A novel technique to prevent intra-operative pneumothorax in awake coronary artery bypass grafting: biomaterial neo-pleura

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Abstract

Objective: Pneumothorax caused by damaged pleura represents the biggest obstacle in awake coronary artery bypass grafting. In order to safely perform this surgery, a new technique was developed to close the damaged pleura. Methods: A rub-and-spray method was employed using polyglycolic acid nonwoven fabric and fibrin glue. At first, some fibrinogen solution was rubbed on the edge of the pleural defect and then the PGA fabric was placed and the fibrinogen and thrombin solutions were sprayed. Using a thorax model, the burst pressure caused by positive pressure and the influence of negative pressure, moisture, time, continuous respiratory movement and pleural defect size were examined. In an animal experiment using pigs, the duration spent on repair was measured and any air leakage from the pleura was also identified. Results: In the thorax model, the burst pressure was $355.9 \pm 55.8$ mmHg with positive pressure and no significant difference in negative pressure, moisture, time and respiratory moment was identified. However, there was a significant difference in the defect size. In the animal model, repair was easily achieved regardless of the defect size or location and air leakage was not seen after repair. The average duration of repair was 21.0 s. Conclusions: The present method achieved a strong closure with sufficient durability. Since the fabric is soft and flexible and suturing is not required, moving and fragile pleura can be easily repaired regardless of the defect location and size. Once established, the present method may be used in other forms of awake thoracic surgery or reconstruction of the thorax.

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Keywords: Coronary artery bypass surgery; Less invasive surgery; Pleura; Pneumothorax; Thoracic general

1. Introduction

Coronary artery bypass grafting (CABG) has been developed as a less invasive treatment method [1]. Currently, off-pump CABG (OPCAB) is a well-established procedure that is known to decrease the occurrence of adverse complications typically associated with cardiopulmonary bypass [2]. Watanabe et al. established endoscopic procedures to make CABG even less invasive [3] and robot surgery has been incorporated. In 2000, Karagoz et al. first reported awake CABG (AOCAB), which is performed without general anesthesia [4]. Under higher epidural anesthesia, AOCAB is performed on awake patients without endotracheal intubation [5–7]. The advantages of AOCAB are that postoperative recovery is fast and surgery can be performed on patients in whom general anesthesia is difficult [8]. AOCAB has been performed since 2003, thus yielding favorable results. Based on the report by Karagoz et al. and our experience in this department, pneumothorax caused by damaged pleura represents the biggest obstacle in AOCAB [9].

Various surgical techniques have been reported for the treatment of such pneumothorax [9]. However, repair by suturing is difficult due to the risk of tearing the mediastinal pleura because it is thin and subject to respiratory movement. Therefore, no effective surgical method for treating pneumothorax has been developed so far. In order to safely perform AOCAB, a new technique was developed to close the pleura using polyglycolic acid (PGA) nonwoven fabric and fibrin glue.

2. Materials and methods

The closure method is based on the dural closure, where the pleural defect is covered with a PGA fabric and closed using fibrin glue [10]. A 0.15 mm thick PGA nonwoven fabric (Neovell, Gunze, Kyoto, Japan) was used. PGA is a homopolymer with a molecular weight of 100,000 and it is
hydrolyzed via pyruvic acid finally to water and carbon dioxide. This material disintegrates by about 50% in 10 days, and thereafter completely disintegrates within about 15 weeks. In addition, fibrin sealant (Bolheal, Chemo-Sero-Therapeutic Research Institute, Kumamoto, Japan) was also used. It is composed of two solutions. Solution A contains 80 mg/ml human fibrinogen, 75 μm/l human plasma-derived coagulation factor XIII and 1000 U bovine aprotinin. Solution B contains 250 U/ml human thrombin and 5.9 ng/ml calcium chloride.

A rub-and-spray method was employed, which was confirmed to be the most rigid procedure \[11\]. First, solution A was rubbed on the edge of the entire hole, then the PGA fabric was placed, surrounded by a 5 mm wide margin and solution A and B were sprayed using an application nozzle with low pressure (0.7 kg/cm\(^2\)) compressed air. The volume of both solutions A and B was 1.0 ml/cm\(^2\).

In the present study, the strength of the new repair method was examined using a thorax model and the usefulness was confirmed in an animal experiment.

2.1. Experiment 1 using a thorax model

A thorax model was prepared (Fig. 1). Using a plastic bottle as a model of a rib cage, an air tube was connected to a manometer and then the bottle was pressurized using a plastic syringe. The upper surface of the bottle was covered using a pleura substitute with a diameter of 40 mm and a circular defect with a diameter of 10 mm was made at the center. The pleura substitute was made of rat skin, a soft and thin biological material that can be easily obtained in the manufacturing process, provided by a supporting facility (Chemo-Sero-Therapeutic Research Institute). The defect was then repaired using PGA fabric and fibrin glue. Three minutes after the application of the fibrin glue, the sealing effect was evaluated by measuring the burst pressure of the membrane. The pressure within the bottle was manually increased by the syringe and the internal pressure was measured by the manometer simultaneously. The pressure when an air bubble was macroscopically observed or the manometer indicated decreased pressure was defined to be the burst pressure. The burst pressure was measured by repeating the following conditions, 10 times each. The control group was the burst pressure with positive pressure described above in order to compare these findings with the following conditions:

1. Burst pressure with negative pressure: the burst pressure was measured by applying negative pressure.
2. Degradation of airtightness with time: the burst pressure was measured by applying positive pressure after leaving the model to stand for 3 h.
3. Degradation of airtightness by moisture: after soaking the model in water for 3 h, the burst pressure was measured by applying positive pressure while the model was wet.
4. Assessment of airtightness with respect to the pleural defect size: a large bottle was covered using a pleura substitute with a diameter of 100 mm. The diameter of the defect was set at 30 and 50 mm and the burst pressure was measured by applying positive pressure while changing the defect size.
5. Effects of continuous respiratory movements: a mechanical ventilator (KMA-1300IIS, Acoma, Tokyo, Japan) was connected to the thorax model. A defect with a diameter of 30 mm was repaired while applying positive pressure from 0 to 150 mmHg at a constant rhythm of 15 times per min. Mechanical ventilation was continued for 3 h and then the burst pressure was measured.

2.2. Experiment 2 using an animal model

An animal experiment using pigs was conducted to ascertain the usefulness of the same method to close damaged pleura. All animals received humane care in compliance with the Principles of Laboratory Animals Care formulated by the National Society for Medical Research and the Guide for the Care and Use of Laboratory Animals prepared by the Institute of Laboratory Animal Resources and published by the National Institute of Health, revised in 1996. All protocols were approved by the animal use and care committee of Kanazawa University and we complied fully with the regulations of this committee.

Five healthy pigs weighing between 25.0 and 35.0 kg (average 29.6 kg) were used. Anesthesia was induced with an intramuscular administration of ketamine hydrochloride (20 mg/kg). After a tracheotomy, a cuffed endotracheal tube was inserted and ventilation was performed with a mechanical ventilator (KMA-1300IIS). Thereafter, muscle relaxation was induced with pancuronium 0.1 mg/kg through peripheral intravenous access. Anesthesia was maintained with 1% halothane.

After a median sternotomy, a defect was made on both sides of the pleura and repaired under the following conditions (Fig. 2):
(1) A 10 mm defect at the center of the pleura ($n = 3$)
(2) A 30 mm defect at the center of the pleura ($n = 3$)
(3) A 30 mm defect at the margin of the pleura adjacent to the rib cage ($n = 4$)

During the repair of the pleura, mechanical ventilation was continued with positive pressure ventilation of 20/min. The time spent on repair was measured and after the repair, the anterior mediastinum was filled with water in order to identify any air leakage from the pleura.

We regard surgeries that take more than 3 h as not being indicated for awake surgery. Therefore, the experiment measured the burst pressure 3 h later and the moisture resistance 3 h later. Due to the ease of detachability of the PGA fabric and fibrin glue, we did not perform histological examinations, as we considered detachment to occur at the time of closure of the chest.

2.3. Statistical analysis

All results were expressed as the mean ± standard deviation. Unpaired t test was used to compare the results. The level of significance was set at $p < 0.05$. The StatView software program (Version 5.0, SAS Institute Inc.) was used for the statistical analysis.

3. Results

3.1. Experiment 1

The burst pressure was 355.9 ± 55.8 mmHg with positive pressure as the control.

(1) The burst pressure was 321.2 ± 48.7 mmHg with negative pressure and no significant difference was identified in comparison to the control ($p = 0.15$).

(2) The burst pressure after 3 h was 316.3 ± 53.5 mmHg and no significant difference was identified in comparison to the control ($p = 0.12$).

(3) The burst pressure when the model was wet was 341.5 ± 54.6 mmHg and no significant difference was identified in comparison to the control ($p = 0.56$; Fig. 3).

(4) The burst pressure was 254.2 ± 63.1 mmHg with a 30 mm defect and 191.5 ± 47.1 mmHg with a 50 mm defect. The larger the defect, the smaller the burst pressure. Significant differences were seen for both 30 and 50 mm defects in comparison to the control ($p = 0.001$ and $p < 0.001$, respectively). Furthermore, a significant difference was seen between 30 and 50 mm defects ($p = 0.02$; Fig. 4).

(5) When repairing under continuous positive pressure respiration, the pleura substitute had repeated continuous horizontal movements within a range of −1 cm to +3 cm from the base line. All defects were repairable and air leakage was not seen during the operation in any cases. After the procedure, the burst pressure was 259.4 ± 64.4 mmHg and no significant differences were identified in comparison to the 30 mm defect ($p = 0.85$; Fig. 5).

All cases of air leakage were caused by air leakage through the PGA fiber mesh, but no fibrin membrane detachment was observed.

3.2. Experiment 2

In the animal models, the moving thin pleura were easily repaired, even in rough or uneven locations, because the fibrin sealant membranes were soft and flexible.

Repair was easily achieved regardless of the defect size or location and the average time of repair for conditions (1), (2) and (3) was 17.3, 22.7 and 22.5 s, respectively. No air leakage was seen after the repair and no progressive pulmonary collapse was observed either.
4. Discussion

Less invasive cardiovascular surgical methods have recently been developed. In CABG, operations without cardiopulmonary bypass and with minimal surgical incisions have become standard procedures [1–3]. In addition, AOCAB is performed without endotracheal general anesthesia, thus further reducing invasiveness [4–9]. Despite the indisputable advantages of general anesthesia in thoracic surgery, this can trigger some adverse effects including an increased risk of pneumonia, impaired cardiac performance, neuromuscular problems and mechanical ventilation-induced injuries, which include barotrauma, volutrauma, atelectrauma and bio-trauma. In order to reduce the adverse effects and cost of general anesthesia, thoracic epidural anesthesia has been employed for AOCAB.

When performing awake surgery, pneumothorax caused by pleural damage is the biggest obstacle. Pneumothorax prevents spontaneous breathing and causes respiratory distress and it has been hypothesized that an increase in carbon dioxide stimulates the medulla oblongata to induce the sensations associated with respiratory distress or that paradoxical thoracic movement and restricted lung dilatation stimulate the brainstem and motor area to cause the sensations associated with respiratory urgency. Subsequently, patients suffer and experience tachypnea. The thoracic movements associated with tachypnea further complicate the surgical procedures. Karagoz et al. and this group have been dealing with pneumothorax by suturing the pleura and then performing drainage of the thoracic cavity or widely opening the chest; however, suturing is very difficult because the damaged pleura is both very thin and always moving due to respiration. According to Karagoz et al., endotracheal intubation was required in 4 of 137 patients (2.9%) [9]. At this center, respiratory assistance was needed due to pneumothorax in 15 of 43 patients and endotracheal intubation was required in 2 patients (4.7%). As a result, no effective techniques are currently available to reliably repair pneumothorax.

In the present study, a new pleural repair method using PGA nonwoven fabric and fibrin glue was proposed and the efficacy was confirmed. In the field of thoracic surgery, fibrin glue is used to achieve hemostasis during surgery or prevent air leakage from the pulmonary parenchyma and the usefulness and safety of this approach have been proven [12–14]. Pressure testing for air leakage confirmed that the strongest technique was the rub-and-spray method combining PGA fabric and fibrin glue [11]. With the rub-and-spray method, by rubbing solution A into PGA fabric, fibrinogen deeply penetrates the fabric and then by spraying solutions A and B, polymerization within the framework of PGA fabric is strong and even. Microscopic experiments also confirmed that the rub-and-spray method achieves the deepest penetration of fibrin glue into the fabric and the surface is covered most evenly [11]. This method is highly resistant to moisture, respiratory movements and chronological degradation in the short term. In the present study, larger defects tended to be associated with smaller burst pressure. Air leakage occurred at the weakest area of the fibrin glue membranes, thus suggesting that even spraying is important for the repair of large defects. However, air leakage should not pose a significant problem in clinical settings, since the burst pressure is much greater than the normal physiological pressure in the thoracic cavity of humans (~1.5 to ~5.9 mmHg).

In the animal study, the PGA fabric and fibrin glue were very flexible and pliable and since suturing was not required, repair was safely achieved on the moving thin pleura regardless of the defect size in not only flat areas, but also rough uneven areas. During surgery, since the PGA fabric alone was permeable, application could be achieved regardless of airflow through the defect due to respiratory movements. PGA is bioabsorbable, but it can be easily removed at the end of surgery. In addition, this method may also be useful for visceral pleural repair.

The limitations of this technique are that preparing an elastic model of a rib cage and an awake animal model is difficult and experiments performed under physiological conditions are difficult to conduct. Identification of the parameters indicating the efficacy of pleural repair in either awake patients or animal models will also be necessary. It is therefore not clear whether these results can immediately be applied to humans. In addition, even after nanofiltering, the infection risk of fibrin glue cannot be completely eliminated [15]. Furthermore, PGA fabric and fibrin glue are also expensive.

5. Conclusions

The present results proved that this novel closure method using PGA fabric and fibrin glue achieved a strong closure with sufficient durability. Once established, the present method may be potentially useful for performing other forms of awake thoracic surgery [8,16] or reconstruction of the thorax. Further investigations are needed, however, to confirm the clinical efficacy of the present method.

References

Pleural tears are a common occurrence in thoracic surgery and a prolonged air leak is often encountered in patients undergoing lung resection or volume reduction when there is associated emphysema [1]. Spontaneous pneumothorax is closely related to pulmonary blebs and interstitial emphysema resulting in variable collapse of lung tissue [2]. Various sealants and glues are available to repair the pleural defects but the optimal treatment and equally, the management of chest tubes are a matter of controversy [1]. Recently, even endobronchial valves have been inserted to control a persistent air leak [3].

In this manuscript the authors address a very specific category of parietal pleural tears; those occurring during awake coronary artery bypass grafting (CABG) [4]. In their clinical experience respiratory assistance because of pneumothorax was necessary in 15 out of 43 patients (34.9%) with endotracheal intubation required in 2 patients (4.7%). In an experimental setting they developed a promising novel technique based on dural closure, repairing the tear by a so-called ‘rub-and-spray method’ using polyglycolic acid (PGA) fabric and fibrin glue.

In a thoracic model using rat skin as pleural substitute a burst pressure of 356 mmHg was measured, which is much higher than normal, physiological intrathoracic pressures. Defects up to 50 mm could be repaired. There were no significant differences regarding the application of negative pressure, moisture, time (with measurements up to 3 h), and respiratory movements. However, there was a significant difference regarding the size of the defect; larger defects having lower burst pressures but still high above physiological values.

In a subsequent pig experiment, sternotomy was performed after endotracheal intubation and mechanical ventilation. Pleural defects of different sizes (10 and 30 mm) were created at different locations and subsequently repaired. This was easily achieved with an average duration of only 21 s. Strong closure with sufficient early durability was obtained.

Although these experiments provide valid information, there are several limitations in the models used. The in vitro thoracic substitute the authors describe, is in fact a rigid plastic bottle, which is quite different from the elastic thoracic cage. In this way, no precise physiological conditions can be applied. Rat skin was used as pleural surrogate but histological similarities and differences with normal pleura are not described. No measurements were made beyond 3 h and histological evaluation of the healing process was not performed. Was this accompanied by a lot of inflammation? PGA disintegrates by about 50% in 10 days and it would be interesting to see if there was a lot of inflammation.

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Pleural tears: are all holes the same?

Keywords: Pleura; Repair; Polyglycolic acid; Fibrin sealant; Air leak; CABG; Thoracic surgery

Editorial comment

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