in TVs were observed after coating with FG via the V/A method during P/D, and that coating with FG using the V/A method contributes to a reduction in air leakage during P/D.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11748-022-01789-4.

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Author contributions Conceptualization, M.H, N.K, and S.H; methodology, M.H and N.K; patient recruitment, M.H, T.N, A.N, A.K, T.T, and S.M; statistical analysis, M.H; data collection, M.H, T.N, A.N, A.K, T.T, and S.M; writing—original draft preparation, M.H; writing—review and editing, N.K and S.H; supervision, S.H; project administration, M.H. All the authors have read and approved the manuscript.

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Declarations

Conflict of interest None of the authors has a conflict of interest.

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