



Randomized Controlled Trial

## Safety and efficacy of carbon dioxide insufflation during gastric endoscopic submucosal dissection

Jun Takada, Hiroshi Araki, Fumito Onogi, Takayuki Nakanishi, Masaya Kubota, Takashi Ibuka, Masahito Shimizu, Hisataka Moriwaki

Jun Takada, Hiroshi Araki, Fumito Onogi, Takayuki Nakanishi, Masaya Kubota, Takashi Ibuka, Masahito Shimizu, Hisataka Moriwaki, Department of Gastroenterology, Gifu University Graduate School of Medicine, Gifu 5011194, Japan

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**Correspondence to:** Hiroshi Araki, MD, PhD, Assistant Professor, Department of Gastroenterology, Gifu University

Graduate School of Medicine, 1-1 Yanagido, Gifu 5011194, Japan. [araara@gifu-u.ac.jp](mailto:araara@gifu-u.ac.jp)  
Telephone: +81-58-2306308  
Fax: +81-58-2306310

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### Abstract

**AIM:** To compare the safety and efficacy of carbon dioxide (CO<sub>2</sub>) and air insufflation during gastric endoscopic submucosal dissection (ESD).

**METHODS:** This study involved 116 patients who underwent gastric ESD between January and December 2009. After eliminating 29 patients who fit the exclusion criteria, 87 patients, without known pulmonary dysfunction, were randomized into the CO<sub>2</sub> insufflation (*n* = 36) or air insufflation (*n* = 51) groups. Standard ESD was performed with a CO<sub>2</sub> regulation unit (constant rate of 1.4 L/min) used for patients undergoing CO<sub>2</sub> insufflation. Patients received diazepam for conscious sedation and pentazocine for analgesia. Transcutaneous CO<sub>2</sub> tension (PtcCO<sub>2</sub>) was recorded 15 min before, during, and after ESD with insufflation. PtcCO<sub>2</sub>, the correlation between PtcCO<sub>2</sub> and procedure time, and ESD-related complications were compared between the two groups. Arterial blood gases were analyzed after ESD in the first 30 patients (12 with CO<sub>2</sub> and 18 with air insufflation) to assess the correlation between arterial blood CO<sub>2</sub> partial pressure (PaCO<sub>2</sub>) and PtcCO<sub>2</sub>.

**RESULTS:** There were no differences in respiratory

functions, median sedative doses, or median procedure times between the groups. Similarly, there was no significant difference in post-ESD blood gas parameters, including PaCO<sub>2</sub>, between the CO<sub>2</sub> and air groups (44.6 mmHg *vs* 45 mmHg). Both groups demonstrated median pH values of 7.36, and none of the patients exhibited acidemia. No significant differences were observed between the CO<sub>2</sub> and air groups with respect to baseline PtcCO<sub>2</sub> (39 mmHg *vs* 40 mmHg), peak PtcCO<sub>2</sub> during ESD (52 mmHg *vs* 51 mmHg), or median PtcCO<sub>2</sub> after ESD (50 mmHg *vs* 50 mmHg). There was a strong correlation between PaCO<sub>2</sub> and PtcCO<sub>2</sub> ( $r = 0.66$ ;  $P < 0.001$ ). The incidence of Mallory-Weiss tears was significantly lower with CO<sub>2</sub> insufflation than with air insufflation (0% *vs* 15.6%,  $P = 0.013$ ). CO<sub>2</sub> insufflation did not cause any adverse events, such as CO<sub>2</sub> narcosis or gas embolisms.

**CONCLUSION:** CO<sub>2</sub> insufflation during gastric ESD results in similar blood gas levels as air insufflation, and also reduces the incidence of Mallory-Weiss tears.

**Key words:** Carbon dioxide; Gastric endoscopic submucosal dissection; Insufflation; Mallory-Weiss tear; Randomized controlled trial

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**Core tip:** The safety and efficacy of carbon dioxide (CO<sub>2</sub>) and air insufflation during gastric endoscopic submucosal dissection (ESD) were compared in a randomized controlled trial. The transcutaneous CO<sub>2</sub> tension and the partial pressure of CO<sub>2</sub> in the arterial blood were measured to directly evaluate CO<sub>2</sub> retention or acidemia. The findings strongly suggest that CO<sub>2</sub> insufflation is as safe as air insufflation with regard to blood gas levels. The present study is the first randomized controlled trial to demonstrate the benefit of CO<sub>2</sub> insufflation in reducing the risk of Mallory-Weiss tears during ESD.

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## INTRODUCTION

Endoscopic submucosal dissection (ESD) for gastric neoplasms enables *en bloc* resection of even an extensive superficial lesion<sup>[1-8]</sup>. However, gastric ESD is technically difficult and time consuming, and therefore, extensive gas insufflation is required to maintain adequate visualization during the procedure. Although air is commonly used for insufflation, it results in the

retention of a large amount of residual gas after ESD. Residual gas in the gastrointestinal tract can induce post-ESD pain or discomfort, and in rare cases can give rise to life-threatening complications such as air embolism and tension pneumothorax<sup>[9-17]</sup>.

It is well known that carbon dioxide (CO<sub>2</sub>) is absorbed faster in the body than air and is also rapidly excreted through the lungs, except in cases of pulmonary dysfunction. Therefore, CO<sub>2</sub> insufflation is expected to reduce the pain and abdominal discomfort associated with endoscopic examination and therapy<sup>[18-25]</sup>.

Perforation and major bleeding are severe complications of ESD. The reported incidence of perforation in ESD ranges from 1% to 6.1%<sup>[1-5]</sup>, and subsequent peritonitis or mediastinitis could be fatal. CO<sub>2</sub> insufflation reportedly minimizes these ESD-related complications<sup>[26]</sup>. The safety and efficacy of CO<sub>2</sub> insufflation during ESD for lesions of the esophagus, stomach, and colorectum have been demonstrated in randomized controlled trials (RCTs)<sup>[27,28]</sup> and prospective studies<sup>[29-31]</sup>. However, these RCTs measured only transcutaneous CO<sub>2</sub> tension (PtcCO<sub>2</sub>) or end-tidal CO<sub>2</sub> pressure, not partial pressure of CO<sub>2</sub> in the arterial blood (PaCO<sub>2</sub>).

The aim of the present prospective RCT was to assess the safety and efficacy of CO<sub>2</sub> insufflation during ESD for gastric neoplasms in patients under conscious sedation. Both PtcCO<sub>2</sub> and PaCO<sub>2</sub> were measured in order to directly evaluate CO<sub>2</sub> retention or acidemia. Furthermore, a continuous PtcCO<sub>2</sub> measuring system to monitor patient safety during CO<sub>2</sub> insufflation was validated.

## MATERIALS AND METHODS

### Study design and participants

This study was designed as a single-center RCT. Between January 2009 and December 2009, all consecutive patients undergoing ESD for gastric neoplasms at Gifu University Hospital in Japan were screened for this study. Gastric ESD was indicated for differentiated adenocarcinoma that was confined to the mucosa with no risk of lymph node metastasis, and for adenoma, regardless of its size or the presence of ulceration.

Patients were excluded if: (1) they had chronic pulmonary dysfunction defined as a forced expiratory volume in 1.0 second/forced vital capacity (FEV<sub>1.0</sub>%) of < 70% or a vital capacity (%VC) of < 80%; (2) they were unable to understand the consent information required for participation; or (3) they declined participation. The study design was approved by the ethics committee for clinical research at Gifu University Hospital. All eligible individuals provided written informed consent prior to study enrollment. Randomization was conducted using sealed envelopes and patients were divided into two groups: the CO<sub>2</sub> insufflation group (CO<sub>2</sub> group) and the air insufflation group (Air group).

### Examination schedule for study events before and after ESD

ESD was conducted during the first afternoon after hospital admission. On the second day in the hospital, blood tests, esophagogastroduodenoscopy, and CT of the chest and abdomen were performed. Blood tests for leukocyte count and C-reactive protein levels were repeated on the third hospital day. Axillary temperature was assessed 1 h after ESD and daily thereafter, at 06:00, 14:00, and 20:00 h.

### ESD procedure and conscious sedation method

The standard ESD procedure was performed using a gastroscope with a single working channel and water jet function (GIF-Q260J; Olympus Optical Co., Tokyo, Japan) and a cap attachment (D-201-11804; Olympus). The gastric lesion was resected using either the DualKnife (KD-630L; Olympus) or the ITKnife2 (KD-611L; Olympus), depending on its location. A 0.4% high-molecular-weight hyaluronic acid solution containing epinephrine was injected into the submucosal layer to raise the lesion. Incision of the mucosal layer around the circumferential markings and subsequent direct dissection of the submucosal layer were performed with the DualKnife and ITKnife2.

Patients received diazepam for conscious sedation and pentazocine for analgesia. At the start of the ESD procedure, 5–10 mg of diazepam and 7.5–15.0 mg of pentazocine were injected intravenously for induction of anesthesia and analgesia, with an additional 5 mg of diazepam or 7.5 mg of pentazocine administered repeatedly as necessary. When the combination of diazepam and pentazocine did not achieve conscious sedation, intravenous midazolam was administered. Oxygen was administered nasally at 2.0 L/min during ESD, and the flow volume was adjusted by monitoring transcutaneous oxygen saturation (SpO<sub>2</sub>). Arterial blood samples were immediately analyzed using a blood gas analyzer (ABL700; Radiometer Medical, Copenhagen, Denmark) after the ESD procedure, for the first 30 consecutive patients.

### CO<sub>2</sub> insufflation and transcutaneous gas analysis

CO<sub>2</sub> was delivered using a CO<sub>2</sub> regulation unit (Olympus UCR; Olympus). The TOSCA measurement system and TOSCA 500 monitor (Linde Medical Sensors, Basel, Switzerland) were used to measure the PtcCO<sub>2</sub> noninvasively and continuously with an earlobe sensor attached by a low-pressure clip. We used a default temperature setting of 42 °C for the sensor and recalibrated the system before each ESD. The low-flow gas tube (MAJ-1742; Olympus) of the Olympus UCR was set at a constant rate of 1.4 L/min for CO<sub>2</sub> insufflation in all patients.

### Definitions of outcome parameters and complications

Operation time was measured from the start of circumferential marking to the completion of resection.

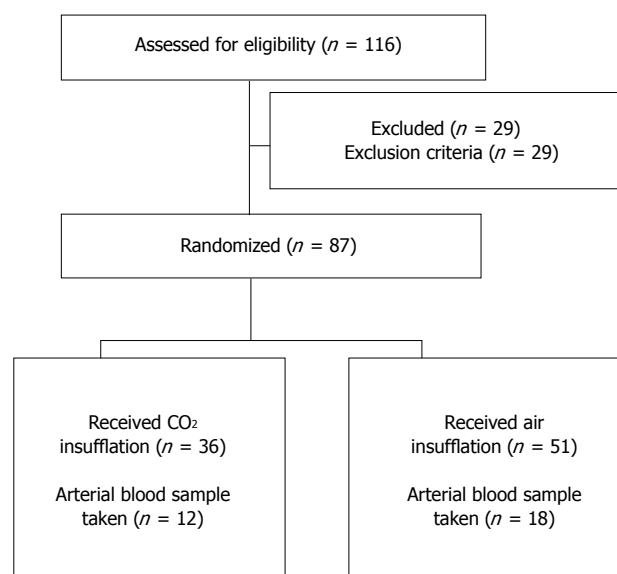


Figure 1 Flow chart of patient enrollment in the study and allocation into groups.

A diagnosis of perforation was made by direct endoscopic observation of visceral organs during ESD or by the presence of free air on follow-up plain chest radiography. Evidence of aspiration pneumonia was determined by the appearance of an obvious pneumonia shadow on a plain chest CT one day after ESD. Bleeding was defined as clinical evidence of bleeding after ESD, such as hematemesis or melena that required endoscopic treatment. A Mallory-Weiss tear (MWT) was defined as a mucosal tear or laceration adjacent to the esophagogastric junction with active bleeding, either spurting or oozing, during ESD.

### Statistical analysis

Values are expressed as the number and percentage of patients or median (range). Differences in distribution of categorical variables between the two groups were analyzed by  $\chi^2$  or by Fisher's exact tests when required. The nonparametric Mann-Whitney *U* test was used for comparing continuous variables. A *P* < 0.05 was considered significant. All statistical analyses were conducted with JMP version 10 (SAS Institute, Cary, NC, United States).

## RESULTS

### Patient enrollment and group allocation

Of the 116 candidate patients for gastric ESD, 87 were enrolled in the trial and randomized. Among them, 36 received CO<sub>2</sub> insufflation and 51 received air insufflation. Twenty-nine patients were excluded due to impaired respiratory function (*n* = 24), severe chronic obstructive pulmonary disease requiring oxygen (*n* = 3), and inability to understand the consent information required for participation (*n* = 2).

**Table 1 Patients and examination characteristics**

Characteristic	CO <sub>2</sub> group (n = 36)	Air group (n = 51)	P value
Age, yr	74 (52-87)	70 (45-93)	NS
Sex, male/female	22/14	36/15	NS
FEV <sub>1.0</sub> %	72 (70-89)	73 (70-93)	NS
%VC	103 (80-102)	109 (80-152)	NS
Location of lesion, n: upper/middle/lower	5/22/9	12/15/24	0.012
En bloc resection, n (%)	36 (100)	51 (100)	NS
Histopathologic type, n: tub1/tub2/por/sig/adenoma	18/3/0/0/15	36/6/2/1/6	0.020
Histologic depth, n: M/SM1/SM2	32/2/2	42/1/8	NS
Histopathologically curative resection, n (%)	31 (86.1)	43 (84.3)	NS
Tumor size, mm	18 (4-75)	17 (3-47)	NS
Resection size, mm	35 (22-110)	37 (23-95)	NS
Procedure time, min	46 (18-194)	48 (15-145)	NS
Dose of diazepam, mg	20 (5-30)	20 (5-30)	NS
Dose of pentazocine, mg	18.8 (7.5-45)	22.5 (7.5-45)	NS
Patients receiving midazolam, n (%)	3 (8.3)	5 (9.8)	NS
Dose of midazolam, mg	10.0 (2.5-20)	7.5 (2.5-10)	NS

Data are presented as n, n (%), or median (range). FEV<sub>1.0</sub> %: Forced expiratory volume 1.0 second/forced vital capacity; %VC: Vital capacity; tub1: Well-differentiated tubular adenocarcinoma; tub2: Moderately differentiated tubular adenocarcinoma; por: Poorly differentiated adenocarcinoma; sig: Signet ring cell carcinoma; M: Tumor confined to the mucosa; SM1: Tumor confined to the submucosa and tumor invasion within 0.5 mm of the muscularis mucosae; SM2: Tumor confined to the submucosa and tumor invasion of 0.5 mm or more into the muscularis mucosae; NS: Not significant.

**Table 2 Patient characteristics and parameters of arterial blood analysis**

Characteristic	CO <sub>2</sub> group (n = 12)	Air group (n = 18)	P value
Age, yr	73 (63-82)	70 (45-87)	NS
Procedure time, min	66 (26-156)	56 (23-107)	NS
Dose of diazepam, mg	17.5 (10.0-22.5)	20.0 (5.0-30.0)	NS
Dose of pentazocine, mg	15.0 (15.0-30.0)	22.5 (15.0-37.5)	NS
Patients receiving midazolam, n (%)	1 (8.3)	1 (5.6)	NS
Dose of midazolam, mg	2.5	5	NS
pH value	7.36 (7.34-7.39)	7.36 (7.33-7.40)	NS
PaCO <sub>2</sub> , mmHg	44.6 (39-53)	45 (40-50)	NS
PaO <sub>2</sub> , mmHg	168 (68-203)	143 (78-259)	NS
HCO <sub>3</sub> <sup>-</sup> , mEq/L	25.1 (23.0-30.0)	25.5 (22.0-27.0)	NS
Base excess, mEq/L	-0.05 (-2.4)	0.3 (-3.1-2.6)	NS

Data are presented as median (range) unless otherwise indicated. PaO<sub>2</sub>: Partial pressure of oxygen in arterial blood; PaCO<sub>2</sub>: Partial pressure of carbon dioxide in arterial blood; NS: Not significant.

The first 30 participants (12 from the CO<sub>2</sub> group and 18 from the Air group) underwent arterial blood gas analysis (Figure 1).

### Baseline characteristics

Baseline characteristics for each treatment group are shown in Table 1. The location ( $P = 0.012$ ) and histopathology ( $P = 0.020$ ) of the gastric lesions were significantly different between the groups. The median procedure time was 46 min in the CO<sub>2</sub> group and 48 min in the Air group (not significant). There were no differences in respiratory function (FEV<sub>1.0</sub> % and %VC) between the groups. No significant differences were observed in the median dose of sedative drugs administered to the patients in each group.

### Arterial blood gas analysis

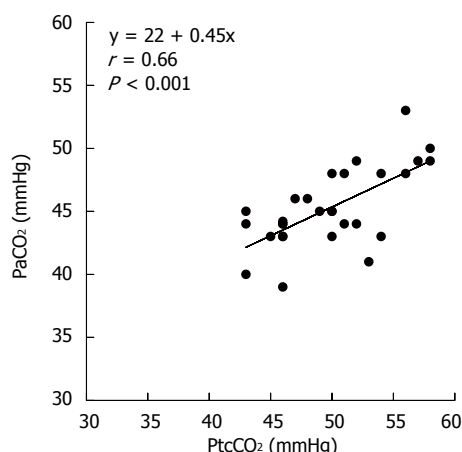
No significant differences were observed between the two groups that received blood gas analysis after ESD with respect to the median procedure time and the

median dose of sedative drugs (Table 2). There was no significant difference between the CO<sub>2</sub> group and the Air group in any blood gas parameters, including PaCO<sub>2</sub> (44.6 mmHg vs 45 mmHg). The median pH values were 7.36 in both groups, and there were no patients with acidemia. As shown in Figure 2, PtcCO<sub>2</sub> was significantly correlated with PaCO<sub>2</sub> ( $r = 0.66$ ;  $P < 0.001$ ). The median difference between PaCO<sub>2</sub> and PtcCO<sub>2</sub> was 4.8 mmHg.

### PtcCO<sub>2</sub> and SpO<sub>2</sub> before and after ESD

The median PtcCO<sub>2</sub> before (baseline) and after ESD was 39 mmHg (28-52 mmHg) and 50 mmHg (41-68 mmHg), respectively, in the CO<sub>2</sub> group, and 40 mmHg (22-51 mmHg) and 50 mmHg (40-64 mmHg), respectively, in the Air group. The PtcCO<sub>2</sub> increased significantly ( $P < 0.001$ ) after the procedure in both groups, though there was no significant difference between the groups. The median peak PtcCO<sub>2</sub> during the procedure was 52 mmHg (43-68 mmHg) in the





**Figure 2** Correlation between partial pressure of carbon dioxide in arterial blood (PaCO<sub>2</sub>) and transcutaneous carbon dioxide tension (PtcCO<sub>2</sub>) after endoscopic submucosal dissection.

CO<sub>2</sub> group and 51 mmHg (40–64 mmHg) in the Air group (not significant, Table 3). There was no correlation between the procedure time and PtcCO<sub>2</sub> elevation in either the CO<sub>2</sub> group or the Air group (Figure 3). The median minimum SpO<sub>2</sub> level and oxygen flow rate were similar between the groups (98% and 2.0 L/min, respectively).

**Incidence of complications and duration of hospital stay**  
ESD-related complications and the duration of the hospital stay are listed in Table 4. CO<sub>2</sub> insufflation did not cause any adverse events such as CO<sub>2</sub> narcosis or gas embolism. No significant difference was observed between the two groups with respect to the incidence of fever (body temperature > 37.5 °C), pneumonia, perforation, or post-ESD hemorrhage. The incidence of MWTs was significantly lower in the CO<sub>2</sub> group than in the Air group ( $P = 0.013$ ). Serum C-reactive protein levels and white blood cell counts on days 1 and 3 after ESD were not significantly different between the groups, and the median hospital stay was equivalent at 7 d for each group.

## DISCUSSION

The safety and efficacy of insufflation using CO<sub>2</sub> as an alternative to air has been demonstrated in several RCTs for various kinds of endoscopic procedures<sup>[18–20,22–24,27,28]</sup>. In gastric ESD, Maeda *et al.*<sup>[28]</sup> reported that CO<sub>2</sub> insufflation significantly reduced the volume of residual gas in the digestive tract compared with air insufflation. In the present study, under similar ESD conditions with regard to procedure time, respiratory function, sedative drug doses, and minimum SpO<sub>2</sub>, neither the post-procedure PaCO<sub>2</sub> nor the median PtcCO<sub>2</sub> differed between the CO<sub>2</sub> group and the Air group. The peak PtcCO<sub>2</sub> during ESD also did not differ between the two groups. Furthermore, we confirmed a strong correlation between PaCO<sub>2</sub> and

PtcCO<sub>2</sub>. Therefore, the PtcCO<sub>2</sub> value can be used as a surrogate marker of CO<sub>2</sub> retention in patients who received CO<sub>2</sub> insufflation during ESD.

In this study, the maximum PtcCO<sub>2</sub> and PaCO<sub>2</sub> reached 68 mmHg and 53 mmHg in the CO<sub>2</sub> group, and 64 mmHg and 50 mmHg in the Air group, respectively. However, no adverse events such as acidemia, CO<sub>2</sub> narcosis, or SpO<sub>2</sub> depression were reported in either group. The elevated PtcCO<sub>2</sub> in both groups after the procedures is likely due to respiratory depression associated with conscious sedation. Several studies have demonstrated that such respiratory depression is involved in the elevation of PaCO<sub>2</sub> or PtcCO<sub>2</sub> in patients undergoing endoscopic treatment<sup>[27,29–31]</sup>. There was no correlation between procedure time and PtcCO<sub>2</sub> elevation in the present study. These results indicate that CO<sub>2</sub> insufflation is as safe as air insufflation for gastric ESD when the CO<sub>2</sub> insufflation rate is 1.4 L/min and the median procedure time is 48 min.

With regard to complications, the incidence of MWTs was significantly lower in the CO<sub>2</sub> group than in the Air group. This may be due to the rapid absorption of CO<sub>2</sub> by the body compared to air. Indeed, CO<sub>2</sub> insufflation in esophagogastroduodenoscopy efficiently reduces MWTs by lowering the tension of the gastric mucosa caused by residual gas in the stomach<sup>[32]</sup>. To our knowledge, the present study is the first RCT to demonstrate the benefit of CO<sub>2</sub> insufflation in reducing the risk of MWTs during ESD.

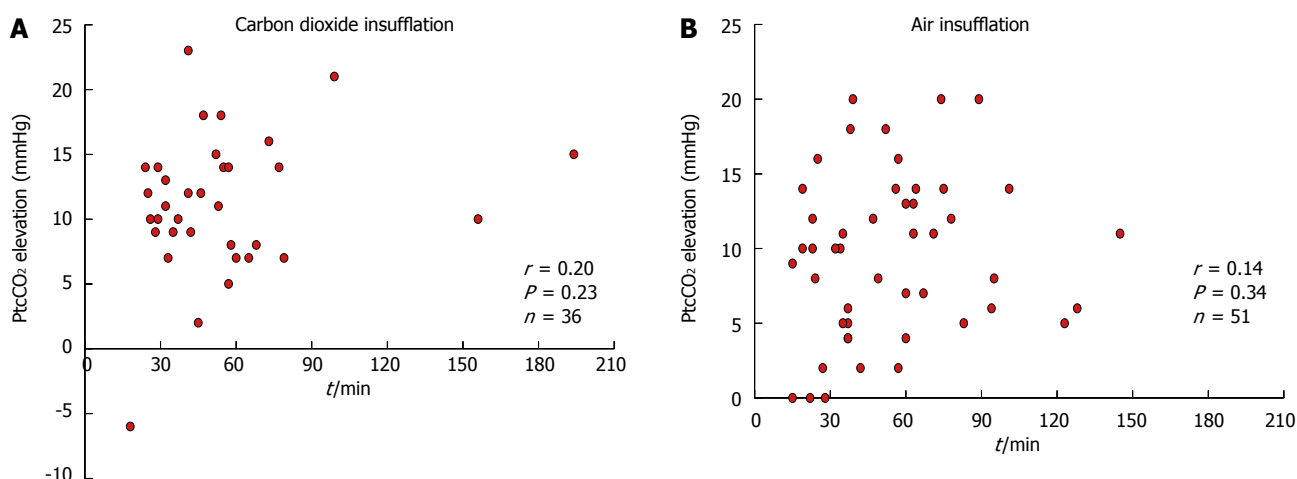
Because respiratory depression due to conscious sedation may lead to CO<sub>2</sub> retention, arterial CO<sub>2</sub> monitoring during lengthy endoscopic procedures is important, even if the patient's respiratory function is normal. However, arterial blood sampling is invasive and it is not practical to measure PaCO<sub>2</sub> serially in all ESD patients. Instead, PtcCO<sub>2</sub>, which correlates well with PaCO<sub>2</sub>, can be measured noninvasively and continuously. PtcCO<sub>2</sub> is usually greater than PaCO<sub>2</sub> by 5–6 mmHg<sup>[33,34]</sup>. Indeed, in the present study, the median difference between these values was 4.8 mmHg. Because of the strong correlation between PtcCO<sub>2</sub> and PaCO<sub>2</sub>, a PtcCO<sub>2</sub> monitoring system is considered a reliable and efficient alternative to PaCO<sub>2</sub> measuring. Thus, arterial blood analysis was not continued after the first 30 patients.

This study has some limitations. First, 27 patients (23.3%) who had chronic pulmonary dysfunction were excluded, as the safety of CO<sub>2</sub> insufflation during gastric ESD has not been established for these patients. We recently reported the safety of CO<sub>2</sub> insufflation during gastric ESD in patients with pulmonary dysfunction (FEV<sub>1.0</sub>% < 70% or %VC < 80%) under conscious sedation<sup>[35]</sup>. However, in patients with severe obstructive pulmonary disease, a longer procedure time may increase the risk of CO<sub>2</sub> retention because there is a significant correlation between PtcCO<sub>2</sub> elevation and ESD procedure time in

**Table 3** Transcutaneous carbon dioxide tension values, transcutaneous oxygen saturation values, and oxygen flow rate

Variable	CO <sub>2</sub> group ( <i>n</i> = 36)	Air group ( <i>n</i> = 51)	<i>P</i> value
Baseline PtcCO <sub>2</sub> , mmHg	39 (28-52) <sup>1</sup>	40 (22-51) <sup>1</sup>	NS
PtcCO <sub>2</sub> after ESD, mmHg	50 (41-68) <sup>1</sup>	50 (40-64) <sup>1</sup>	NS
Peak PtcCO <sub>2</sub> , mmHg	52 (43-68)	51 (40-64)	NS
PtcCO <sub>2</sub> > 60 mmHg during ESD	3 (8.3)	2 (3.9)	NS
Minimum SpO <sub>2</sub> , %	98 (90-100)	98 (89-100)	NS
Oxygen flow rate, L/min	2 (1-5)	2 (2-4)	NS

<sup>1</sup>The PtcCO<sub>2</sub> increased significantly (*P* < 0.001) after the procedure. Data are presented as *n* (%) or median (range). ESD: Endoscopic submucosal dissection; PtcCO<sub>2</sub>: Transcutaneous carbon dioxide tension; SpO<sub>2</sub>: Transcutaneous oxygen saturation.



**Figure 3** Elevation of transcutaneous carbon dioxide tension (PtcCO<sub>2</sub>) in the carbon dioxide and air insufflation groups. There was no significant correlation between the procedure time and PtcCO<sub>2</sub> elevation in either group.

**Table 4** Complications from endoscopic submucosal dissection, blood parameters, and duration of hospital stay

Variable	CO <sub>2</sub> group ( <i>n</i> = 36)	Air group ( <i>n</i> = 51)	<i>P</i> value
Fever (body temperature > 37.5 °C)	9 (25.0)	9 (17.6)	NS
Pneumonia	3 (8.3)	5 (9.8)	NS
Perforation	1 (2.7)	1 (1.9)	NS
Post-procedure hemorrhage	0	4 (7.8)	NS
Mallory-Weiss tears	0	8 (9.8)	0.013
CRP on day 1 after ESD, mg/dL	0.30 (0.09-6.19)	0.40 (0.04-3.62)	NS
CRP on day 3 after ESD, mg/dL	2.00 (0.18-7.83)	2.00 (0.08-14.20)	NS
WBC on day 1 after ESD, n/μL	9020 (3730-15680)	8090 (4510-13450)	NS
WBC on day 3 after ESD, n/μL	6310 (2560-11200)	6260 (3100-10660)	NS
Hospital stay, d	7 (7-16)	7 (7-20)	NS

Data are presented as *n* (%) or median (range). ESD: Endoscopic submucosal dissection; CRP: C-reactive protein; WBC: White blood cell.

patients with pulmonary dysfunction<sup>[35]</sup>. Therefore, PtcCO<sub>2</sub> should be carefully monitored in these patients to avoid severe complications such as CO<sub>2</sub> narcosis and acidemia. Second, the number of patients who underwent arterial blood gas analysis in the present study may be too small. The present study was also a single-center trial. Therefore, further larger prospective multicenter studies are required to confirm the safety and efficacy of CO<sub>2</sub> insufflation for gastric ESD by evaluating both PtcCO<sub>2</sub> and PaCO<sub>2</sub> values.

In conclusion, this study strongly suggests that CO<sub>2</sub> insufflation is safe and effective during gastric ESD under conscious sedation in patients without

pulmonary dysfunction. Furthermore, CO<sub>2</sub> insufflation reduces the incidence of MWTs compared to air insufflation. However, conscious sedation might increase the risk of CO<sub>2</sub> retention and the PtcCO<sub>2</sub> should be monitored carefully in these cases.

## COMMENTS

### Background

The safety and efficacy of insufflation using carbon dioxide (CO<sub>2</sub>) as an alternative to air has been demonstrated in several randomized controlled trials for various kinds of endoscopic procedure. However, there has been no report on the safety and efficacy of CO<sub>2</sub> insufflation for gastric endoscopic submucosal

dissection (ESD) based on the measurement of both the partial pressure of CO<sub>2</sub> in the arterial blood and transcutaneous CO<sub>2</sub> tension.

### Research frontiers

Based on the observation that CO<sub>2</sub> is rapidly absorbed from the bowel, this study investigated the effect of CO<sub>2</sub> insufflation on patients undergoing gastric ESD.

### Innovations and breakthroughs

CO<sub>2</sub> insufflation remarkably reduced the incidence of Mallory-Weiss tears without any adverse events.

### Applications

The safety and efficacy of CO<sub>2</sub> insufflation during gastric ESD in patients under conscious sedation were demonstrated in this study. Further investigation in patients with pulmonary dysfunction is necessary.

### Peer-review

The present study is the first randomized controlled trial to demonstrate that CO<sub>2</sub> insufflation can reduce the risk of Mallory-Weiss tears during ESD, and represents a major contribution to this field.

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