

# Invasive CO<sub>2</sub> monitoring with arterial line compared to end tidal CO<sub>2</sub> during peroral endoscopic myotomy\*



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## ABSTRACT

**Background and study aims** Peroral endoscopic myotomy (POEM) has become a recognized treatment for achalasia.

The technique requires CO<sub>2</sub> insufflation. It is estimated that the partial pressure of CO<sub>2</sub> (PaCO<sub>2</sub>) is 2 to 5 mm Hg higher than the end tidal CO<sub>2</sub> (etCO<sub>2</sub>), and etCO<sub>2</sub> is used as a surrogate for PaCO<sub>2</sub> because PaCO<sub>2</sub> requires an arterial line. However, no study has compared invasive and noninvasive CO<sub>2</sub> monitoring during POEM.

**Patients and methods** Seventy-one patients who underwent POEM were included in a prospective comparative study. PaCO<sub>2</sub> plus etCO<sub>2</sub> was measured in 32 patients (invasive group) and etCO<sub>2</sub> only in 39 matched patients (noninvasive group). Pearson correlation coefficient (PCC) and Spearman's Rho were used to calculate the correlation between PaCO<sub>2</sub> and ETCO<sub>2</sub>.

**Results** PaCO<sub>2</sub> and ETCO<sub>2</sub> were strongly correlated: PCC R value: 0.8787  $P \leq 0.00001$ , Spearman's Rho R value: 0.8775,  $P \leq 0.00001$ . Within the invasive group, the average difference between PaCO<sub>2</sub> and ETCO<sub>2</sub> was 3.39 mm Hg (median 3, standard deviation 3.5), within the 2- to 5-mm Hg range. The average procedure time (scope in to scope out) was increased 17.7 minutes ( $P=0.044$ ) and anesthesia duration was 46.3 minutes. Adverse events (AEs) included three hematomas and one nerve injury in the invasive group and one pneumothorax in the noninvasive group. There were no differences in AE rates between the groups (13% vs 3%  $P=0.24$ ).

**Conclusions** Universal PaCO<sub>2</sub> monitoring contributes to increased procedure and anesthesia times without any decrease in AEs in patients undergoing POEM. CO<sub>2</sub> monitoring with an arterial line should only be performed in patients with major cardiovascular comorbidities; in all other patients, ETCO<sub>2</sub> is an appropriate tool.

## Introduction

Achalasia is a motor disorder of the esophagus characterized by impaired relaxation of the lower esophageal sphincter, as a consequence of the loss of myenteric neurons. There are multiple options available for its treatment, including medications,

pneumatic balloon dilation, and surgical myotomy [1,2]. POEM is an endoscopic technique that evolved from the concept of natural orifice transluminal endoscopic surgery. The procedure involves the creation of a submucosal tunnel and then myotomy of the muscular fibers of the distal esophagus, including the lower esophageal sphincter. First described in humans more than a decade ago, the reported safety and clinical efficacy of this treatment modality in all types of achalasia, as

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well as in other spastic disorders of the esophagus, has been well demonstrated [3, 4].

Carbon dioxide (CO<sub>2</sub>) insufflation is a crucial component of third space endoscopy, and permits work in the submucosal space with less risk of barotrauma because it is reabsorbed faster than air [3, 5]. Controlled or minimized CO<sub>2</sub> insufflation during the creation of the submucosal tunneling, as well as during the myotomy, can still be associated with complications [6]. The recognition and treatment of the physiological changes that occur as a consequence of CO<sub>2</sub> is of utmost importance to improve patient safety. End tidal CO<sub>2</sub> (ETCO<sub>2</sub>) offers an acceptable estimate of alveolar CO<sub>2</sub> measured as arterial CO<sub>2</sub> (PaCO<sub>2</sub>) [7], and is recommended as a surrogate for PaCO<sub>2</sub> in most patients, although its reliability can be compromised in patient with pulmonary diseases [7, 8].

PaCO<sub>2</sub> provides the most accurate evaluation of alveolar CO<sub>2</sub> but requires the presence of an arterial line. Interestingly, no study has evaluated whether there are any differences between invasive and noninvasive CO<sub>2</sub> monitoring during POEM. The aim of our study was to elucidate if the use of an arterial line with direct measurement of PaCO<sub>2</sub> was of any benefit, when compared to only ETCO<sub>2</sub>.

## Patients and methods

### Patient population

A prospective comparative study was performed in our institution. Information on all patients 18 years or older who underwent POEM for the treatment of achalasia and were able to provide consent was included in a prospectively collected database. Information on patients with known pulmonary disease or advanced cardiovascular disease was excluded. A total of 71 patients were included in the study. In the group in which PaCO<sub>2</sub> plus ETCO<sub>2</sub> was measured, also known as invasive group, included 32 patients, an arterial line was placed prior to starting the POEM and the PaCO<sub>2</sub> was checked on average every 28 minutes. The group in which only ETCO<sub>2</sub> was measured, also known as the noninvasive group, included 39 matched patients. ETCO<sub>2</sub> was recorded every 12 minutes on average in both groups.

### Periprocedure details

All the patients at our institution require a thorough evaluation before a diagnosis of achalasia is made, which includes a history and physical focusing on the Eckardt score, esophagogastro-duodenoscopy, high-resolution manometry and endoluminal impedance measurement. Absolute contraindications for POEM are severe coagulopathy unable to be reversed as well as end-stage cirrhosis with sequelae of portal hypertension such as esophageal or gastric varices.

After the decision has been made for POEM, patients are placed on a full liquid diet for 2 days prior to the procedure, and then nil per os (NPO) for at least 8 hours. Preprocedurally patients are given a high-dose proton pump inhibitor (PPI), scopolamine patch and ondansetron to prevent nausea as well as prophylactic antibiotics, usually a quinolone.

The procedure is performed under general anesthesia with endotracheal intubation, paralytics are usually administered throughout the procedure, and pressure-controlled ventilation is favored over volume-controlled ventilation. In the pediatric population, the available evidence about the best anesthetic practices for POEM is scarce, and usually management is driven by the available data from adult patients [9]. The patient is placed in the supine position, and the endoscopist performs the procedure at the head of the bed, which allows for continuous visualization of the patient's abdomen to monitor for the development of capnoperitoneum [10]. A high-definition gastroscope is required, with 4-mm transparent cap attached to the distal end. Several endoscopic knives and an electro-surgical generator are used for dissection; however, a hybrid knife (ERBE, Marietta, Georgia, United States) is preferred to allow simultaneous injection and dissection. A posterior approach is usually chosen for dissection and myotomy, and submucosal injection is performed using a solution consisting of normal saline and methylene blue. A coag gasper (Olympus, Center Valley, Pennsylvania, United States) is used to prevent or treat bleeding. CO<sub>2</sub> is used for insufflation with an insufflator with adjustable output flow rate ranging from ultralow to high (ERBE). Medium flow is used before tunneling and then is switched to low during submucosal dissection and myotomy; if there is persistent elevation of CO<sub>2</sub> on ETCO<sub>2</sub>, the flow is switched to ultralow. There is also continuous communication with the anesthesia team and the respiratory rate is also increased to decrease the CO<sub>2</sub>. When there is persistent CO<sub>2</sub> elevation along with elevated peak pressure despite the aforementioned measures, the neck, chest and abdomen are examined to look for signs of CO<sub>2</sub> extravasation at those sites. When there is significant abdominal distention, suctioning of the stomach is performed using the endoscope, and then percutaneous needle decompression of pneumoperitoneum is carried out with a 14G needle to decrease the level of CO<sub>2</sub> on ETCO<sub>2</sub>. If there is persistent elevation of CO<sub>2</sub>, the procedure is temporarily stopped until the CO<sub>2</sub> on ETCO<sub>2</sub> drops below 40 mm Hg. After the myotomy is performed, the tunnel can be lavaged with diluted gentamycin on a case-by-case basis. Finally, the tunnel is closed using endoscopic clips or endoscopic suturing.

Patients are extubated post procedure and recover in the postprocedure area of the endoscopy unit. Most of our patients are admitted to the hospital 1 night for observation and kept NPO until a gastrografen esophagram is performed the next day to rule out contrast extravasation. After a negative study, a clear liquid diet is started and if the diet is tolerated, patients are discharged home on antibiotics to complete 5 days of treatment. High-dose PPI and antiemetics are continued on discharge. Patients continue a clear liquid diet for 3 days, and then transition to a full liquid diet for another 3 days and then a soft diet, which is advanced as tolerated.

### Statistical analysis

Data were captured in a registry (NCT05051358) deemed exempt by WCG IRB (February 17, 2021).

Information on demographics, procedural details, post-procedure outcomes, and adverse events (AEs) was collected and

► **Table 1** Demographics of both groups, PaCO<sub>2</sub> plus ETCO<sub>2</sub> and ETCO<sub>2</sub> only.

Groups	PaCO <sub>2</sub> + ETCO <sub>2</sub> group			ETCO <sub>2</sub> only group		
Cases	N = 32			N = 39		
Males/females	14/18 (44%/56%)			15/24 (38%/62%)		
Age (standard deviation)	54.41 mean (16.04)			58.6 mean (19.44)		
Esophageal myotomy	13 cm mean			13 cm mean		
Gastric myotomy	3 cm mean			3 cm mean		
Achalasia subtypes	I n = 10 (31%)	II n = 17 (53%)	III n = 5 (16%)	I n = 12 (31%)	II n = 21 (54%)	III n = 6 (15%)
Severe tortuosity/sigmoid esophagus	3%			5%		

PaCO<sub>2</sub>, partial pressure of CO<sub>2</sub>; ETCO<sub>2</sub>, end tidal CO<sub>2</sub>.

► **Table 2** Comparison between both groups, PaCO<sub>2</sub> plus ETCO<sub>2</sub> and ETCO<sub>2</sub> only.

Groups	PaCO <sub>2</sub> + ETCO <sub>2</sub> group			ETCO <sub>2</sub> only group			P value
Cases	N = 32			N = 39			
Males/females	14/18			15/24			
	Average	Median (range)	SD	Average	Median (range)	SD	
Procedure time in minutes (scope in and out)	96.7	80 (50 to 291)	50.7	79	70 (22–172)	33.2	0.04
Age	54.41	58 (22–88)	16.04	58.6	63 (18–94)	19.44	0.33
pH	7.37	7.38 (7.22 to 7.5)	0.064	N/A	N/A	N/A	
PaCO <sub>2</sub> (mm Hg)	41.23	41 (26 to 64)	7.3	N/A	N/A	N/A	
PaCO <sub>2</sub> frequency in minutes	Every 28	Every 27 (14.5 to 56)	7.8	N/A	N/A	N/A	
ETCO <sub>2</sub> (mm Hg)	37.8	38 (26 to 60)	5.6	36.7	37 (27 to 48)	4.21	0.27
ETCO <sub>2</sub> frequency in minutes	Every 12.3	Every 11.6 (4.9 to 29.2)	4.9	Every 11.9	Every 12.8 (3 to 14.5)	3.6	0.74
Adverse event	13% (3 hand hematoma, 1 nerve injury)			3% (1 pneumothorax <sup>1</sup> )			0.24

PaCO<sub>2</sub>, partial pressure of CO<sub>2</sub>; ETCO<sub>2</sub>, end tidal CO<sub>2</sub>; SD, standard deviation; N/A, not applicable.

<sup>1</sup> Inadvertent use of air instead of CO<sub>2</sub> during the procedure.

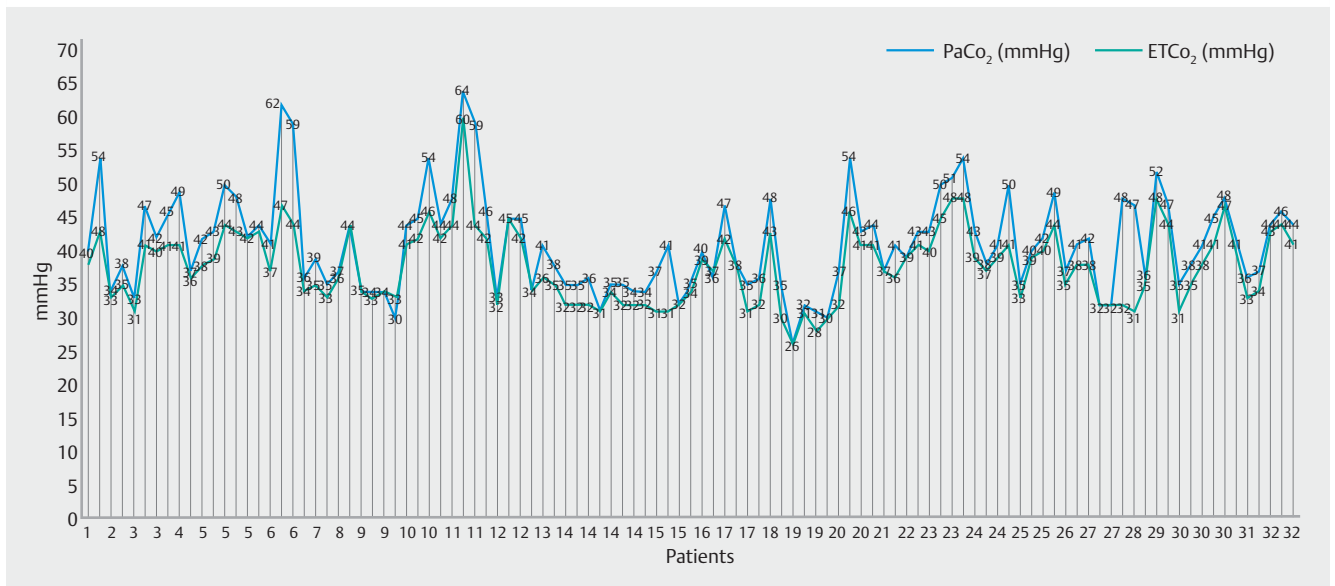
compared. Results are reported as mean ± standard deviation (SD) or median (range) for quantitative variables and percentages for categorical variables. The difference in procedure time, anesthesia time as well as AEs were reported in both groups. Significant associations were defined as  $P < 0.05$ .

We calculated Pearson correlation coefficient (PCC) and Spearman's Rho to calculate the correlation between PaCO<sub>2</sub> and ETCO<sub>2</sub>. PaCO<sub>2</sub> plus ETCO<sub>2</sub> were measured in 32 patients (invasive group) and ETCO<sub>2</sub> only in 39 matched patients (noninvasive group).

Two-sided  $P < 0.05$  were considered statistically significant. All descriptive and statistical analyses were conducted using MedCalc V18.9 (MedCalc Software, Ostend, Belgium).

## Results

Both groups had similar demographics and there were no significant differences in age, length of myotomy, subtype of achalasia or severe tortuosity when comparing the groups (► **Table 1**). The average procedure time (scope in and out) was increased 17.7 minutes ( $P = 0.04$ ) in the invasive monitoring group (► **Table 2**). Anesthesia duration was increased 46.3 minutes in addition to endoscopy time in the invasive monitoring group ( $P \leq 0.00001$ ). Within the PaCO<sub>2</sub> group, the average difference between PaCO<sub>2</sub> and ETCO<sub>2</sub> was 3.39 mm Hg (Median 3, SD 3.5), within the 2- to 5-mm Hg range (► **Fig. 1**). The frequency of ETCO<sub>2</sub> monitoring in the two groups was not significantly different ( $P = 0.74$ ). PaCO<sub>2</sub> and ETCO<sub>2</sub> were strongly correlated in patients undergoing POEM, PCC R value: 0.8787  $P \leq 0.00001$ , Spearman's Rho R value: 0.8775,  $P \leq 0.00001$ .



► Fig. 1 Correlation between PaCO<sub>2</sub> and ETCO<sub>2</sub>.

There were no differences between the groups in AEs (13% vs 3%  $P=0.24$ ). AEs included three hematomas and one nerve injury related to arterial line placement in the invasive group and one pneumothorax due to inadvertent air insufflation in the noninvasive group. The episode of pneumothorax in the noninvasive group was caused by inadvertent use of air instead of CO<sub>2</sub> insufflation, and required stopping the procedure as well as chest tube placement. After the pneumothorax resolved the patient decided not to pursue another procedure.

The three hematomas in the invasive group were managed conservatively while the patient with nerve injury is undergoing ambulatory physiotherapy.

## Discussion

Appropriate distention is required for good visibility during endoscopy. Initially air was being used for insufflation during endoscopy and in the 1970s, it was discovered that use of electrosurgical instruments during air insufflation could lead to a fatal explosion in the bowels and barotrauma, [11]. CO<sub>2</sub> happens to be less expensive and more rapidly absorbed than regular air, because CO<sub>2</sub> is absorbed 160 times faster than nitrogen and 12 times faster than oxygen, the two main components of air. After being absorbed, the CO<sub>2</sub> is transported by the blood to the lungs and then exhaled [12].

POEM involves the creation of a tunnel across the submucosal space with frequent exposure of the mediastinum. The most common AEs associated with POEM are related to excess insufflation, including pneumomediastinum, pneumothorax, pneumoperitoneum, and subcutaneous emphysema because endoscopically insufflated gas may be inadvertently absorbed into surrounding tissues, compromising cardiorespiratory function. According to prior studies, insufflation-related AEs are quite variable in incidence, ranging from 7.5% to 55.5% [13–17].

Initial studies of POEM showed that use of CO<sub>2</sub> was associated with less risk of insufflation-related complications when compared to air, and although its use did not completely eliminate the risk, it was decreased substantially [18, 19]. The use of general anesthesia also facilitates achievement of positive intrathoracic pressure and decreases risk of mediastinal emphysema [20].

CO<sub>2</sub> plays various roles in the human body, including regulation of blood pH, respiratory drive, and affinity of hemoglobin for oxygen; therefore, CO<sub>2</sub> levels should be closely monitored to maintain them under 45 mm Hg [13, 21]. It is estimated that partial pressure of CO<sub>2</sub> (PaCO<sub>2</sub>) is 2 to 5 mm Hg higher than ETCO<sub>2</sub> [22, 23], and the recommended level of ETCO<sub>2</sub> during POEM is approximately 40 mm Hg. Another parameter to consider is the peak inspiratory pressure or P<sub>max</sub>; elevated peak pressure (>38 cm H<sub>2</sub>O or 20% above the baseline) along with abdominal distention could represent increased abdominal pressure, and the need for percutaneous needle decompression of pneumoperitoneum [21, 24].

Previous studies have demonstrated the adequacy of ETCO<sub>2</sub> to evaluate hypercapnia and monitor ventilation during anesthesia because it is continuous and noninvasive [7, 8, 22, 25, 26].

This prospective comparative study confirmed that, among patients undergoing POEM, ETCO<sub>2</sub> correlates strongly with PaCO<sub>2</sub> with an average difference that is within the expected 2- to 5-mm Hg range as reported in studies in non-POEM patients [22, 23]. The gradient between ETCO<sub>2</sub> and PaCO<sub>2</sub> is directly proportional to the degree of physiologic dead space [27–29]. Although the typical alveolar CO<sub>2</sub> concentration is slightly greater than PaCO<sub>2</sub>, ETCO<sub>2</sub> is normally 2 to 5 mm Hg lower than PaCO<sub>2</sub> due to mixing of CO<sub>2</sub>-containing alveolar gas with exhaled gas devoid of CO<sub>2</sub> from the anatomical dead space. As a result, ETCO<sub>2</sub> levels are maintained in a normal physiologic range (30–40 mm Hg), corresponding to a PaCO<sub>2</sub> range

of 35 to 45 [21–23]. Because the observed average difference in  $\text{ETCO}_2$  and  $\text{PaCO}_2$  in our study was within the 2- to 5-mm Hg range,  $\text{ETCO}_2$  can be used as a noninvasive surrogate measure for  $\text{PaCO}_2$  in patients undergoing POEM. In patients with concurrent lung disease, the reliability of  $\text{ETCO}_2$  can be compromised because the 2- to 5-mm Hg gradient can increase with any increase in the dead space volume; indeed, the addition of alveolar dead space further dilutes  $\text{ETCO}_2$  relative to  $\text{PaCO}_2$ . In such patients, endoscopists should exercise caution because the same  $\text{ETCO}_2$  values may reflect greater  $\text{PaCO}_2$  values, and thus, increased risk of hypercapnia-related complications [7, 8].

Although it is recognized that POEM poses unique anesthesia-related challenges, standardized management has yet to be established and the necessity for arterial line placement has not previously been investigated. In our study, there was no significant difference in AEs between the invasive and noninvasive groups, suggesting that using  $\text{ETCO}_2$  as a safe surrogate measure for  $\text{PaCO}_2$  allows for prompt recognition and response to emergent hypercapnia-related complications. While there was an instance of pneumothorax in the noninvasive group due to use of air for insufflation instead of  $\text{CO}_2$ , it was inadvertent and not due to using  $\text{ETCO}_2$  as a surrogate measure for  $\text{PaCO}_2$ . However, compared to POEM procedures performed in the invasive group, those performed in the noninvasive group had a significantly shorter mean procedure time and anesthesia duration. Longer procedure times and anesthesia durations among the invasive group due to the placement of an arterial line may increase the risk of complications. In our study, the widespread placement of arterial line was associated with an increased incidence of hematoma and nerve injuries.

A retrospective case series review by Loser et al demonstrated that insufflation-related cardiorespiratory responses are likely inevitable during POEM. The cardiorespiratory response tends to include an increased peak inspiratory pressure,  $\text{ETCO}_2$  levels, mean arterial pressures, and heart rate [24]. The goal of periprocedural monitoring is to identify abnormalities at an early stage to prevent or mitigate harm to the patient [7]. Previous studies have reported the safety of  $\text{ETCO}_2$  during POEM [13, 21, 24]. Our study has several strengths, including being the first to compare invasive versus noninvasive  $\text{CO}_2$  monitoring in patients undergoing POEM, demonstrating that  $\text{ETCO}_2$  correlates strongly with  $\text{PaCO}_2$  and should be used as a surrogate of  $\text{PaCO}_2$  in patients undergoing POEM, and universal  $\text{PaCO}_2$  monitoring contributes to increased duration of anesthesia, as well as total procedure and turnover time.

## Conclusions

In conclusion, POEM is a relatively new procedure, continuously evolving. It has unique perioperative aspects that need to be understood by the team performing the procedure, which includes the endoscopist, the anesthesiologist, anesthetist, perioperative nurses and endoscopy technician.

One of the limitations of our study is that it was not randomized. However, it demonstrates the viability of  $\text{ETCO}_2$  as a surrogate measure for  $\text{PaCO}_2$ , allowing recognition of  $\text{CO}_2$ -related

complications without the need for arterial line placement during the POEM procedure. Invasive  $\text{CO}_2$  monitoring with an arterial line should be performed in patients with major cardiopulmonary comorbidities on a case-by-case basis.

## Competing interests

Dr. Tyberg is a consultant for Ninepoint Medical, Endogastric Solutions, and Obalon Therapeutics. Dr. Sarkar has done consulting work for US Endoscopy and Obalon Therapeutics. Dr. Shahid has done consulting work for US Endoscopy. Dr. Kahaleh has received grant support from Boston Scientific, Fujinon, W.L. Gore, Apollo Endosurgery, Cook Endoscopy, GI Dynamics, Merit Medical, Interscope Med, Olympus, ERBE, and MI Tech. He is a consultant for Boston Scientific and Laboratories Inc., AbbVie. None of that funding was related to this paper. Dr. Gaidhane is a consultant for 3D Matrix.

## Clinical trial

ClinicalTrials.gov (<http://www.clinicaltrials.gov/>)  
NCT05041608

**TRIAL REGISTRATION:** Retrospective study NCT05041608 at ClinicalTrials.gov (<http://www.clinicaltrials.gov/>)

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