Evaluation of Regional Pulmonary Function Using a Bronchoscopic Capnometer in Patients with COPD

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Abstract

Background: Partial pressure of carbon dioxide (PCO\textsubscript{2}) measured by capnometer is mainly used to evaluate the respiratory condition of the lungs under ventilator control. Recently, the use of bronchoscopy has been reported in the evaluation of lung function after lobectomy in patients with lung cancer and those with chronic obstructive pulmonary disease (COPD), who underwent bronchoscopic lung volume reduction (BLVR).

Objectives: To determine the usefulness of bronchoscopic capnometry to assess treatment sites for BLVR.

Method: Twenty patients with COPD suspected of having lung cancer who underwent transbronchial biopsy were included. PCO\textsubscript{2} was measured at the healthy side of the segmental bronchus under room air with a capnometer. Distribution of the percentage of low attenuation area (%LAA) as measured by chest computed tomography (CT), was calculated and compared to end-tidal CO\textsubscript{2} (EtCO\textsubscript{2}) distribution obtained by the capnometer.

Results: All 20 patients displayed homogeneous patterns on CT, but the distribution of EtCO\textsubscript{2} as measured by capnometer was uneven in 3 patients. There was no significant correlation between %LAA and EtCO\textsubscript{2} in the 20 patients, but in 9 patients with higher %LAA values, %LAA correlation significantly with EtCO\textsubscript{2} ($r = -0.437$, $p = 0.023$).

Conclusions: Capnography was useful in physiologically evaluating local ventilation and perfusion status of the lung. We recommend capnography as an adjunct to CT to assess functional heterogeneity in patients potentially undergoing BLVR.

Key words

Capnography, emphysema, end-tidal CO\textsubscript{2}, heterogeneity, homogeneity.

Introduction

In recent years, bronchoscopic lung volume reduction (BLVR) has been performed on patients with chronic obstructive pulmonary disease (COPD) to reduce disease symptoms when standard therapies have failed\cite{1}. The application of BLVR is determined by the evaluation of lung heterogeneity by computed tomography (CT). Evaluations of ventilation and perfusion status are also important in patients with an indication for lung volume reduction surgery\cite{2}.

Capnometers are mainly used to evaluate the condition of the lungs during ventilator management. However, local lung function has been utilized to assess the remaining lung function after pulmonary resection by measuring the partial pressure of carbon dioxide (PCO\textsubscript{2}) from expiratory gas via bronchoscopy\cite{3}. Furthermore, Nishine et al. reported that intrabronchial capnography could to predict the outcome of stent implantation by assessing ventilation/perfusion status\cite{4}.

In a 2014 study, Freitag et al. found that the use of local endocapnometry and endooximetry curves resulted in better identification of target zones for endoscopic emphysema treatments\cite{5}. Currently however, no studies have examined the relation between...
the degree of emphysema and end-tidal CO\(_2\) (EtCO\(_2\)) using capnography. In the present study, we evaluated the distribution of EtCO\(_2\) and the relation between EtCO\(_2\) and the percentage of low attenuation area (%LAA) to identify the indication for BLVR in patients with COPD.

Materials and Methods

Patient selection

Twenty-five patients with COPD who were suspected of having lung cancer and underwent transbronchial biopsy were recruited at St. Marianna School of Medicine between February 2017 and September 2018. Inclusion criteria were patients over 20 years old, and with a diagnosis of COPD including airflow obstruction assessed by pulmonary function tests with post-bronchodilator inhalation (GOLD)\(^5\).

Written informed consent was obtained from all patients. Research Ethics Committee at St. Marianna University School of Medicine approved this study (#1905).

Clinical assessments

Prior to bronchoscopy, 2mg of midazolam was administered intravenously in the endoscopy suite. A guide sheath (PW-2L-1 or PR-2B-1; Olympus, Tokyo, Japan) was inserted through the working channel of the bronchoscope. Subsequently, the partial pressure of oxygen (PO\(_2\)) and PCO\(_2\) were measured by capnometer, (FB-8010 Multi Pulmonary Functional Monitor; Cosmosweb, Miyagi, Japan) (Fig. 1). PCO\(_2\) was measured at the healthy side of the segmental bronchus over 5 breaths under room air with the capnometer. EtCO\(_2\) and oxygen amplitude were then calculated on the basis of the obtained PO\(_2\) and PCO\(_2\) measurements. In this study, functionally non-uniform EtCO\(_2\) was defined as a difference of 25% or more between adjacent measurement sites.

Pulmonary function tests

Spirometry was performed according to the guidelines of the American Thoracic Society and European Respiratory Society\(^7\).

CT measurements of %LAA

%LAA measurements were performed as follows. The threshold technique was adopted with attenuation between -500 and -1024 Hounsfield units (HU). These images were then converted into binary images with a window level of -950 HU and the range of circularity set from 0 to infinity. %LAA was calculated using the Analyze Particles function of ImageJ software for each image slice (Image J, version 1.15, Bethesda, MD, USA). The total lung area was obtained using threshold values between -500 to -1024 HU\(^8\). Goddard’s classification was used as a two-dimensional semi-quantitative evaluation for emphysematous lesions\(^9\).

Statistical analysis

Results are presented as mean ± SD, and p-values of <0.05 were considered statistically significant. The correlation between EtCO\(_2\) and %LAA was evaluated using Pearson’s correlation coefficient. All statistical analyses were performed using JMP 13 software (SAS Institution, Cary, NC, USA).

Fig. 1. Schematic of PO\(_2\) and PCO\(_2\) measurements in patients with COPD. A guide sheath was inserted through the working channel of the bronchoscope. Subsequently, PO\(_2\) and PCO\(_2\) were measured by capnometer.
Results

Of the 25 patients originally recruited for this study, 20 satisfied the clinical course, symptoms, and laboratory data requirements for a clinical diagnosis of COPD. Of the 5 patients who were excluded, 3 required oxygen during bronchoscopy and 2 did not meet the criteria for a diagnosis of COPD. Patient characteristics are shown in Table 1. Thus, 20 patients with COPD (16 men, 4 women), with an average age of 75 years were analyzed. GOLD guideline staging for the patients was as follows: Stage I = 6 patients, II = 9 patients, and III = 5 patients.

Capnography was measured at 20 points at each of the upper, middle, and lower sections of the healthy lung. There was no correlation between EtCO$_2$ and %LAA for all 60 lung measurement points (Fig. 2a). Subsequently, we separated the patients into 2 groups, the more severe (%LAA≥21.8%) and milder emphysematous (%LAA<21.8%) groups, by measuring the total average %LAA at each segmental bronchus. Significant correlations were seen for the more severe emphysematous group (r = −0.4370; p<0.023) (Fig. 2b), but no correlation was seen for the lower emphysematous group (Fig. 2c). In all cases, CT revealed homogeneity at the upper, middle, and lower sections of the lung. The following is a typical homogenous case.

A 72-year-old man with stage I COPD and a smoking history of 37.1 pack years (Fig. 3) underwent CT scanning that revealed homogeneity with an %LAA of 16.7% upper, 3.5% middle, and 8.7% for the lower lung. Capnography measurements revealed uniform distribution of EtCO$_2$ between the upper (27.7 mmHg), middle (25.5 mmHg), and lower (25.7 mmHg) lung segments.

However, capnography showed non-uniform distributions of EtCO$_2$ in 3 emphysema cases, which are described below.

The first case was a 72-year-old man with stage II COPD and a smoking history of 78 pack years (Fig. 4). A CT scan revealed homogeneity with a %LAA of 24% upper, 21.9% middle, and 36.5% for the lower lung. However, capnography measurements revealed that a non-uniform difference in distribution was present for EtCO$_2$ between the upper (30.5 mmHg) and middle (21.5 mmHg) lung segments.

The second case was an 82-year-old man with stage II COPD and a smoking history of 70 pack years (Fig. 5). CT scanning again revealed homogeneity with a %LAA of 7.6% upper, 10.6% middle, and 19.4% for the lower lung. However, capnography

| Table 1. Patient Characteristics |
|-------------------------------|
| Characteristics | Value |
| Age, years | Mean ± SD 75.75 ± 5.79 |
| | Range 60-84 |
| Sex, n | Male 16 |
| | Female 4 |
| BMI, kg/m$^2$ | 22.4 |
| Brinkman Index | 1222.80 ± 859.93 |
| VC, %predicted | 99.99 ± 14.48 |
| FRC, L | 3.38 ± 0.83 |
| RV, L | 2.31 ± 0.67 |
| TLC, L | 5.39 ± 1.03 |
| RV/TLC | 0.43 ± 0.09 |
| FVC, L | 2.96 ± 0.72 |
| FEV1, L | 1.61 ± 0.54 |
| FEV1/FVC, % | 53.77 ± 10.19 |
| FEV1, % predicted | 68.31 ± 17.64 |

Abbreviations: BMI, body mass index; VC, vital capacity; FRC, functional residual capacity; RV, residual volume; TLC, total lung capacity; RV/TLC, residual volume to total lung capacity ratio; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 sec; FEV1/FVC, forced expiratory volume in 1 sec to forced vital capacity ratio.

Values are represented as mean ± standard deviation.
Fig. 2. Correlation between EtCO$_2$ and %LAA. (a) Scatter plot of EtCO$_2$ and %LAA in all cases. (b) Correlation between EtCO$_2$ and %LAA in the more severe emphysematous cases. (c) There was no correlation between EtCO$_2$ and %LAA in the milder emphysematous cases. EtCO$_2$, end-tidal CO$_2$; %LAA, percentage of low attenuation area.

Fig. 3. Typical homogeneous case. CT slices showing the %LAA at (a) the upper lobe, (b) the middle lobe, and (c) the lower lobe. CO$_2$ waveform measured at (d) the upper lobe, (e) the lingular bronchus, and (f) the lower lobe. O$_2$ amplitude measured at (g) the upper lobe, (h) the lingular bronchus, and (i) the lower lobe. CT, computed tomography; EtCO$_2$, end-tidal CO$_2$; %LAA, percentage of low attenuation area.
**Fig. 4.** Heterogeneous case 1. CT slices showing the %LAA at (a) the upper lobe, (b) the middle lobe and (c) the lower lobe. CO₂ waveform measured at (d) the upper lobe, (e) the lingular bronchus, and (f) the lower lobe. O₂ amplitude measured at (g) the upper lobe, (h) the lingular bronchus, and (i) the lower lobe. CT, computed tomography; EtCO₂, end-tidal CO₂; %LAA, percentage of low attenuation area.

**Fig. 5.** Heterogeneous case 2. CT slices showing the %LAA at (a) the upper lobe, (b) the middle lobe, and (c) the lower lobe. CO₂ waveform measured at (d) the upper lobe, (e) the middle lobe, and (f) the lower lobe. O₂ amplitude measured at (g) the upper lobe, (h) the middle lobe, and (i) the lower lobe. CT, computed tomography; EtCO₂, end-tidal CO₂; %LAA, percentage of low attenuation area.
measurements revealed the presence of a non-uniform difference in distribution for EtCO₂ between the middle (41.9 mmHg), and lower (30.9 mmHg) lung segments.

The final case was a 78-year-old woman with stage I COPD and a smoking history of 15 pack years (Fig. 6). A CT scan revealed homogeneity with a %LAA of 47% upper, 29.6% middle, and 5.3% for the lower lung. Again, capnography measurements revealed the presence of a non-uniform difference in distribution for EtCO₂ between the middle (37.7 mmHg), and lower (48.1 mmHg) lung segments.

**Discussion**

To our knowledge, this is the first study to compare CT imaging and physiological assessment using capnography to measure exhaled gas at the segmental bronchus. This study succeeded in evaluating local lung function using capnography to physiologically confirm heterogeneity in patients with emphysema. The indication for BLVR is determined by CT evaluation, which includes heterogeneity and fissure completeness. Generally, when considering the outcome of BLVR, heterogeneity assessed by CT is an important factor for treatment. In the present study, all cases were assessed as homogeneous by CT using the Goddard classification, but there were 3 cases of heterogeneity, which was identified as functionally non-uniform EtCO₂ measured by capnography. This discrepancy between imaging and physiological evaluations could potentially be an indication for BLVR in patients with COPD.

We identified a significant correlation of %LAA with EtCO₂ in the severely emphysematous patients. In a report by Matsuura et al., the relation between emphysematous change and the pulmonary vascular cross-sectional area was examined. They concluded that the emphysematous change was more severe than mild, and that the destruction of the lung vascular bed was high. As a result, the pulmonary blood flow decreased as the emphysematous change worsened. The decrease in lung blood flow caused the further uneven distribution of ventilation blood flow.

As described above, milder emphysematous changes cause mild destruction of the pulmonary vascular bed and less reduction in pulmonary blood flow, but more severe emphysematous changes result in greater destruction of the pulmonary vascular bed, and a decrease in EtCO₂ is also noticeable.

**Limitations**

This study has some limitations. First, damping
of the catheter due to mucus plugging was observed to affect the 
EtCO₂ measurements. However, this was easily detected as a flat line for EtCO₂ by the software and could be corrected by flushing the catheter with air. Another concern was that the curves for gas concentrations were not in real-time. Because the curves are displayed on a laptop, there is a time lag of approximately 1.5 seconds due to the length of the catheter. Finally, this study recruited only a small number of patients and therefore, future studies with larger cohorts are necessary to confirm a potential indication for BLVR.

**Conclusion**

In this study, capnography was useful in the physiological assessment of ventilation and perfusion status. We found that CT was unable to discrimination between homogeneous and heterogeneous patterns in three patients. Therefore, we believe that capnography as an adjunct assessment may contribute to the expansion of therapeutic indications for BLVR in patients with COPD.

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**Conflicts of interest**

The authors have nothing to disclose.

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