Ther Adv Respir Dis
2018, Vol. 12: 1–7
DOI: 10.1177/1753465818756564

Use of endo-bronchial end-tidal CO_2 test for location of the pleural air leakage in patients with intractable pneumothorax

Yi-Ming Zeng, Yun-Feng Chen, Hui-Huang Lin and Xiao-Bin Zhang

Abstract

Background: Location of the affected bronchus of pleural air leaks is the most important step of trans-bronchoscopic bronchial occlusion for the treatment of intractable pneumothorax. The balloon occlusion test is the most commonly used technique, but has failed in some cases. The aim of the present study was: (1) to determine if endo-bronchial end-tidal CO_2 ($EtCO_2$) measurement can identify the affected bronchus that is the source of a persistent pleural air leak; and (2) to establish a methodology for endo-bronchial $EtCO_2$ testing in locating affected bronchus in intractable pneumothorax.

Methods: A total of 28 patients with intractable pneumothorax underwent bronchoscopy with (1) the balloon occlusion test for the identification of the affected bronchus; and (2) endo-bronchial $EtCO_2$ measurement ($EtCO_2$ test) at the orifices of the bronchus of the affected lung. The effectiveness of these two methods of affected bronchus identification were compared. The threshold $EtCO_2$ (T-$EtCO_2$) was determined.

Results: The positive rates of locating the affected bronchus by the endo-bronchial $EtCO_2$ test, balloon occlusion test, and combination of the two techniques were 60.7% (17/28), 64.3% (18/28) and 96.4% (27/28), respectively. The average differences in $EtCO_2$ between the affected bronchus and the main carina, main bronchus, and non-affected bronchus were (in mmHg) 4.41 ± 1.99 (95% confidence interval: 3.5, 5.3), 4.73 ± 2.10 (3.80, 5.66) and 5.57 ± 2.53 (4.45, 6.69), respectively.

Conclusions: (1) The endo-bronchial $EtCO_2$ test is complementary to the balloon occlusion test of the leading bronchus. (2) A threshold (T-$EtCO_2$) value of >5 mmHg is optimal for this technique.

Keywords: balloon occlusion, bronchoscope, end-tidal CO_2, interventional pulmonology, pneumothorax

Received: 24 July 2017; revised manuscript accepted: 16 October 2017.

Correspondence to:
Yi-Ming Zeng
Department of Pulmonary and Critical Care Medicine, Second Affiliated Hospital of Fujian Medical University, Respiratory Medicine Center of Fujian Province, No. 34, Zhongshanbei Road, Licheng District, Quanzhou 362000, Fujian Province, China
ymzeng08@163.com

Yun-Feng Chen
Hui-Huang Lin
Xiao-Bin Zhang
Department of Pulmonary and Critical Care Medicine, Second Affiliated Hospital of Fujian Medical University, Respiratory Medicine Center of Fujian Province, China

Introduction

Intractable pneumothorax or prolonged pulmonary air leak is defined as persistent pleural air leak for more than 7 days. Common causes of intractable pneumothorax are COPD, lobectomy and trauma. The bronchial occlusion technique has been proven to be an effective method for treating intractable pneumothorax.[1–4] One of the key steps in bronchial occlusion is to detect the bronchus leading to pleural air leakage – that is, the affected bronchus. In previous clinical research, the balloon occlusion test has been the most frequently used method for detecting the affected bronchus. In our previous research, the detection power of this technique was found to be 85%.[4] However, in subsequent clinical practice, we found that the balloon occlusion test failed to locate the affected bronchus in pneumothorax patients with multiple pleural leakages or collateral ventilation. The aim of the present study was to explore the value of endo-bronchial end-tidal CO_2 ($EtCO_2$) measurement in the detection of the affected bronchus, and furthermore to establish the exact methodology of trans-bronchoscopic $EtCO_2$ detection.

Methods

A prospective observational study was conducted to evaluate the value of endo-bronchial $EtCO_2$ test in identifying the affected bronchus. $EtCO_2$ values at different anatomic sites of the tracheobronchial tree were checked, and the occlusion effectiveness of the combination of $EtCO_2$ test and balloon occlusion test was also evaluated.

Recruitment criteria

Patients with persistent pleural air leaks from intercostal drainage for more than 7 days were included.

Exclusion criteria: (1) Patients were unable to tolerate the bronchoscopic procedure due to poor cardiopulmonary function. (2) Patients refused to undergo the bronchoscopic procedure. (3) Any other contraindications to bronchoscopy.

This research has been approved by the Institutional Review Board of the Second Affiliated Hospital of Fujian Medical University (approval number 2012-022). All procedures were performed in the same hospital and by the same bronchoscopists. Eligible patients were informed about the present study, and written informed consent was obtained from each participant. Participants were all from the Department of Pulmonary and Critical Care Medicine of the Second Affiliated Hospital of Fujian Medical University, treated between July 2012 and September 2015. There were 42 pneumothorax patients with intercostal drainage for more than 7 days. Of these, 31 patients agreed to participate in the present study, 3 of whom quit due to lack of tolerance of the bronchoscopic procedure; the remaining 28 patients completed the study.

Instruments

An Olympus CV-260SL flexible bronchoscope, MTN-SRB 3-lumen balloon catheter (Micro-Tech, Nanjing, China), and an $EtCO_2$ detector (Microstream®, Oridion, Needham, MA, USA; Figure 1) were employed during the procedures.

Figure 1. Instruments for the endo-bronchial $EtCO_2$ test.

Determination of the affected bronchus

Flexible bronchoscopy (⩾2.8 mm i.d.) was performed in all patients under local anesthesia with 2% lidocaine and mild sedation (midazolam). Both the balloon occlusion test and $EtCO_2$ detection were used to detect the affected bronchus according to the following procedures. For balloon detection, a balloon catheter was introduced through the working channel of a flexible bronchoscope, and the affected bronchus was detected as described in our previous publication.[4] Briefly, the balloon was inflated to achieve complete occlusion in the lobar, segmental and sub-segmental bronchus. The affected bronchus was identified by reduction or elimination of the air leak through the chest tube 15–20 s after occlusion. The $EtCO_2$ test was performed as follows: an $EtCO_2$ sampling catheter was introduced through the working channel of a flexible bronchoscope. The proximal end of the catheter was connected to an $EtCO_2$ detector (Microstream®), and the exhaled gas was sampled from the distal end of the catheter with the help of the air pump inside the Microstream® (Figure 1). The $EtCO_2$ was sampled at different anatomical sites (Figure 2): the lower segment of the trachea (above the main carina), the main bronchus of the affected lung, and the bronchial orifices for each lobe of the affected lung. At each site, the $EtCO_2$ values usually stabilized within 10 cycles of breathing; subsequently, $EtCO_2$ values were recorded for five cycles of relaxed breathing, and the average value at each site was calculated and recorded. A bronchus was considered as the suspected affected bronchus if its $EtCO_2$ value was significantly

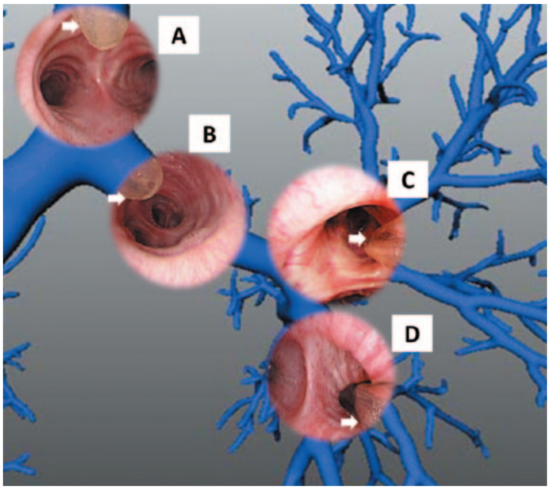

Figure 2. Example of the endo-bronchial $EtCO_2$ test. The arrow points to the tip of the $EtCO_2$ sampling catheter. Sampling sites: carina (A), main bronchus of left lobe (B), orifice of left upper lobe (C), orifice of left basal segments (D).

lower than values from the other sites; further measurements were performed at the constituent segmental bronchial orifices if necessary.

Occlusion of the affected bronchus

Once the affected bronchus was located, bronchial occlusion was performed to stop pleural air leakage. Materials for bronchial occlusion include either or both of autologous blood plus thrombin and endo-bronchial spigot. Technical details are offered in the literature.[3–5] When injected into the affected bronchus, autologous blood can coagulate in the sub-segmental bronchus in a short time, and the air leak can be stopped. The advantages of autologous blood are as follows: it does not cause immunoreactions in one's own body; the blood clots can stop the air leak; and the blood clots can be absorbed within 1–2 weeks, in which time the bronchopleural fistula may be cured. Thrombin can accelerate the coagulation of autologous blood. Autologous blood plus thrombin for treatment of intractable pneumothorax has been proven to be an effective treatment choice in the clinic.[4,5]

Criteria for positive $EtCO_2$ test

The $EtCO_2$ test was ultimately defined as positive when the $EtCO_2$ value at the orifice of one or more specific bronchus was lower than the values at other bronchial orifices, and the following criteria were met: (1) the result was consistent with the positive result of the balloon occlusion test; (2) the pleural fistula was successfully sealed after bronchial occlusion guided by the result of a reduction in $EtCO_2$ value.

Determination of the reference point and the reference $EtCO_2$ value (R-$EtCO_2$)

After a specific bronchus (affected bronchus) was judged to be positive according to the positive criteria of the $EtCO_2$ test as described above, its $EtCO_2$ value was compared with $EtCO_2$ values from the main carina, main bronchus, and other bronchus of the affected lung. When the $EtCO_2$ value at any one of the three sites stated above was statistically higher than the $EtCO_2$ value at the affected bronchus, the site with statistically higher value was determined to be the reference point, and the $EtCO_2$ value at this site was labeled the reference $EtCO_2$ value (R-$EtCO_2$ value).

Establishment of the threshold value of $EtCO_2$ (T-$EtCO_2$) test

The difference of $EtCO_2$ value between the R-$EtCO_2$ and that of the affected bronchus was defined as the T-$EtCO_2$. In other words, when the difference between $EtCO_2$ of a specific bronchus and R-$EtCO_2$ is more than T-$EtCO_2$, this specific bronchus was diagnosed as the affected bronchus.

Statistical analysis

The detection powers of the $EtCO_2$ test, balloon occlusion test and $EtCO_2$ test plus balloon occlusion test were expressed as percentages. Different $EtCO_2$ values between the affected bronchus and the non-affected bronchus, main bronchus and main carina were expressed as mean (95% confidence interval), and were assessed by independent sample Student's t test. Statistical analysis was performed using the SPSS statistical software version 22.0 for Windows (SPSS, Inc., Chicago, IL, USA). A p value <0.05 was considered as statistically significant.

Results

Clinical characteristics of participants

A total of 28 male patients (64.7 ± 12.8 years old) with intractable pneumothorax were included in

Table 1. Power of endo-bronchial $EtCO_2$ test and balloon detection.

$EtCO_2$ test	Balloon occlusion test ($n = 28$)		Sum (%)#
($n = 28$)	Positive (n)	Negative (n)	
Positive	8	9	17 (60.7)*
Negative	10	1	11 (39.2)
Sum (%)	18 (64.3)*	10 (35.7)	28 (100)

*There is a significant difference between positive rates of $EtCO_2$ and balloon occlusion test ($p = 0.041$), tested by exact chi-square test. #Combination of the positive rate of the balloon occlusion test and the $EtCO_2$ test was 96.4% (27/28).

Table 2. $EtCO_2$ values among different sites.

Site of sampling	$EtCO_2$ values ($\bar{x} \pm SD$)	t-values (p) compared with affected bronchial	t-values (p) compared with non-affected bronchial
Affected bronchial	34.27 ± 8.49	–	−3.477 ($p < 0.05$)
Non-affected bronchial	41.45 ± 7.49	−3.337 ($p < 0.05$)	–
Main carina	40.00 ± 8.37	−2.102 ($p = 0.042 < 0.05$)	−0.652 ($p = 0.517$)
Main bronchus of affected lung	40.35 ± 8.24	−2.246 ($p = 0.031 < 0.05$)	−0.496 ($p = 0.622$)

the present study. Of the 28 patients, 18 had right pneumothorax and 10 had left pneumothorax. Primary comorbidities of these patients were: chronic obstructive pulmonary disease ($n = 18$), old pulmonary tuberculosis ($n = 4$), pneumosilicosis ($n = 5$), lung cancer ($n = 2$), peripheral pleural fistula after left upper lobe wedge resection ($n = 1$) and idiopathic pneumothorax ($n = 1$).

Results of balloon occlusion and endo-bronchial $EtCO_2$ test

The results for both the balloon occlusion test and the $EtCO_2$ test are listed in Table 1. The balloon occlusion test successfully identified the affected bronchus in 18 cases and failed in 10 (positive rate 64.3%); the $EtCO_2$ test showed reduction in $EtCO_2$ values in 17 cases (positive rate 60.7%). The combined techniques failed in one case (positive rate 96.4%).

Effectiveness of $EtCO_2$ in patients with negative balloon occlusion results

Ten cases had negative results by the balloon occlusion test, nine of which showed positive results by the $EtCO_2$ test; one case showed a negative result by both detection techniques.

Different values of $EtCO_2$

The affected bronchus was successfully identified by $EtCO_2$ test in 19 lobes or segments among 17 cases. The $EtCO_2$ values recorded at different sites of the bronchial tree are listed and compared in Table 2. The $EtCO_2$ values at the affected bronchus were significantly lower than those at the non-affected bronchus, main carina and main bronchus of the affected lung (all $p < 0.05$).

Therapeutic results of bronchial occlusion

According to the results of the balloon occlusion test and the $EtCO_2$ test, 27 patients underwent bronchial occlusion by the use of bronchial spigot, autologous blood and thrombin, or both. The overall successful rate was 24/28 (85.7%) (Figure 3). And air leak disappeared during the bronchoscopic procedure in all 24 successfully treated patients.

Discussion

Selective bronchial occlusion has been reported to be an effective technique for treating intractable pneumothorax.[1–4,6] Before bronchial occlusion can be performed, the affected bronchus must be located. Methods for identifying the

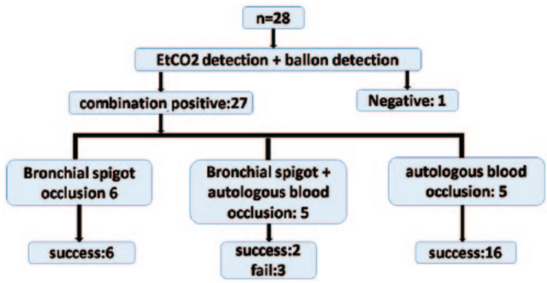

Figure 3. Bronchial occlusion results: according to the combination detection results of the balloon occlusion test with $EtCO_2$ detection, 27 patients underwent bronchial occlusion by the use of bronchial spigot, autologous blood or both. The successful rate of occlusion was 85.7%.

affected bronchus include balloon detection, bronchography, Xe-133 detection and helium detection.[7] The balloon occlusion test is the most frequently used method, and it was associated with a positive detection rate of 85% in our previous study.[4] However, Sasada and colleagues reported that only 10 out of 23 patients showed apparent improvement in air leaks when treated with the balloon occlusion test.[8] The balloon occlusion test failed in >30% of cases of intractable pneumothorax in the present study. Reasons for failure of the balloon occlusion test might include multiple fistulas in different lobes and collateral ventilation between lobes,[9] neither of which can be detected when using a balloon catheter to occlude the orifice of a single lobar or segmental bronchus. Accordingly, there is a need for the development of a new technique to improve detection power in patients with multiple pleural fistulas in different lobes or collateral ventilation. In our study, the $EtCO_2$ test was evaluated as a new technique for improving detection power, and we tried to establish a methodology for the test.

The endo-bronchial $EtCO_2$ test was previous reported by Bhattacharyya and colleagues[10] as an effective technique for detecting the affected bronchus in patients with bronchopleural fistula. The authors stated that a particular affected bronchus was located when capnographic tracing showed rapid flattening of the curve to a straight line. In the present study, our tasks were to establish two standards: (1) the $EtCO_2$ reference point; and (2) the threshold $EtCO_2$ or T-$EtCO_2$, which is the breakpoint of the diagnoses. First, the $EtCO_2$ reference point: the $EtCO_2$ sampled from this reference point (one or more of the following sites: main carina, main bronchus and other bronchus from the affected lung) is regarded as the standard or reference $EtCO_2$ value (R-$EtCO_2$) and can be compared with the $EtCO_2$ value obtained from other points within the bronchial tree of the affected lung. Second, T-$EtCO_2$ is the difference in $EtCO_2$ between the affected bronchus and the reference point. In other words, T-$EtCO_2$ allows us to determine the leading bronchus: when the difference in $EtCO_2$ between a specific bronchus and the reference point is larger than the T-$EtCO_2$, the specific bronchus can be labeled as the leading bronchus.

The $EtCO_2$ values from the orifices of different bronchi may vary between patients because patients with intractable pneumothorax can have a variety of underlying diseases (e.g. chronic obstructive disease, old tuberculosis and pneumosilicosis) and have different gas exchange efficacies. This is why the establishment of R-$EtCO_2$ is important. To date, no previous data on this topic have been reported. The main carina and main bronchus of the affected lung were candidate reference points in this study. There are significant differences in $EtCO_2$ between the main carina and affected bronchus ($p = 0.042$), main bronchus and affected bronchus ($p = 0.037$), and non-affected bronchus (average $EtCO_2$ of all bronchi other than the leading bronchus) and affected bronchus ($p < 0.05$). The $EtCO_2$ values were similar between the main carina and main bronchus of the affected lung, main carina and non-leading bronchus, and main bronchus and non-leading bronchus. The above results suggested the main carina and main bronchus of the affected lung should be used as reference points.

Although there was a significant difference between the $EtCO_2$ of the affected bronchus and the average $EtCO_2$ of all non-leading bronchi, it is time-consuming to detect and calculate the $EtCO_2$ values at the orifices of all the non-affected bronchi. Additionally, the $EtCO_2$ from different non-affected bronchi may vary greatly. Thus, in clinical practice, it is not feasible to detect and calculate the average $EtCO_2$ of the non-affected bronchus (R-$EtCO_2$). The difference of $EtCO_2$ between the main bronchus and the affected bronchus was 4.73 ± 2.10 (95% confidence interval: 3.80, 5.66) mmHg in the present study, suggesting that a specific bronchus can be determined to be the affected bronchus when its $EtCO_2$ value is about 5 mmHg lower than that of the main bronchus of the affected lung. In other words, a 5 mmHg reduction in $EtCO_2$ is considered to be the T-$EtCO_2$ or diagnostic value for an affected bronchus according to our results. Our results demonstrated that the affected bronchus can be located in 60.7% of cases by the $EtCO_2$ test and 64.3% of cases by the balloon occlusion test.

Theoretically, the balloon occlusion test is indicated for a single fistula without collateral ventilation, while the $EtCO_2$ test is intended for multiple fistulas or fistulas with collateral ventilation. In the present study, the balloon occlusion test failed in 35.7% of cases of intractable pneumothorax. For this reason, the $EtCO_2$ test was employed as a new technique for searching the affected bronchus. We found a positive detection rate of 60.7% with this new method, lower than that of balloon detection. However, as shown in Table 1, when we combined the $EtCO_2$ test with balloon detection, the combined positive rate of the detection of the affected bronchus rose to 96.4% (27/28), indicating that these two techniques are complementary. The $EtCO_2$ test is thus recommended to be an effective technique when the balloon occlusion test fails.

Some improvements in technical details are needed for the use of the trans-bronchial $EtCO_2$ test in future clinical investigations. First, how to minimize the fluctuation of $EtCO_2$ due to an unstable respiration state or cough; second, how to make the trans-bronchial $EtCO_2$ test more feasible by shortening the procedure time; third, how to prevent the $EtCO_2$ sampling catheter from becoming blocked with mucus. Further well-designed study is required to investigate these issues.

Some limitations of the present study should be mentioned. First, the sample size of the present study was small, with only 28 patients enrolled in the study. However, most patients with pneumothorax can be cured by intercostal drainage within 7 days – that is, the number of patients with intractable pneumothorax is relatively small. Multiple centers and a large sample size study is needed. Second, we did not conduct artery gas analysis for detecting $PaCO_2$ when detecting $EtCO_2$ from the affected bronchus. Third, the $EtCO_2$ values were only detected in large bronchi rather than smaller bronchi, which may not be precise enough.

In summary, the $EtCO_2$ test can be taken as a complementary technique in the event of failure of the balloon occlusion test. Combination of the $EtCO_2$ test with the balloon occlusion test can significantly improve the positive detection rate in locating affected bronchi in patients with intractable pneumothorax. According to the result, the $EtCO_2$ values measured at the main carina or main bronchus of the affected lung can be taken as the R-$EtCO_2$ value for comparison with the $EtCO_2$ value obtained at the orifice of the suspected leading bronchus. A particular bronchus can be determined to be the affected bronchus when its $EtCO_2$ value is 5 mmHg less than the R-$EtCO_2$ value.

Acknowledgements

Study concept and design: Yi-Ming Zeng; data collection and interpretation: Yi-Ming Zeng and Yun-Feng Chen; drafting of the manuscript: Yi-Ming Zeng, Hui-Huang Lin and Xiao-Bin Zhang. All authors read and approved the manuscript.

Funding

The present study was funded by the Natural Science Foundation of Fujian Province, China (No. 2016Y0033).

Conflict of interest statement

The authors declare that there is no conflict of interest.

References

1. Kabanov AN and Astafurov VN. Temporary occlusion of the bronchi in the treatment of nonspecific spontaneous pneumothorax. *Sov Med* 1979; 10: 60–62.
2. Zeng Y, Zhang H, Lv L, *et al.* Balloon detection and selective bronchial occlusion for the management of intractable pneumothorax. *Chin J Intern Med* 2003; 42: 193–195.
3. Watanabe Y, Matsuo K, Tamaoki A, *et al.* Bronchial occlusion with endobronchial Watanabe spigot. *J Bronchol Interv Pulmonol* 2003; 10: 264–267.
4. Zeng Y, Hong M, Zhang H, *et al.* Transbronchoscopic selective bronchial occlusion for intractable pneumothorax. *Respirology* 2010; 15: 168–171.
5. Mizumori Y, Nakahara Y, Kawamura T, *et al.* Intrabronchial infusion of autologous blood plus

thrombin for intractable pneumothorax after bronchial occlusion using silicon spigots: a case series of 9 patients with emphysema. *J Bronchol Interv Pulmonol* 2016; 23: 199–203.

6. Brichon PY, Poquet C, Arvieux C, *et al*. Successful treatment of a life-threatening air leakage, complicating severe abdominal sepsis, with a one-way endobronchial valve. *Interact Cardiovasc Thorac Surg* 2012; 15: 779–780.

7. Lillington GA, Stevens RP and DeNardo GL. Bronchoscopic location of bronchopleural fistula with xenon-133. *J Nucl Med* 1982; 23: 322–323.

8. Sasada S, Tamura K, Chang YS, *et al*. Clinical evaluation of endoscopic bronchial occlusion with silicone spigots for the management of persistent pulmonary air leaks. *Intern Med* 2011; 50: 1169–1173.

9. Higuchi T, Reed A, Oto T, *et al*. Relation of interlobar collaterals to radiological heterogeneity in severe emphysema. *Thorax* 2006; 61: 409–413.

10. Bhattacharyya P, Dutta A, Sarkar D, *et al*. Endobronchial sealing of bronchopleural fistula following capnographic detection: a new mode of therapy. *Indian J Chest Dis Allied Sci* 2008; 50: 203.