—Original Article—

# Transcutaneous partial pressure of carbon dioxide monitoring during EUS-guided drainage of peripancreatic fluid collections using carbon dioxide insufflation: A prospective study

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## ABSTRACT

**Background:** Carbon dioxide ($CO_2$) insufflation has become more commonly used in EUS-guided interventions in recent years. However, there is a paucity of information regarding methods by which to monitor *in vivo* $CO_2$ levels. This study aimed to assess the feasibility of a novel noninvasive method to monitor transcutaneous partial pressure of $CO_2$ ($P_{CO_2}$) ($P_{tcCO_2}$) levels during EUS-guided drainage of peripancreatic fluid collections (PFCs). The safety of $CO_2$ insufflation in EUS-guided interventions was also investigated. **Patients and Methods:** Patients who underwent EUS-guided PFC drainage between September 2015 and December 2016 at Shengjing Hospital of China Medical University were prospectively enrolled in this study. $P_{tcCO_2}$ was measured in all patients using a noninvasive sensor throughout the procedure. **Results:** There were 25 patients eligible to be included in this study. The mean procedure time was 53.1 min. The mean $P_{tcCO_2}$ level was 40 ± 4 mmHg and 48 ± 5 mmHg before and after the procedure, respectively. The mean peak $P_{tcCO_2}$ during the procedure was significantly higher at 53 ± 6 mmHg ($P < 0.0001$). No complications associated with $CO_2$ insufflation such as $CO_2$ narcosis, gas embolism, or arrhythmias were encountered. **Conclusions:** $P_{tcCO_2}$ monitoring can accurately reflect the level of $P_{CO_2}$ continuously and noninvasively. $CO_2$ insufflation is safe for patients undergoing relatively complicated EUS-guided drainage of PFCs.

**Key words:** Carbon dioxide, EUS, peripancreatic fluid collections, transcutaneous partial pressure of carbon dioxide monitoring

## INTRODUCTION

Carbon dioxide ($CO_2$) is quickly absorbed *in vivo* and is excreted rapidly through respiration.[1] $CO_2$ insufflation is expected to reduce abdominal discomfort during an endoscopic procedure.[2-4] The use of $CO_2$ insufflation during endoscopic procedures such

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as gastrointestinal endoscopy, endoscopic mucosal resection, and endoscopic submucosal dissection was recently reported to be safe and efficacious.[3,5-10] These studies demonstrated that $CO_2$ insufflation not only provided greater comfort than air insufflation, but the incidence of complications associated with the endoscopic procedure was also reduced.[3,5,6,10] EUS-guided interventions are more technically difficult and time-consuming than basic endoscopic examinations and therapies. EUS-guided transluminal drainage of peripancreatic fluid collections (PFCs) has an increased risk of perforation and leakage of gas into the abdomen, leading to abdominal distension.[11] To our knowledge, there is no study evaluating the monitoring of levels of partial pressure of $CO_2$ ($P_{CO_2}$) during $CO_2$ insufflation as part of EUS-guided interventional procedures. However, real-time monitoring of arterial blood gases (ABGs) is cumbersome and is not feasible in many clinical settings. Recently, a novel device that monitors transcutaneous measurements of $P_{CO_2}$ ($P_{tc_{CO_2}}$) has been developed. In this study, we used this simple and noninvasive equipment to continuously monitor $CO_2$ levels in order to evaluate the safety of $CO_2$ insufflation during EUS-guided PFC drainage.

## PATIENTS AND METHODS

### *Patient enrollment*

Consecutive patients at Shengjing Hospital who underwent EUS-guided drainage of PFCs between September 2015 and December 2016 were enrolled. Suspected pancreatic pseudocysts (PPCs) and walled-off pancreatic necrosis (WON) were considered for treatment based on imaging findings. The inclusion criteria were (1) well-encapsulated PFCs; (2) PFCs that persisted at least 6 weeks following the initial event; (3) a distance between the cystic wall and gastroduodenal wall of <1 cm; (4) a diameter of PFC of >5 cm; and (5) symptomatic PFC, such as infection or obstruction of a surrounding hollow viscus injury (gastroduodenal or biliary obstruction). The exclusion criteria were (1) unencapsulated PFCs; (2) PFCs with vascular pseudoaneurysms; (3) PFCs >1 cm away from the gastroduodenal tract; and (4) suspected malignancy. Patients with severe cardiopulmonary disease, known $CO_2$ retention, or abnormal ABG measurements were excluded from the study. All EUS-guided procedures were performed by a highly experienced endoscopist.

The study design was approved by the Ethics Committee for Clinical Research at Shengjing Hospital of China Medical University. All eligible individuals underwent preoperative laboratory testing as well as enhanced computed tomography (CT) scan of the abdomen to measure the size of the collection, its position relative to the wall of the stomach or duodenum, and the distribution of peripheral vasculature. All patients provided written informed consent prior to study enrollment.

### *EUS-guided pancreatic collection drainage procedure*

A therapeutic linear EUS with Doppler (Pentax Precision Instrument, Tokyo, Japan) was advanced into the stomach or duodenum. After measuring the distance between the collection and the luminal wall and identifying intervening vessels along the assumed puncture way, the optimal puncture site was determined. Transmural puncture was performed under direct EUS guidance with the use of color flow to avoid disruption of mural blood vessels lying in the line of puncture [Figure 1a].[12,13] A 19G fine needle (Echo tip Ultra™, Cook Medical, Limerick, Ireland) was utilized to access the collection, and the contents were aspirated for visual assessment as well as for laboratory analysis (including bacterial cultures, amylase levels, and carcinoembryonic antigen levels). Following the needle puncture, a 0.035" guidewire (CookMedical, Winston-Salem, North Carolina, USA) was coiled into the cavity under EUS guidance [Figure 1b]. When necessary, a bent needle knife via the guidewire was utilized to obtain a wider channel. Then, single or multiple 7 Fr or 10 Fr double-pigtail plastic stents (CookMedical, Limerick, Ireland) were placed for the treatment of

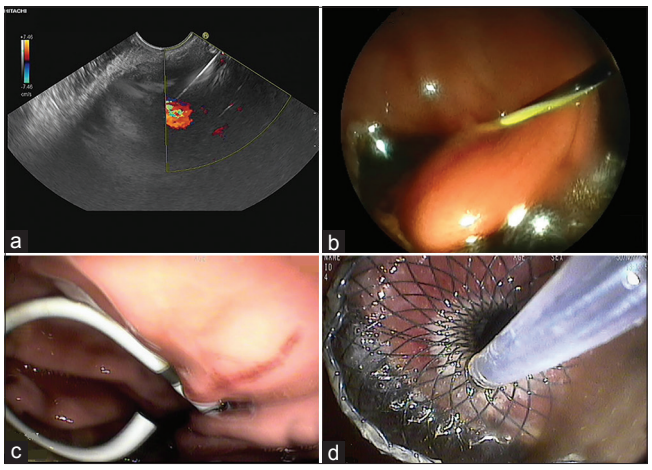


**Figure 1.** EUS-guided pancreatic collection drainage procedure. (a) A 19G EUS fine-needle puncture of a cyst using EUS guidance. (b) A 0.035″ guidewire being inserted into a peripancreatic fluid collection. (c) A double-pigtail plastic stent in place. (d) A fully covered self-expanding metallic stent in place

PPCs [Figure 1c], whereas fully covered self-expanding metallic stents (WallFlex™ Biliary, Boston Scientific Corporation, Galway, Ireland) were placed for the treatment of WON. The use of a nasocystic drain (CookMedical, Limerick, Ireland) followed by the placement of stents was performed at the discretion of the endoscopist [Figure 1d].

Before the procedure, broad-spectrum intravenous antibiotics were administered. Every patient received 3 mg of midazolam for sedation just prior to the procedure. During the procedure, inhaled supplemental oxygen was administered at 3 L/min, and pulse oximetry oxygen saturation ($SpO_2$), blood pressure, heart rate, and respiratory rate were monitored simultaneously.

### *Carbon dioxide insufflation and transcutaneous carbon dioxide monitoring*

$CO_2$ was insufflated during the procedure using the CR4500 (Hangzhou AGS MedTech Co., Ltd., Hangzhou, China) endoscopic $CO_2$ regulation unit. The flow rate of $CO_2$ was set at 1.5 L/min for $CO_2$ insufflation in all cases.

The TCM4 detector (Radiometer™, Copenhagen, Denmark) was used to measure the $P_{tcCO_2}$ noninvasively and continuously with a sensor attached by a low-pressure clip. We chose the internal aspect of the left lower arm as the site for sensor placement. The default skin probe temperature was adjusted to 44°C to heat the local skin. After localized disinfection of the site, a sensor with a gas-permeable membrane was closely attached to the body surface with no air bubbles remaining. Then, the electrodes began to heat the skin, resulting in an increased permeability to gas and a dilatation of the capillary bed, allowing for $CO_2$ diffusion. $CO_2$ passed through the membrane and modified the pH of the electrolyte solution. Thus, proportional electrode signals directly reflected the $P_{CO_2}$ concentration of the subcutaneous tissue. $P_{CO_2}$ was detected, and measurements were recorded automatically on a screen every 30 s. The data were exported for further analysis.

Before midazolam administration, the patient clinically needed a rest period, and the membrane required approximately 5 min for stabilization, during which time the baseline data were collected. $P_{tcCO_2}$ was monitored for a 15-min recovery time following completion of the procedure.

### *Therapeutic outcomes and complications*

For all patients, procedural time was recorded from the time of insertion of the endoscope to its withdrawal. Technical success was defined as achieving access and drainage of the PFCs, as well as correct placement of the stents. Clinical success was defined as a decrease in the size of the PFCs during follow-up radiological examinations with resolution of the patients' symptoms. Bleeding was defined as the clinical evidence of hematemesis or melena requiring endoscopic intervention. Infection was defined as a postoperative temperature >38.5°C with significant elevation of white blood cells for >2 days. A diagnosis of perforation and stent migration was made by direct endoscopic observation of visceral organs during drainage or by a follow-up abdominal CT scan.

### *Statistical analysis*

All variables in this study were described as mean ± standard deviation. The continuous variable data were analyzed using the paired *t*-test. All statistical analyses were performed using SPSS 16.0 statistical software (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

## RESULTS

Of the 27 patients who were candidates for EUS-guided drainage of PFCs, 25 patients met the inclusion criteria and were enrolled in the study. Two patients were excluded: one due to severely impaired respiratory function and the other due to unwillingness to participate in the trial. The mean PFC size was 82.6 mm (mean: 82.6 mm; range: 24–220 mm), and the median procedural time was 53.1 min (mean: 53.1 min; range: 20–150 min). EUS-guided drainage procedures were performed on all of the patients. The details are summarized in Table 1.

### *Transcutaneous carbon dioxide monitoring*

The mean $P_{tcCO_2}$ values pre- and post-procedure were 40 ± 4 mmHg (range: 34–48 mmHg) and 48 ± 5 mmHg (range: 36–55 mmHg), respectively. The mean peak $P_{tcCO_2}$ was 53 ± 6 mmHg (range: 38–61 mmHg) during the procedures, which was significantly higher than the mean $P_{tcCO_2}$ values before and after the procedures ($P < 0.0001$). Although the $P_{tcCO_2}$ peak value exceeded 60 mmHg in one case, neither $CO_2$ narcosis nor any other complications of $CO_2$ retention occurred in any of the patients. $P_{tcCO_2}$

values were saved automatically by the monitor every 30 s. The trend of average $P_{tcCO_2}$ values during the first 20 min of the procedure and during the first 10 min of recovery following procedure completion is shown in Figures 2, 3 and Table 2.

### *Complications*

EUS procedure-related adverse events occurred in five patients (20%), including bleeding with stent migration ($n$ = 1) and infection ($n$ = 4). For the patient who developed bleeding and stent migration, secondary EUS-guided stent implantation and endoscopic hemostasis were necessary. For patients with postoperative infections, appropriate antibiotics were administered according to the results of bacterial culture and drug sensitivities. When necessary, saline solution was administered daily through the nasocystic catheter to prevent the accumulation of pus and debris ($n$ = 1). If infection was caused by the contamination of an incompletely drained WON or PPCs arising from premature stent occlusion or uneven collapse ($n$ = 2), balloon and basket catheters were subsequently placed using endoscopy for dilation of the fistula and removal of the pus or necrotic contents inside, followed by repeated irrigation of the cyst using normal saline.

All patients were treated conservatively without surgical intervention. The criteria for discharge from the hospital included either a decrease in size or complete resolution of the fluid collection as visualized on the CT scan combined with the resolution of clinical symptoms.

**Table 1. Background characteristics of patients**

| Variable name | *N* |
|---|---|
| Number of cases (*n*) | 25 |
| Number of lesions (PPCs/WON) | 26 (15/11) |
| Gender (male/female) | 11/14 |
| Mean age, years (range) | 47.0 (15-67) |
| Mean procedural time, min (range) | 53.1 (20-150) |
| Mean hospital stay, day (range) | 16.2 (4-39) |
| Mean PFC size, mm (range) | 82.6 (24-220) |
| Single plastic stent, *n* (PPCs/WON) | 14 (12/2) |
| Double plastic stents, *n* (PPCs/WON) | 4 (3/1) |
| Fully covered self-expanding metallic stents, *n* (PPCs/WON) | 8 (0/8) |
| Combined with nasocystic catheter | 4 |

WON: Walled-off pancreatic necrosis, PPCs: Pancreatic pseudocysts, PFC: Peripancreatic fluid collection

**Table 2. Transcutaneous partial pressure of carbon dioxide levels before, during, and after the procedure in mmHg (range)**

| $P_{CO_2}$ | Results (mmHg) |
|---|---|
| Mean $P_{tcCO_2}$ before the procedure | 40±4 (34-48) |
| Peak $P_{tcCO_2}$ during the procedure | 53±6 (38-61) |
| Mean $P_{tcCO_2}$ after the procedure | 48±5 (36-55) |

$P_{CO_2}$: Partial pressure of $CO_2$, $CO_2$: Carbon dioxide, $P_{tcCO_2}$: Transcutaneous $P_{CO_2}$

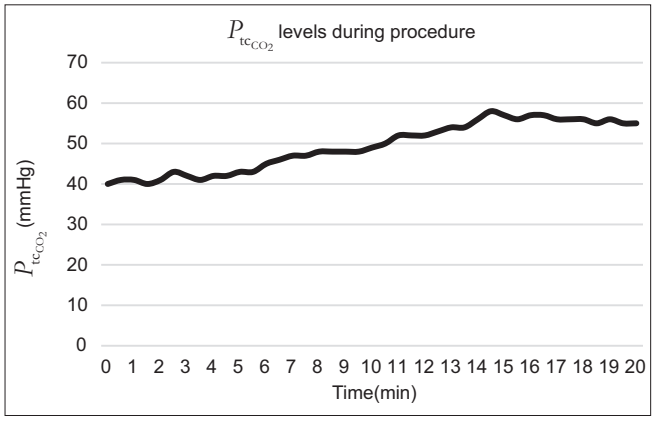


**Figure 2.** The trend of mean transcutaneous partial pressure of carbon dioxide values during EUS-guided drainage of peripancreatic fluid collections

## DISCUSSION

To the best of our knowledge, this is the first study to monitor $P_{CO_2}$ during EUS-guided drainage of PFCs and to subsequently show that $CO_2$ insufflation during this procedure does not lead to a clinically significant rise in the $P_{tcCO_2}$ level.

Monitoring of pulmonary gas exchange is crucial for the effective management of patients' ventilatory function when $CO_2$ insufflation is used during endoscopic procedures. It is essential to note that insufflation of $CO_2$ into the gastrointestinal (GI) tract could lead to arterial $CO_2$ retention which could theoretically result in the development of severe

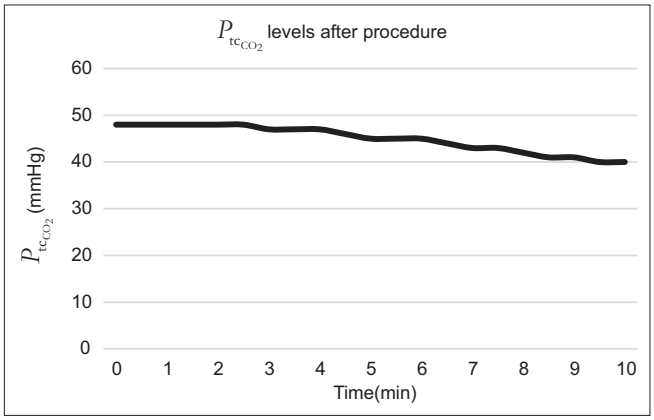


**Figure 3.** The trend of mean transcutaneous partial pressure of carbon dioxide values during the first 10 min following procedure completion

acidosis, leading to cardiac arrhythmia and circulatory collapse. For this reason, it is essential to carefully monitor $Pa_{CO_2}$ levels during this procedure. Oxygen saturation, as measured by $SpO_2$, is widely used as a surrogate of arterial oxygen saturation ($SaO_2$).[14] Similarly, there is also a need for an analogous, reliable, noninvasive, immediate, and continuous assessment of arterial $P_{CO_2}$.

ABG measurement is considered the gold standard for assessing $Pa_{CO_2}$ levels. It involves arterial puncture, a procedure that requires skilled technicians to ensure the accuracy of the samples. ABG monitoring can cause pain during the procedure and also may require multiple procedures when serial measurements are indicated. Moreover, arterial puncture has inherent risks and potential complications such as bleeding, vasospasm, and nerve injury. Transcutaneous measurement of $P_{tcCO_2}$ is a novel method to determine $CO_2$ levels in arterial blood. Perioperative monitoring of pulmonary gas exchange using this method is continuous and noninvasive. It is based on the principle that $CO_2$ gas can be detected after diffusing through body tissue and skin. Heat applied to the skin accelerates blood flow within the subcutaneous capillaries, which induces a local hypermetabolic state, leading to a local increase in $CO_2$ production that can be detected by a sensor at the skin surface.[15,16] For accurate correlation with ABG values, there are several potential sites for sensor placement including the earlobe, the chest (second right intercostal space at the midclavicular line), and the forearm.[17,18] Measurements of $P_{tcCO_2}$ by this device have been shown to correlate closely with arterial blood $CO_2$ values in virtually all clinical conditions.[10,19] Typically, corrected $P_{tcCO_2}$ measurements are 5–6 mmHg higher than those obtained by ABG. This difference between $P_{tcCO_2}$ and $Pa_{CO_2}$ may be attributable to skin metabolism and the arteriole–cellular $CO_2$ difference.[20,21] In this study, there was only one peak $P_{tcCO_2}$ value that exceeded 60 mmHg, while all others were in the normal range of $P_{CO_2}$ values. The range of $P_{CO_2}$ values was within clinically acceptable levels. $P_{tcCO_2}$ monitoring has the benefit of being reliable, efficacious, and pain free. Aarrestad *et al.* summarized the groups of patients in which $P_{tcCO_2}$ was evaluated and concluded that $P_{tcCO_2}$ is an appropriate alternative to repeated blood gas analyses.[22]

Conventionally, air has been used for insufflation during procedures to maintain adequate visualization. This results in the retention of a large amount of residual gas in the GI tract after the procedure. Gas retention within the GI tract often causes abdominal pain or bloating, and in rare cases can give rise to life-threatening complications such as air embolism[23-25] and tension pneumothorax.[26,27] $CO_2$ is absorbed across the GI tract 160 times more rapidly than nitrogen and 13 times faster than oxygen so that $CO_2$ has the benefit of being rapidly absorbed from the intestinal lumen into the bloodstream and then eliminated from the body via respiration.[1] The first use of $CO_2$ insufflation in endoscopic procedures was performed in colonoscopy. It has been reported that $CO_2$ insufflation applied during colonoscopy is useful for reducing intestinal gas retention as well as for reducing pain.[2,3,28] In one study, the $CO_2$ insufflation group showed no significant residual abdominal gas on plain radiographs performed 30 min after colonoscopy and had much less discomfort than the air insufflation group, which showed large amounts of residual postprocedural gas on radiographs.[2]

EUS-guided drainage of PFCs results in excellent technical and clinical outcomes in the majority of cases.[29] It has been widely recognized as a safe and efficacious therapy because of improved physical and mental health outcomes, lower complication rates, and lower mortality as compared to surgery.[30,31] However, this procedure is relatively complicated and time-consuming. Moreover, gas can leak into the abdomen through fistulas, leading to more severe abdominal distention or even pneumoperitoneum and peritonitis. Knowledge of these risks led to an interest in the insufflation of $CO_2$ during EUS-guided drainage of PFCs. This method can minimize leakage-related complications because leaked $CO_2$ is rapidly absorbed into the surrounding tissues, delaying or obviating the increase in abdominal pressure. In this study, on examining ABG values during the procedure, all recorded data were in the normal range after 5–6 mmHg correction,[10,19] without significant increases in $CO_2$. By analyzing the trends of $P_{tcCO_2}$ before, during, and after the procedures, it was found that $P_{tcCO_2}$ peaked in the first 15–20 min of surgery, and then stabilized with only minimal fluctuations for the remainder of the procedure. This may be because $CO_2$ stimulates the respiratory center, resulting in hyperventilation and respiratory compensation for the acid–base disturbance in order to maintain a steady-state $P_{CO_2}$ level. In addition, a 10–15 min period of postoperative observation during the recovery period

revealed that $P_{tcCO_2}$ levels generally returned to the patients' preoperative baseline levels in no >10 min. Throughout the periods of observation, no respiratory depression, arrhythmias, or other complications associated with $CO_2$ ventilation were encountered.

There are some limitations to this study, including its single-center design and its small sample size. We also used only one type of sensor device that did not offer additional information provided by ABG measurements, including pH or buffer excess. Therefore, further larger prospective multicenter studies are required. Future trials should randomly compare $CO_2$ insufflation with air insufflation during the procedure. In addition, the patient-oriented outcomes also should be more detailed including an examination of mortality, serious adverse events, and length of hospital stay, with a longer follow-up period of 2–3 years.

## CONCLUSIONS

$CO_2$ insufflation is as safe as air insufflation for patients undergoing EUS-guided drainage of PFCs. $P_{tcCO_2}$ monitoring correlates closely with $P_{CO_2}$ values and reflects dynamic changes in $P_{CO_2}$ continuously and noninvasively. This study recommends using $CO_2$ insufflation during EUS-guided operation in conjunction with $P_{tcCO_2}$ as a valid tool to continually assess real-time $P_{CO_2}$ levels.

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### *Conflicts of interest*

There are no conflicts of interest.

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