CASE REPORT

OPEN

Monitoring the Resolution of Acute Exacerbation of Airway Bronchoconstriction in an Asthma Attack Using Capnogram Waveforms

Mio Shikama, MD

Miyuki Yamamoto, MD, PhD

Itsuki Osawa, MD

Takuya Sato, MD

Ichiro Hirayama, MD, PhD

Naoki Hayase, MD, PhD

Takehiro Matsubara, MD, PhD

Kent Doi, MD, PhD

BACKGROUND: Patients with acute bronchospasm can show a distinct slope of the capnogram ("shark fin") as a result of asynchronous alveolar excretion. Although the slope of the upward alveolar plateau (phase III) in the capnogram waveforms of non-intubated patients is known to help monitor the therapeutic response to acute bronchospasm, little is known about the significance of its slope among intubated patients. Therefore, we quantified the phase III slope of an intubated patient with acute asthma to investigate whether capnogram waveforms could be useful for identifying the response to antibronchospasm treatment in real time.

CASE SUMMARY: The patient was a 53-year-old man who had a history of asthma. He presented to the emergency department with the primary complaint of respiratory distress. He was diagnosed with severe asthma attack and required invasive mechanical ventilation for 10 days, during which we quantified the phase III slope of the capnogram. The phase III slope decreased during treatment, with a significant reduction from the third to the fourth day; however, a significant decrease in end-tidal carbon dioxide ($EtCO_2$) was observed from the fifth to the sixth day. We found that the slope values decreased earlier than $EtCO_2$ reduction, although the absolute $EtCO_2$ values eventually decreased in response to antibronchospasm treatment.

CONCLUSION: There were several reports that evaluated the phase III slope in non-intubated patients with asthma, but this is the first report measuring the phase III slope in an intubated patient over several days. Capnogram waveforms may serve as useful real-time indicators to monitor acute bronchospasm among mechanically ventilated patients.

KEY WORDS : asthma attack; asthma; capnogram waveforms; end-tidal carbon dioxide

A capnogram is the curve obtained by the continuous measurement of the partial pressure of carbon dioxide in a sample of expiratory air. The expiratory cartography waveform consists of three phases. Phase I (latency phase) reflects dead space ventilation in nonrespiratory bronchi. Phase II is marked by a very rapid rise in PCO_2 ($PexpCO_2$), which reflects the mixture of dead space and alveolar gas. Phase III is the plateau phase and reflects the elimination of alveolar air (slightly increasing $PexpCO_2$), resulting in a peak at the end of tidal expiration (1, 2).

Patients with obstructive airway disease exhibit an upward alveolar plateau (phase III) slope in the capnogram as a result of asynchronous alveolar excretion (3). Several studies have quantified the phase III slope in the capnogram waveforms of nonintubated patients and suggested that the phase III slope may help monitor the therapeutic response to acute bronchospasm (1, 3–9).

DOI: 10.1097/CCE.0000000000000899

KEY POINTS

Question: Is the slope of the upward alveolar plateau (phase III) in the capnogram waveforms helpful to evaluate the therapeutic response for mechanically ventilated patients with severe asthma?

Findings: As the slope of phase III values decreased earlier than $EtCO_2$ reduction, the phase III slope could reflect early resolution of an acute exacerbation of airways bronchoconstriction.

Meaning: For acute bronchospasm among mechanically ventilated patients, capnogram waveforms could serve as a useful real-time indicator of overall medium and small airways resistance.

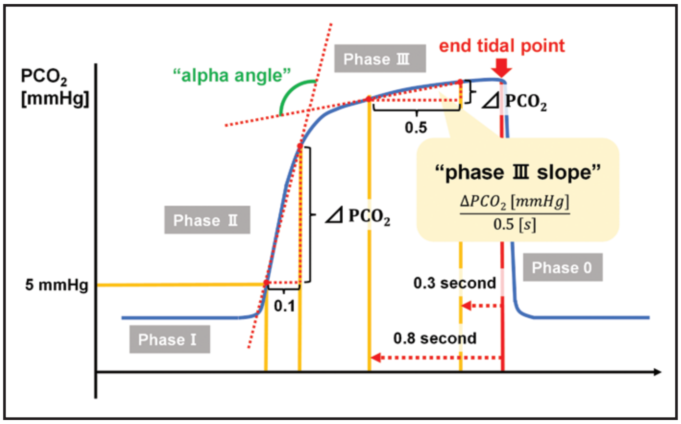

Figure 1. Capnogram waveform indices. The phase III slope in the capnogram waveform was calculated using $PaCO_2$ values between 0.8 and 0.3 s (total time 0.5 s) before the end-tidal peak. The slope of phase II was measured for 0.1 s from the first point when the measured CO_2 rose above 5 mm Hg, and the alpha angle was formed by the slopes of phases II and III.

However, little is known about the utility of the phase III slope in the capnogram waveforms among intubated patients. Therefore, we quantified the phase III slope in the capnogram waveforms of an intubated patient with severe asthma attack (**Fig. 1**).

CASE

The patient was a 53-year-old man who had a history of asthma. He suffered from asthma attacks lasting for 20 years. He presented to the emergency department with a primary complaint of respiratory distress. Blood gas analysis revealed severe respiratory acidosis (pH, 7.142; $PaCO_2$, 96.3 mm Hg). He was diagnosed with severe asthma attack and was administered inhaled, short-acting β2-agonists. However, he was eventually intubated and placed on invasive mechanical ventilation due to progressive hypercapnia. We initially tried pressure-controlled ventilation, but failed to achieve sufficient tidal volume because of extremely high airway resistance. Rather, pressure-supported ventilation for utilizing spontaneous breathing was more successful than pressure-controlled ventilation in maintaining sufficient ventilation, so he was continuously ventilated in the pressure-support (PS) mode. We did not change the ventilator setting of positive end-expiratory pressure and adjusted the setting of PS to match his inspiratory effort and tidal volume, as shown in **Figure 2**. With frequent inhalation of short-acting β2-agonists, intravenous steroids, ketamine as a bronchodilator sedative, and analgesics, the patient's respiratory obstructive disorder gradually improved. He was extubated and discharged on the 10th and 13th day of hospitalization, respectively.

MATERIALS AND METHODS

The phase III slope was calculated using $PaCO_2$ values between 0.8 and 0.3 s (total time 0.5 s) before the end-tidal peak to ensure consistency in measurements (Fig. 1) according to a previous study (4). In this case, we used the median of phase III slope for 10 consecutive breaths within the same period of each day (i.e., 12:00 P.M.) for 10 days while the patient was on mechanical ventilation in the ICU. In addition, to compare the utility of the phase III slope with other clinical parameters at the same period, we evaluated the alpha angle formed by the slopes of phases II and III, end-tidal carbon dioxide ($EtCO_2$), and the difference between $PaCO_2$ and $EtCO_2$. The slope of phase II was measured for 0.1 s from the first point when the measured CO_2 rose above 5 mm Hg (4).

RESULTS

The median phase III slope was 21.5 mmHg/s on the first day and 2.1 mmHg/s on the 9th day before extubation. The decrease in phase III slope appears to track the improvement in the patient's condition. Remarkably, given that phase III slope considerably

mode	PSV	PSV	PSV	PSV	PSV	PSV	PSV	PSV	PSV
PS	25	25	25	30	30	15	10	8	5
PEEP	5	5	5	5	5	5	5	5	5
FiO_2	50	45	50	35	35	35	35	35	30

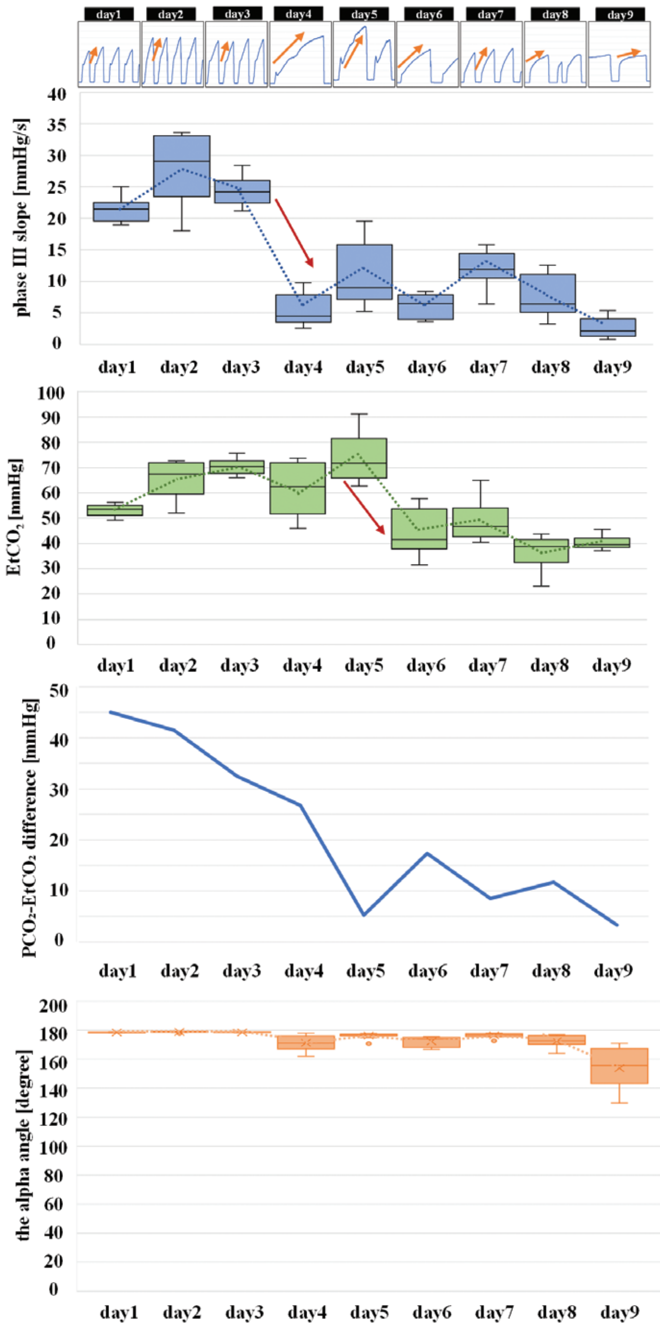

Figure 2. Phase III slope changes, end-tidal carbon dioxide (EtCO2) changes, the difference between EtCO2 and PaCO2 during intubation, and the alpha angle changes during intubation. **A**, The ventilator settings of each day. **B**, The typical daily waveforms. **C**, The median (center line), 25th and 75th percentiles, and the range of the phase III slope of each day. **D**, The median (center line), 25th and 75th percentiles, and range of EtCO2 of each day. **E**, The difference between EtCO2 and PaCO2 during intubation. **F**, The median (center line), 25th and 75th percentiles, and the range of the changes of alpha angle changes during intubation. PEEP = positive end-expiratory pressure, PS= pressure support, PSV = pressure-support ventilation.

decreased from the third to the fourth day and other parameters (e.g., blood gas and observed respiratory tidal volumes) were also improved accordingly, we performed spontaneous awaking trial and breathing trial and gradually weaned from mechanical ventilator. Finally, the patient was extubated on the 10th day (Fig. 2). Furthermore, the median $EtCO_2$ level during the same period was 53.5 mm Hg on the first day and 39.5 mm Hg on the ninth day. $EtCO_2$ levels also decreased with treatment; however, a notable reduction was observed from the fifth to the sixth day. The difference between $EtCO_2$ and $PaCO_2$ also decreased with treatment, and decreased significantly from the fourth to the fifth day. In addition, the results of the tidal volume, respiratory rate, and expiratory time are shown in **Supplementary Figure 1** (http://links.lww.com/CCX/B175). The changes in respiratory rate and expiratory time from the third to the fourth day were also observed as in phase III slope and tidal volume, but the relationship among these parameters after the fourth day was not clearly observed. On the other hand, the alpha angle did not show any remarkable change during the treatment (Fig. 2). Although we used the bronchodilator for this patient every 6–8 hours, we did not find any remarkable change of phase III slope shape after each bronchodilator administration.

DISCUSSION

We quantified the phase III slope in the capnogram waveform of a patient with acute bronchospasm under mechanical ventilation. The phase III slope decreased during treatment, with a significant reduction from the third to the fourth day; however, a significant decrease in $EtCO_2$ was observed from the fifth to the sixth day. The difference between $EtCO_2$ and $PaCO_2$ decreased significantly from the fourth to the fifth day, which indicated the decrease in dead space along with the improvement of bronchospasm and suggested the utility of capnography. Taken together, our findings suggested that the phase III slope could be a better indicator reflecting the early improvement of bronchospasm than the $EtCO_2$ value.

Several reports have evaluated the phase III slope in nonintubated patients with asthma. You et al (1) demonstrated in a case series that the phase II and III slopes notably change with improvements in total respiratory system airflow resistance. They reported strong correlations between capnographic indices and spirometric parameters, suggesting that capnographic waveform analysis is useful for monitoring asthma improvement. Howe et al (4). reported that capnogram waveform indices reflect improvement in overall medium and small airways resistance in nonintubated patients with acute asthma in the emergency department, and found significant differences in phase III slope and alpha angle (opening of the angle between phases II and III) between pre- and posttreatment capnogram waveforms. This is the first report measuring the phase III slope in an intubated patient over several days. Since this case involved an intubated patient, $PexpCO_2$ could be measured more accurately than in nonintubated patients reported in previous studies (1, 3–9).

We could observe temporal changes in the phase III slope in capnogram waveforms in real time because continuous capnographic monitoring is possible with a bedside patient monitoring system in the ICU. This study provides evidence for the potential utility of the phase III slope to easily and visually evaluate the improvement in bronchospasm in patients with exacerbated asthma. It should be noted that the phase III slope is an early indicator of clinical recovery, but is not superior to existing parameters (e.g., $PaCO_2 - EtCO_2$) in this preliminary study. Further research to develop an automated calculation of the Phase III slope with standardization with physiological parameters (e.g., respiratory rate, expiratory time, and I:E ratio) may enhance its utility to visually monitor the resolution process of bronchospasm in a real time manner. On top of that, utilizing all information on the phase III slope as well as existing parameters such as $PaCO_2 - EtCO_2$ may be able to more accurately monitor the resolution of acute exacerbation of airway bronchoconstriction.

The study has several limitations. First, we used the time from the end-tidal peak to calculate the phase III slope according to the previous study (4), which could be influenced by physiologic parameters such as respiratory rate and expiratory time. However, another method of calculating the phase III slope, identifying the phase II–III inflection point, may be subject to measurement error. Given our method was validated by Howe et al (4), we believe our approach may be a practical way to estimate the phase III slope. In order to develop a more validated method for estimating the slope including standardization with respiratory rate or expiratory time, further research is needed. Second, we acknowledged that other waveform indices might provide more accurate information on improvement in airway resistance; for example, the dynamic compliance and ventilatory ratio decreased during treatment (**Supplementary Fig. 2**, http://links.lww.com/CCX/B175) (10). Third, although our findings were based on the data on a mechanically ventilated patient under PS mode, capnogram waveforms under assist-control mode are more stable than those under PS mode, and we can measure other respiratory physiological variables (e.g., static compliance) under assist-control mode. Fourth, improvement of bronchospasm can be detected by expiratory flow curve, but the specific data of the expiratory flow curve were not available. We did not find remarkable air trapping in expiratory flow curve during intubation.

CONCLUSIONS

We decided the treatment strategy based on many clinical factors related to respiratory systems, and the phase III slope could be one of them due to the ease of assessment. Further studies should be conducted to investigate and integrate monitoring other respiratory factors and generalize our findings in monitoring acute bronchospasm of mechanically ventilated patients using capnogram waveforms in real time.

All authors: Department of Emergency and Critical Care Medicine, The University of Tokyo Hospital, Tokyo, Japan.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccejournal).

The authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail: mshikama.eme@gmail.com

The patient provided informed consent.

REFERENCES

1. You B, Peslin R, Duvivier C, et al: Expiratory capnography in asthma: Evaluation of various shape indices. *Eur Respir J* 1994; 7:318–323
2. Pertzov B, Ronen M, Rosengarten D, et al: Use of capnography for prediction of obstruction severity in non-intubated COPD and asthma patients. *Respir Res* 2021; 22:154
3. Yaron M, Padyk P, Hutsinpiller M, et al: Utility of the expiratory capnogram in the assessment of bronchospasm. *Ann Emerg Med* 1996; 28:403–407
4. Howe TA, Jaalam K, Ahmad R, et al: The use of end-tidal capnography to monitor non-intubated patients presenting with acute exacerbation of asthma in the emergency department. *J Emerg Med* 2011; 41:581–589
5. Nik Hisamuddin NA, Rashidi A, Chew KS, et al: Correlations between capnographic waveforms and peak flow meter measurement in emergency department management of asthma. *Int J Emerg Med* 2009; 2:83–89
6. Sun X, Yang W, Gong S, et al: Diagnostic value of volumetric capnography in patients with chronic cough variant asthma. *Clinics (Sao Paulo)* 2020; 75:e1662
7. Cracco O, Degrugilliers L, Rames C, et al: Change in capnogram waveform is associated with bronchodilator response and asthma control in children. *Pediatr Pulmonol* 2019; 54:698–705
8. Almeida CC, Almeida-Júnior AA, Ribeiro MA, et al: Volumetric capnography to detect ventilation inhomogeneity in children and adolescents with controlled persistent asthma. *J Pediatr (Rio J)* 2011; 87:163–168
9. Almeida-Junior A, Marson FAL, Almeida CCB, et al: Volumetric capnography versus spirometry for the evaluation of pulmonary function in cystic fibrosis and allergic asthma. *J Pediatr (Rio J)* 2020; 96:255–264
10. Sinha P, Fauvel NJ, Singh P, et al: Analysis of ventilatory ratio as a novel method to monitor ventilatory adequacy at the bedside. *Crit Care* 2013; 17:R34