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# Changes in Pedicle Pericardial Fat Tissue around the Anastomotic Site after Tracheobronchoplasty

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**Abstract**

*Purpose* Pericardial fat is an appropriate tissue to cover the bronchial anastomotic site because its harvesting is minimally invasive. We investigated the changes in pericardial fat tissue around the anastomotic site after pulmonary resection with tracheobronchoplasty.

*Methods* The study included 43 lung cancer patients who had undergone pulmonary resection with tracheobronchoplasty. We measured the maximum cross-sectional area and average CT values of the pedicle pericardial fat pad around the anastomotic site one week and 6 months after the operation.

*Results* Average rate of residual pedicle pericardial fat pad was 61% at 6 months postoperatively. Body mass index (BMI) < 21.2 kg/m$^2$ ($P$ = 0.031) and blood albumin level < 3.4 g/dl ($P$ = 0.005) were significant predictive factors for pedicle flap shrinkage. Patients with fat tissue shrinkage showed significantly elevated CT values 6 months postoperatively ($P$ = 0.029), whereas those without shrinkage maintained low CT values.

*Conclusions* Preoperative nutritional conditions, reflected in high BMI and blood albumin levels, correlated with a high rate of residual pedicle pericardial fat pad. In patients with pedicle flap

shrinkage, CT values significantly increased, suggesting that fat might have taken on another form (e.g., scar tissue).

## Introduction

Various autologous tissues have been used to prevent the occurrence of bronchopleural fistula (BPF) (1-3). However, whether to perform bronchial coverage has been assessed in only one small randomized trial (4). Bronchovascular fistula is the most critical event after lung cancer surgery, and bronchial coverage may be a means to avoid this occurrence. Because pulmonary resection with tracheobronchoplasty places the patient at high risk of developing a BPF (5), the pulmonary artery should be separated from the bronchial anastomotic site. Some patients had complication such as ileus after harvesting the omentum (3). Complications have been reported for the intercostal muscle flap, including heterotopic ossification (6, 7). We suggest that pericardial fat tissue is an appropriate covering tissue, because its harvesting will be less invasive and safety.

Although changes in the covering free pericardial fat tissue were investigated in a previous study (8), changes in the covering pedicle pericardial fat tissue have never been addressed. This study aimed to investigate changes in the pedicle pericardial fat tissue used to cover the anastomotic site. The findings may contribute to selecting more appropriate covering material after tracheobronchoplasty.

## Methods

Altogether, 57 patients with primary lung cancer underwent pulmonary resection with tracheobronchoplasty at our institution from January 2010 to December 2019. In this retrospective study, we evaluated the qualitative and quantitative changes in the pedicle pericardial fat tissue around the anastomotic site in 43 of the patients who had undergone plain computed tomography (CT) of the chest both one week and 6 months after the operation. Patients who had not undergone both CT evaluations were excluded from the study. Because of secondary surgery, four patients with BPF were also excluded. Preoperatively, all patients provided informed consent for use of their examination outcomes and data in clinical studies. The local institutional ethics committee approved this study (approval no. 4403; approval date, October 3, 2019).

Mediastinal lymph nodes with a short axis of > 10 mm on enhanced CT scans were diagnosed as clinically positive for metastasis. Our criteria for selecting surgical resection were the absence of distant metastasis, no cancer cell-positive pleural or pericardial effusion, no N2 disease at two or more mediastinal levels, no bulky N2 disease, no N3 disease, and a predicted postoperative vital capacity of > 40%. Patients with T4 lung cancer with N0 or N1 nodal extension and tumors that could be removed completely were candidates for surgery.

Patients with pathological stage II or III lung cancer underwent adjuvant platinum-based doublet chemotherapy, and those with stage I lung cancer received oral tegafur-uracil adjuvant chemotherapy. Initiation of treatment in each case was based on the empirical decisions of the physician in charge. Induction chemoradiotherapy was planned for patients with enlarged, but completely removable, N2 lymph node metastasis. Hence, in this study, 18 patients had adjuvant chemotherapy, and 3 underwent induction chemoradiotherapy.

Tracheobronchoplasty was performed using interrupted or continuous 4-0 absorbable monofilament sutures. Layer-to-layer bronchial anastomosis is standard method. After airway reconstruction, the mediastinal pleura of the pre-phrenic nerve and behind the sternum was cut in a double line from the diaphragm to the brachiocephalic vein. The pericardial fat tissue was harvested with the mediastinal pleura, which showed blood capillaries under the pleura (Fig. 1). The pedicle is on the cranial side of the flap. Each anastomotic site was covered circumferentially with a fat pad.

When radiographic findings are subtle or equivocal, CT frequently allows more accurate identification of the disease process as well as prompt and appropriate treatment (9). Chest CT was routinely performed one week after the pulmonary resection with tracheobronchoplasty. After discharge, all patients had follow-up examinations every 2–4 months that included chest radiographs. Plain CT was performed 6 months postoperatively and every year thereafter as a usual postoperative surveillance.

CT images with a section thicknesses of 5 mm were obtained. These CT images were acquired using 32-row or 320-row multislice CT scanner. The maximum cross-sectional area and average CT values of the pedicle pericardial fat pad around the anastomotic site were measured using a SYNAPSE SCOPE (Fujifilm Co, Tokyo, Japan) (Fig. 2a). CT values of fat tissue ranged from −45 to −195 HU (10). The volume of the residual pericardial fat pad at 6 months postoperatively has been reported at 40% (8). When the volume of the fat tissue was considered to vary in equal proportions, a cutoff value for residual rate of fat tissue area was set at 54% ($0.4^{2/3} = 0.54$) (Fig. 2b). A rate of residual fat tissue area < 54% at 6 months postoperatively was defined as pedicle flap shrinkage.

Changes in areas and CT values of the pedicle pericardial fat pad are analyzed by paired t-test. Differences in clinicopathological factors between patients with and without shrinkage of the pedicle flap were assessed using the Mann–Whitney U-test and the $\chi 2$ test. Cutoff values of body mass index (BMI), albumin and triglyceride levels were calculated using receiver operating characteristic curve analysis. Logistic regression analyses were used for univariate analyses, and a multiple logistic regression analysis was used for the multivariate analysis. Hazard ratios were used to estimate the relative risks for pedicle flap shrinkage. A value of $P < 0.05$ was considered to indicate statistical significance. Statistical analyses were performed using JMP statistical software (version 10; SAS Institute, Cary, NC, USA).

**Results**

The patients' surgical details are shown in Table 1. Right upper sleeve lobectomy was the most common method. Maximum cross-sectional areas of the pedicle pericardial fat pads one week and six months after the operation are shown in Figure 3. The areas of pedicle pericardial fat pad decreased significantly ($P < 0.017$) and the average rate of residual area at 6 months was 61%. These changes were not measured in four patients with anastomotic leakage because of secondary surgery. Four patients with anastomotic leakage did not develop a bronchovascular fistula, which is the most critical adverse event after lung cancer surgery. There were no treatment-related deaths during the study period.

Patients' characteristics according to the presence of fat tissue shrinkage are shown in Table 2. Decreased BMI ($P$ = 0.020), blood albumin ($P$ = 0.017) and blood triglyceride levels ($P$ = 0.041) significantly correlated with fat tissue shrinkage.

Table 3 shows the results of the univariate and multivariate analyses of risk factors for fat pad shrinkage. The BMI < 21.2 g/m2 ($P$ = 0.031) and blood albumin level < 3.4 g/dl ($P$ = 0.005) were significant predictive factors for fat tissue shrinkage in the univariate analysis. Among these factors, a blood albumin level of < 3.4g/dl was an independent predictive factor for fat tissue shrinkage ($P$ = 0.020).

Figure 4 shows time-dependent change in the CT values at the pedicle pericardial fat pad. For patients with pedicle flap shrinkage, the CT values were significantly elevated 6 months after the surgery ($P$ = 0.010), whereas they remained low in patients without pedicle flap shrinkage ($P$ = 0.091).

**Discussion**

The results showed changes in the pedicle pericardial fat tissue around the anastomotic site over time. In particular, the BMI and blood albumin levels were significant predictive factors for pedicle pericardial fat tissue shrinkage. Of the two, the blood albumin level proved to be a significant independent predictive factor for fat tissue shrinkage. These results suggested that nutritional conditions might correlate with the residual volume of the fat pad around the anastomotic site. We also showed that the CT values of the fat tissue were significantly elevated in patients who experienced pedicle flap shrinkage.

It was reported that BPF developed 180 days after anatomical lung resection (11). A bronchovascular fistula developing 163 days after bronchoplasty have been reported (12). Because it is important that the pedicle flap intervenes for a long term between the bronchial anastomotic site and the pulmonary artery, we measured the changes in the fat tissue 6 months after the operation. Average rate of residual fat tissue area at 6 months was 61%. When the volume of the covering fat tissue varied in equal proportions, the average residual volume at 6 months was estimated at 47% ($0.61^{3/2} = 0.47$). The residual volume 6 months postoperatively was 40% (8). Those authors used a free fat pad to cover the bronchial stump. This difference in the rates of residual fat tissue may be associated with the way pericardial fat tissue is harvested.

Pericardial fat tissue contains blood capillaries (Fig. 1), suggesting that the pedicle tissue has micro blood flow, which would contribute to maintaining the fat tissue. The blood supply of the intercostal muscle flap has been evaluated using indocyanine green fluorescence (13). Blood flow in pedicle pericardial fat has not been investigated, perhaps because the blood supply is insufficient to be measured using indocyanine green. Hattori and colleagues (14) reported a novel method for monitoring arterial blood supply using a capillaroscope (a microscope that aids visualization of capillaries and their blood flow) during autologous breast reconstruction surgery using a deep inferior epigastric perforator flap. We suggest that a capillaroscope may be useful for evaluating the blood supply of the pedicle pericardial fat tissue. If we can measure the blood supply intraoperatively, we could regulate the tension and fixation of the pedicle pericardial fat tissue to maintain sufficient blood flow, thereby increasing the rate of residual fat tissue.

CT values range from −1000 to +1000 HU, depending on the density of the assessed item. For example, the CT value for air is −1000 HU, for water 0 HU, and for bone 1000 HU. CT value of fat tissue range from −45 to −195 HU (10). Our data showed a correlation between an increased CT value and shrinkage of pericardial fat tissue around the anastomotic site. It was reported that the CT value increase in pericardial fat tissue was induced by inflammatory cell infiltration (15). We showed that the median CT value of shrunken pericardial fat tissue was more than −45 HU, possibly indicating that the shrunken pericardial fat tissue was no longer adipose tissue but had transformed into some other form, such as scar tissue.

Preoperative nutritional conditions—such as those reflected in a lower BMI value and serum albumin level—were significant predictive factors for pericardial fat tissue shrinkage around the anastomotic site. Pulmonary resection with tracheobronchoplasty is commonly indicated for patients with locally advanced primary lung cancer. These patients do not have enough time to improve their nutritional status before surgery. A preoperative evaluation of nutritional conditions may provide valuable information to guide the selection of appropriate covering tissue around the anastomotic site.

Kwek and colleagues (6) studied changes in the CT appearance of the intercostal muscle flap. They concluded that the flap remained unchanged on subsequent CT scans. Thus, the intercostal muscle flap is expected to separate the pulmonary artery from the anastomotic site for a long time. These authors also showed that all intercostal flaps had evidence of calcification. Deeb and colleagues (7) reported that some patients with an intercostal muscle flap developed airway stenosis due to ossification of the flap. We suggest that the intercostal muscle flap may be unfit for circumferential coverage of a bronchial anastomotic site.

This study had some limitations. First, it was a retrospective trial and included only a small number of patients. Accumulation of patients' data is warranted. Second, this study did not include patients developing the BPF. We did not find out whether the shrinkage of fat tissue doesn't actually mean the decrease in its protection for the anastomotic site. Prospective trials may be necessary to address this lack. Finally, we showed quantitative and qualitative changes in the fat pad postoperatively by measuring the cross-sectional area and determining the average CT values, but we did not investigate the volume or CT values of the whole tissue of the fat pad. Because the flap is connected mediastinally through the pedicle, it is difficult to identify the actual range of the pericardial fat pad. Nevertheless, we suggest that the method we described is both simple and reproducible.

In conclusion, we showed changes in the pedicle pericardial fat tissue around the anastomotic site after tracheobronchoplasty. The average rate of residual fat tissue 6 months after the operation was 61%. A preoperative nutritional condition, such as low BMI and low blood albumin level, correlated with the rate of residual fat. This finding may contribute to the selection of more appropriate material for covering the site after tracheobronchoplasty. In patients with flap shrinkage, CT values of the fat tissue are significantly elevated, indicating that fat tissue might have taken on another form, such as scar tissue.

**Conflict of interest statement:** Takuma Tsukioka and other co-authors have no conflict of interest.

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**Figure legends**

**Figure 1** A pedicle pericardial fat pad was harvested from the left thoracic space. Blood capillaries were observed in the surface of the flap.

**Figure 2** **a** Maximum cross-sectional area and average computed tomography (CT) values for the pedicle pericardial fat pad around the anastomotic site were measured using plain CT. **b** When the volumes of the covering fat tissue varied in equal proportion, the fat tissue volume decreased to 40%. It was 54% in the cross-sectional area ($0.4^{2/3} = 0.54$)

**Figure 3** Maximum cross-sectional areas of the pedicle pericardial fat pad one week and 6 months after the operation

**Figure 4** Changes in computed tomography values were analyzed per the presence of fat tissue shrinkage. Values are presented as medians ± SEMs. Values at one week after the operation are shown in the filled columns. Values at 6 months after the operation are shown in the open columns.