Changes in the Cross-sectional Area of Pulmonary Small Vessels Assessed via Chest Computed Tomography after Interventional Bronchoscopy in Patients with Airway Obstruction Due to a Malignant Disease

Hiromi Muraoka¹, Hiroki Nishine¹, Takeo Inoue¹, Teruomi Miyazawa¹, and Masamichi Mineshita¹

(Received for Publication: August 18, 2016)

Abstract

Background: Pulmonary perfusion scintigraphy is a useful method to assess improvements in airflow limitation. However, the number of institutions equipped with pulmonary perfusion scintigraphy equipment is limited. Computed tomography (CT) scans are quick to perform and can be performed in severe cases. Recently, it has been reported that the percentage of the cross-sectional area of pulmonary small vessels (%CSA<5) can be measured by analyzing CT images that correlate with the radionuclide uptake rate shown by pulmonary perfusion scintigraphy.

Methods: We retrospectively reviewed CT scans of 14 patients with unilateral bronchial obstruction due to malignant disease to measure the %CSA<5 before and after interventional bronchoscopy using the semi-automatic image-processing program (ImageJ). In 5 cases, we examined the correlation between the %CSA<5 and the radionuclide uptake rate visualized by pulmonary perfusion scintigraphy.

Results: The %CSA<5 in the obstructed side of the lung after treatment displayed significant improvements after intervention (p = 0.04). Among the 5 cases that underwent pulmonary perfusion scintigraphy before and after the treatment, the radionuclide uptake rate of the obstructed side improved in all patients, whereas the %CSA<5 improved in 4 of the 5 patients.

Conclusion: Measurement of the %CSA<5 might be useful to assess the outcome of interventional bronchoscopy.

Key words

Interventional bronchoscopy, computed tomography, cross-sectional area, pulmonary vessels

Introduction

Severe airway obstruction due to malignant disease can cause symptoms such as dyspnoea, wheezing, and failure to expectorate mucus, and is often associated with complicated atelectasis and lung abscess. Patients suffering from airway obstruction can receive significant relief from life-threatening symptoms via interventional bronchoscopy, and performing interventional bronchoscopy at the exact location of the obstruction can provide the greatest functional benefit to patients¹⁻¹⁰. It is essential to improve obstructions, usually using chemotherapy and radiation as the first choice of treatment¹¹,¹². However, if the airway obstruction is predominantly due to extrinsic compression by tumour or metastatic lymph nodes, interventional bronchoscopy should be considered.

In physiological assessments, we have noted distinct flow-volume curve patterns specific to the type of obstruction¹⁰. Although flow-volume curves are widely used and easy to generate in daily clinical set-
tings, they cannot discriminate between the left and right lungs. Furthermore, in patients with bronchial obstructions, pulmonary function tests may not show significant changes after intervention\(^\text{13}\).

Hauck et al. reported that the normalization of blood flow via interventional bronchoscopy in patients with bronchial obstruction showed improvements for ventilation in the obstructed side of the lung\(^\text{14}\). Pulmonary perfusion scintigraphy requires approximately 30 minutes to perform, and it is diffi-
cult for patients with airway obstructions to remain in a supine position for long periods of time. Furthermore, there are few institutions that are equipped with the necessary equipment to perform pulmonary perfusion scintigraphy. On the other hand, the time required for CT imaging is very short, making it suitable even in severe cases. Recently, it was reported that the cross-sectional area (CSA) measured by ana-
lyzing CT images correlates with the radionuclide uptake rates shown by pulmonary perfusion scintigraphy\(^\text{15}\).

In this study, we retrospectively investigated the changes in CSA in patients with unilateral bronchial obstruction due to a malignant disease to evaluate the effects of interventional bronchoscopy.

Material and Methods

Subjects

We retrospectively reviewed CT scans of pa-
tients who were referred to our institution between April 2008 and March 2016. This study was approved by our institutional review board, waiving the need for informed consent (approval number 3126). We selected CT scans of adult patients who met all the following criteria: patients with unilateral bronchial obstruction due to a malignant disease who underwent interventional bronchoscopy, and patients with CT scans performed within 7 days before and after the interventional procedures. We excluded cases with abnormal parenchymal lesions or unclear CT images that prevented analysis using the software. We examined correlations between CSA and the radionuclide uptake rate shown by pulmonary perfusion scintigraphy.

Computed Tomography (CT)

CT examinations were performed using a 16-, 64-, or 80-detector CT scanner (Aquilion 16, Aqui-
lion 64, and Aquilion Prime, Nasu, Japan, Toshiba Medical Systems). CT was performed during a breath-hold at a deep inspiration with the patient in the supine position. The MDCT parameters were as follows: 120 kV and 80–300 mA; collimation, 0.5 mm; gantry rotation time, 0.5 s; and a beam pitch of 0.81–0.94. All images were reconstructed using a standard reconstruction algorithm with a slice thickness of 1 mm\(^\text{15}\).

CT Measurement of Pulmonary Small Vessels

CT measurements of pulmonary CSA have been described in previous literature\(^\text{17,18}\). In brief, the fol-
lowing procedures were performed. For measure-
ments of pulmonary CSA, all CT images (1-mm slice thickness) at 1-cm intervals were selected from approximately 1 cm below the apex to approximately 1 cm above the base of the lung. Measurements were performed for the upper, middle and lower regions of the affected lung. CT images were divided into upper, middle and lower zones. The upper zone was defined as CT sections located above the aortic arch, the middle zone located below the carina, and the lower zone located below the inferior pulmonary vein. These CT images were analyzed using a semiautomatic image-
processing program, ImageJ version 1.49v (im-
agej.nih.gov).

CSA measurements were conducted as follows: first, the lung field was segmented using a threshold technique with all pixels between −500 and −1024 HU on each CT image (Fig. 1A). Next, the segmented images were converted into binary images with a window level of −720 HU. Using the Analyze Parti-
cles function of ImageJ, which can count and measure objects into binary images, the number of vessels of a specified size, and the CSA of each size range on every CT slice were determined. Simultaneously, ves-
sels that ran oblique or parallel to the slice were ex-
cluded using the Circularity function of ImageJ, where circularity was calculated as \(4\pi \times \text{[area / (perimeter)]}^2\) of the structure of interest. Circularity val-
ues can range from 0 (straight line) to 1.0 (circle), and a range of circularity from 0.9 to 1.0 was used so that only vessels that ran essentially perpendicular to the plane of the CT slice, based on their shape in the image, were analyzed.

We measured the CSA of vessels less than 5 mm\(^2\) (CSA<5), which showed the highest correlation with pulmonary blood flow\(^\text{15}\). Measurements were performed for the upper, middle and lower zones of the affected lung. The areas of all vessels with a CSA<5 were calculated and summed in each image slice and expressed as a percentage of the area in the measured field of the affected-side lung (%CSA<5).
Figure 1. Measurement of the cross-sectional area of pulmonary small vessels using ImageJ software

A) CT image shows the lung field segmented within threshold values from –500 to –1024 HU. B) CT image segments in A with a window level of ~720 HU. C) Binary image converted from B. D) Mask image was obtained for a particle analysis after setting the vessel size parameters to within 0–5 mm$^2$ and circularity levels to within 0.9–1.0 (circularity was calculated as $4\pi \times \text{area} / \text{perimeter}^2$, and values range from 0 [straight line] to 1.0 [circle]).

for each image.

**Pulmonary Perfusion Scintigraphy**

Six static views with anterior, posterior, and right-to-left lateral, oblique posterior, and anterior projections were acquired immediately after an IV injection of 115–233 MBq of 99mTc-MAA using gamma cameras. Using anteroposterior and posteroanterior projections, regions of interest were manually drawn around the right and left lungs. Lung counts were averaged for anterior and posterior projections. We determined right, left and total lung counts and then calculated the percentage of the affected side relative to the whole lung (%MAA affected/W).

**Statistical Analysis**

All statistical analyses were performed using SPSS Statistics version 19 (SPSS Inc., Chicago, IL, USA). The %CSA<5 of the affected side was statistically analyzed. P values were considered significant at less than 0.05. Significant differences in %CSA<5 and %MAA affected/W before and after interventional bronchoscopy were evaluated using Wilcoxon signed-rank tests.

**Results**

Of the 30 cases considered for assessment, 3 cases were excluded because interventional bronchoscopy was undertaken at the healthy lung side, and 13 cases were excluded due to a change in lung lesions after bronchoscopy, making them unsuitable for image analysis. The characteristics of the remaining 14 cases included in this study are shown in Table 1. Symptoms and pulmonary function test (PFT) results significantly improved for all patients (Table 2). There was no statistical correlation between PFTs and %CSA<5 in the 9 cases in which PFTs could be performed.

The %CSA<5 of the obstructed side of the lung displayed significant improvements after intervention ($p = 0.04$) (Fig. 2).

In addition, of the 5 cases that underwent pulmonary perfusion scintigraphy and CT within 7 days before and after treatment, improvements in %CSA<5 were seen in 4 cases, while the %MAA im-

<table>
<thead>
<tr>
<th>Table 1. Patient Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex, n (%)</strong></td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td><strong>Median age (range)</strong></td>
</tr>
<tr>
<td>59.93(40-72)</td>
</tr>
<tr>
<td><strong>Disease, n (%)</strong></td>
</tr>
<tr>
<td>Lung Cancer</td>
</tr>
<tr>
<td>Oesophageal Cancer</td>
</tr>
<tr>
<td>Cervical Cancer</td>
</tr>
<tr>
<td>Malignant lymphoma</td>
</tr>
<tr>
<td>Malignant melanoma</td>
</tr>
<tr>
<td><strong>Affected side, n (%)</strong></td>
</tr>
<tr>
<td>Right</td>
</tr>
<tr>
<td>Left</td>
</tr>
<tr>
<td><strong>Treatment, n (%)</strong></td>
</tr>
<tr>
<td>Stenting</td>
</tr>
<tr>
<td>Ballooning</td>
</tr>
<tr>
<td>Argon plasma coagulation</td>
</tr>
</tbody>
</table>
Table 2. Changes in Pulmonary Function Test Results and Modified Medical Research Council Scale Scores

<table>
<thead>
<tr>
<th></th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PFTs (n = 9)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FVC(l)</td>
<td>2.12±0.61</td>
<td>2.55±0.78*</td>
</tr>
<tr>
<td>(FVC/predicted FVC,%)</td>
<td>70.2±19.45</td>
<td>84.4±20.86*</td>
</tr>
<tr>
<td>FEV1(l)</td>
<td>1.02±0.44</td>
<td>1.63±0.57*</td>
</tr>
<tr>
<td>(FEV1/predicted FEV1, %)</td>
<td>41.9±15.65</td>
<td>71.5±16.15*</td>
</tr>
<tr>
<td>FEV1/FVC%</td>
<td>70.94±22.09</td>
<td>69.11±11.35</td>
</tr>
<tr>
<td>PEF</td>
<td>2.39±0.83</td>
<td>3.29±1.41*</td>
</tr>
<tr>
<td><strong>MMRC (n = 13)</strong></td>
<td>3±1.26</td>
<td>1±0.93*</td>
</tr>
</tbody>
</table>

Definition of abbreviation: FVC = forced vital capacity, FEV1 = forced expiratory volume in one second, PEF = peak expiratory flow, MMRC = Modified Medical Research Council Scale. Mean values(±SD) are given for FVC, FVC/predicted FVC, FEV1, FEV1/predicted FEV1, FEV1/FVC%, PEF and MMRC.

* p < 0.04 after treatment vs. before treatment.

Figure 2. Changes in the %CSA<5 before and after treatment
Each line represents the change in %CSA<5 before and after treatment.

Figure 3B. Changes in the %CSA<5 before and after treatment
Each line represents the change in %CSA<5 before and after treatment.

Discussion

In this study, the cross-sectional area of pulmonary small vessels improved after interventional bronchoscopy in cases of unilateral bronchial obstruction. CT is non-invasive and can be performed in many hospitals, and it is applicable in severe cases. Thus, CT analysis appears to be useful in evaluating the effectiveness of treatment in cases where PFTs or quantitative pulmonary perfusion scintigraphy could not be performed. Furthermore, evaluation of the %CSA <5 via CT was effective to assess treatment effects in emergent cases. This is the first report to demonstrate improvements in the %CSA<5 after removing airflow limitations.

Matsuoka reported that the %CSA<5 was found to have a negative correlation with the extent of emphysema, degree of airflow limitation, and severity of pulmonary hypertension. Further, Karayama reported that the %CSA<5 significantly decreased after chemotherapy and mentioned that this result was indicative of the potential vascular toxicity induced by
## Table 3. Results of 5 Cases that Underwent Both CT and Pulmonary Perfusion Scintigraphy

<table>
<thead>
<tr>
<th>No.</th>
<th>Disease</th>
<th>Affected side</th>
<th>Pre-%MAA affected/W (%)</th>
<th>Post-%MAA affected/W (%)</th>
<th>Pre-%CSA&lt;5 (%)</th>
<th>Post-%CSA&lt;5 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cervical Ca</td>
<td>right</td>
<td>17.2</td>
<td>38.3</td>
<td>4.427</td>
<td>4.476</td>
</tr>
<tr>
<td>2</td>
<td>Lung Ca</td>
<td>left</td>
<td>59.5</td>
<td>66.7</td>
<td>3.200</td>
<td>2.850</td>
</tr>
<tr>
<td>3</td>
<td>Oesophageal Ca</td>
<td>left</td>
<td>8.7</td>
<td>31.1</td>
<td>1.530</td>
<td>1.882</td>
</tr>
<tr>
<td>4</td>
<td>Lung Ca</td>
<td>left</td>
<td>13.0</td>
<td>50.4</td>
<td>1.528</td>
<td>1.885</td>
</tr>
<tr>
<td>5</td>
<td>Lung Ca</td>
<td>left</td>
<td>18.3</td>
<td>33.7</td>
<td>3.612</td>
<td>4.202</td>
</tr>
</tbody>
</table>

Definition of abbreviations: Ca = cancer, Pre-%MAA affected/W = the percentage of the affected side relative to the whole lung before treatment, Post-%MAA affected/W = the percentage of the affected side relative to the whole lung after treatment, Pre-%CSA<5 = the percentage of the cross-sectional area of pulmonary vessels less than 5 mm² before treatment, Post-%CSA<5 = the percentage of the cross-sectional area of pulmonary vessels less than 5 mm² after treatment

%MAA significantly improved after treatment (p=0.04). %CSA<5 did not improve significantly after treatment (p=0.138).

Chemotherapy(18). In this study, the %CSA<5 improvement in the affected side of the lung was observed after the dilation of a unilateral bronchial obstruction via interventional bronchoscopy. A possible mechanism for this improvement is the amelioration of the hypoxic pulmonary vasoconstriction (HPV) caused by airway obstruction. HPV is a fundamental physiological process whereby ventilation/perfusion matching is optimized through the constriction of the pulmonary circulation supplying poorly ventilated lung units(19). Airway obstruction caused by malignant diseases may cause HPV, leading to decreases in blood flow perfusion. After interventional bronchoscopy, the improvement of hypoxic conditions in the affected lung may relieve HPV. The %CSA improvement observed in this study is considered to be indicative of increases in lung perfusion due to the elimination of HPV.

Case 2 in Table 3 did not show a correlation between %CSA<5 and %MAA. For this case, the left bronchus was obstructed on CT, but intraoperative endoscope revealed a stenosis in the right bronchus confirming bilateral airway obstruction. Therefore, there was no reduction in %MAA prior to treatment. Thus, %CSA<5 cannot be used in cases of bilateral airway obstruction that cannot be found before treatment.

In conclusion, the %CSA<5 of the affected lungs significantly improved after the removal of airflow limitations, and the %CSA<5 assessed via CT might be a useful measure to evaluate improvements in pulmonary blood flow after treatment.

### References

4. Saad CP, Murthy S, Krizmanich G, Mehta AC.
Figure 3. 72-year-old woman with bronchial stenosis
A) 3D image of the bronchial stenosis before stenting. B) 3D image of the bronchial stenosis after stenting. C) Pulmonary perfusion scintigraphy before stenting; a decrease in left pulmonary perfusion is evident. D) Pulmonary perfusion scintigraphy after stenting. The CSA<5 measurements of pulmonary vessels are shown in CT image E) before treatment and F) after treatment. F) Plots of the increases compared with values in E.


Changes in cross-sectional area of pulmonary vessels after interventional bronchoscopy
