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CLINICAL ENDOSCOPY

Carbon Dioxide versus Air Insufflation in Gastric Endoscopic Submucosal Dissection: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Background/Aims: Endoscopic submucosal dissection (ESD) with air insufflation is commonly used for the staging and treatment of early gastric carcinoma. However, carbon dioxide (CO_2) use has been shown to cause less post-procedural pain and fewer adverse events. The objective of this study was to compare the post-procedural pain and adverse events associated with CO_2 and air insufflation in ESD.
Methods: A systematic search was conducted for randomized control trials (RCTs) comparing the two approaches in ESD. The Mantel-Haenszel method was used to analyze the data. The mean difference (MD) and odds ratio (OR) were used for continuous and categorical variables, respectively.
Results: Four RCTs with a total of 391 patients who underwent ESD were included in our meta-analysis. The difference in maximal post-procedural pain between the two groups was statistically significant (MD, -7.41; 95% confidence interval [CI], -13.6 – -1.21; p=0.020). However, no significant differences were found in the length of procedure, end-tidal CO_2, rate of perforation, and post-procedural hemorrhage between the two groups. The incidence of overall adverse events was significantly lower in the CO_2 group (OR, 0.51; CI, 0.32–0.84; p=0.007).
Conclusions: CO_2 insufflation in gastric ESD is associated with less post-operative pain and discomfort, and a lower risk of overall adverse events compared with air insufflation. **Clin Endosc 2017;50:464-472**

Key Words: Carbon dioxide insufflation; Air insufflation; Endoscopic submucosal dissection; Early gastric carcinoma; Post-procedural pain

INTRODUCTION

The lifetime risk of developing gastric cancer in the United States is 0.9%. It is estimated that 26,370 new cases of gastric cancer were diagnosed in 2016 alone, and that 10,730 people died of it.[1] Worldwide, it is the third highest leading cause of cancer-related death.[2] Early gastric carcinoma in the United States accounts for about 20% of the total cases of gastric cancer.[3]

Endoscopic submucosal dissection (ESD) helps in both the staging and treatment of early gastric carcinoma. It is a well-established technique for *en bloc* removal of gastrointestinal (GI) epithelial lesions.[4-10] However, this procedure is technically demanding and time consuming. Extensive gas insufflation is required to maintain optimal visualization during the procedure. Compared with standard air insufflation, carbon dioxide (CO_2) insufflation has been found to be safe and effective in various studies.[11-16] CO_2 is absorbed 160 times more rapidly than nitrogen and 13 times more rapidly than oxygen across the intestine into the blood. Hence, it is easily excreted by the lungs.[17] Our aim was to evaluate the safety and efficacy of CO_2 insufflation in terms of maximal end-tidal CO_2 during the procedure, procedure length, and

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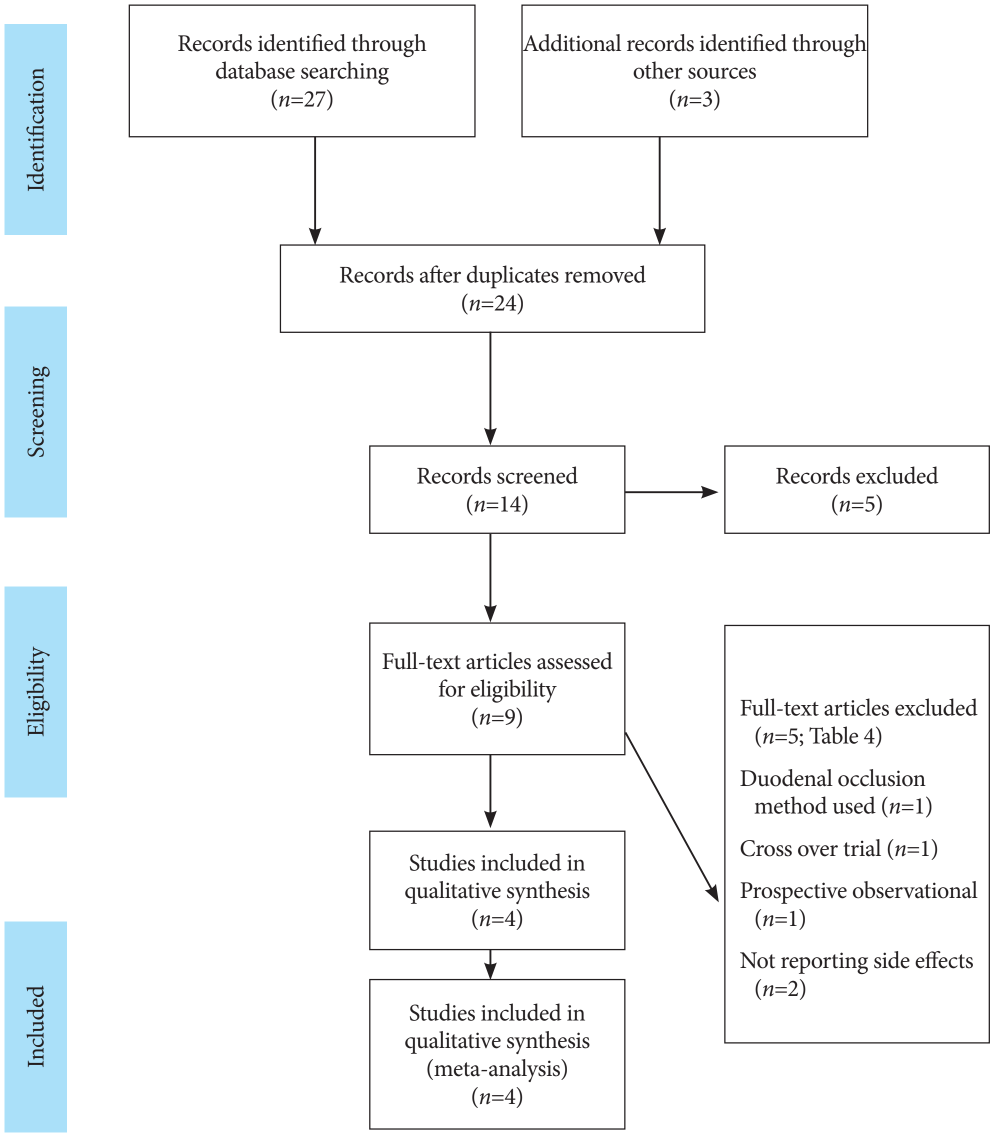

Fig. 1. Preferred reporting items for systematic reviews and meta-analysis statement of systematic search.

Table 1. Results of Quality Assessment by Delphi Consensus Criteria

Final Delphi List	Tanioka et al.[23]	Kim et al.[24]	Maeda et al.[25]	Takada et al.[26]
Treatment allocation				
a) Was a method of randomization performed?	Y	Y	Y	Y
b) Was the treatment allocation concealed?	NA	N	NA	NA
Were the groups similar at baseline regarding the most important prognostic indicators?	NA	Y	Y	Y
Were the eligibility criteria specified?	NA	Y	Y	Y
Was the outcome assessor blinded?	NA	NA	NA	NA
Was the care provider blinded?	NA	Y	Y	NA
Was the patient blinded?	NA	Y	Y	NA
Were point estimates and measures of variability presented for the primary outcome measures?	Y	Y	Y	Y
Did the analysis include an intention to treat?	Y	Y	Y	Y

Y, yes; N, no; NA, not available.

incidence of adverse events as compared with air insufflation in gastric ESD.

MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement for reporting meta-analysis and systemic reviews, as recommended by the Cochrane Collaboration, was used for this meta-analysis (Fig. 1).[18] We included all relevant studies published up to November 2016. Medline, Embase, Cochrane library, and *clinicaltrials.gov* databases were used to identify the studies. The search was conducted using four broad themes. For the theme of carbon dioxide, the all field terms "carbon dioxide" and "CO_2" were used. For the theme of air, the all field terms "air" and "room air" were used. For the theme gastric cancer, all field terms "gastric", "stomach", "early gastric carcinoma", "gastric carcinoma", and "gastric tumor" were used. For endoscopic submucosal dissection, the all field terms "endoscopic submucosal dissection", "ESD", "endoscopic treatment", and "endoscopic procedure" were used. The results were combined using the Boolean operator "AND".

All results were reviewed. No language restrictions were used and all necessary measures to prevent data duplication were taken. Two different investigators (RB and SU) conducted the search and excluded the studies that did not meet the inclusion criteria. Relevant data extracted by the two investigators was corroborated by two other investigators (JK and SKS). A fifth investigator was consulted whenever any issue arose (TSM). The eligibility criteria for the included studies relied on previously published guidelines for systematic reviews and was based on the PICO framework; P (population–patients with early gastric cancer undergoing ESD), I (interventions–CO_2 insufflation), C (comparative interventions–control group, air insufflation), and O (outcomes–procedure-related primary or secondary adverse events including post-procedural pain and discomfort and pulmonary dysfunction).[19] Studies that did not compare CO_2 insufflation with air were excluded.[11,20-22] A total of four randomized control trials (RCTs) met the inclusion criteria.[23-26] Three of them had been

Table 2. Characteristics of the Included Trials

Trials	Tanioka et al. (2008)[23] Single-center RCT, Japan		Maeda et al. (2013)[25] Single-center RCT, Japan		Kim et al. (2015)[24] Single-center RCT, Korea		Takada et al. (2015)[26] Single-center RCT, Japan	
Variable	CO_2 group	Air group	CO_2 group	Air group	CO_2 group	Air group	CO_2 group	Air group
Total no. of patients	50	50	54	48	50	52	36	51
Age, mean±SD/median (range), yr	-	-	72.5±9.0	72.0 ±10.2	61.8±9.0	72.0±10.2	74 (52–87)	70 (45–93)
Sex, M:F	-	-	40:14	35:13	34:16	38:14	22:14	36:15
History of smoking (%)	-	-	12 (24.0)	15 (28.8)	NA	NA	NA	NA
FEV1 (%)	-	-	NA	NA	NA	NA	72 (70–89)	73 (70–93)
Tumor size, mean±SD/ median (range), mm	-	-	17.3±10.3	17.7±12.4	13.7±7.0	16.7±9.9	18 (4–75)	17 (3–47)
Resection size, mean±SD/ median (range), mm	-	-	37.7±10.3	39.2±15.6	32.2±8.3	35.1±10.3	35 (22–110)	37 (23–95)
Sedation/Analgesic used	Propofol	Propofol	Propofol/pentazocine± droperidol	Propofol/pentazocine± droperidol	Propofol+midazolam/ tramadol or diclofenac	Propofol+midazolam/ tramadol or diclofenac	Diazepam± midazolam/pentazocine	Diazepam± midazolam/pentazocine
Procedure time, mean±SD/ median (range), min	119±58	107±46	69.4±27.6	62.1±28.9	48.8±26.9	48.6±31.1	46 (18–194)	48 (15–145)
Histo-pathologic type	-	-						
Adenoma			1	4	25	27	15	6
Adenocarcinoma			53	43	24	21	21	44
Signe- ring cell carcinoma			0	1	1	2	0	1
Others			NA	NA	0	2	NA	NA

RCT, randomized control trial; CO_2, carbon dioxide; SD, standard deviation; NA, not available.

Table 3. Adverse Events of Endoscopic Submucosal Dissection in the Carbon Dioxide Insufflation and Air Groups

Trials	Tanioka et al. (2008)[23]		Maeda et al. (2013)[25]		Kim et al. (2015)[24]		Takada et al. (2015)[26]	
Adverse events	CO_2 group	Air group	CO_2 group	Air group	CO_2 group	Air group	CO_2 group	Air group
Abdominal pain post procedure on 100-mm visual analog scale	14.3±20.5 (1 hr)	24.3±25.3 (1 hr)	4 (0 hr) 4 (1 hr) 3 (3 hr) 1 (next day)	3 (0 hr) 4 (1 hr) 3 (3 hr) 4 (next day)	2.0 (baseline) 35.2 (1 hr) 27.8 (3 hr) 9.2 (24 hr)	1.9 (baseline) 48.5 (1 hr) 42.5 (3 hr) 21.9 (24 hr)	NA	NA
Volume of residual gas in the digestive tract post-procedure/ change in abdominal girth	NA	NA	643 mL	1,037 mL	+0.9 cm	+1.5 cm	NA	NA
Post-procedure hemorrhage	0	0	1	1	9	15	0	4
Perforation	1	4	1	3	0	0	1	1
Aspiration pneumonia	0	0	0	0	0	0	3	5
Mallory-Weiss tears	0	0	NA	NA	NA	NA	0	8
Paroxysmal atrial fibrillation	0	0	1	0	NA	NA	-	-
Other adverse events	0	0	Fever (23)	Stricture with dysphagia (1) Fever (25)	None	None	Fever (9)	Fever (9)
End-tidal CO_2 partial pressure, mean±SD/median (range), mm Hg								
Baseline	-	-	37.1±3.8	38.2±4.6	NA	NA	39 (28–52)	40 (22–51)
Maximum	48.8±4.8	50.0±5.5	40.6±4.3	41.5±4.4	NA	NA	52 (43–68)	51 (40–64)
Minimum oxygen saturation, mean±SD/median (range), %	-	-	94.3±3.0	94.0±2.4	NA	NA	98 (90–100)	98 (89–100)

CO_2, carbon dioxide; SD, standard deviation; NA, not available.

published in peer-reviewed journals,[24-26] and one was a published abstract.[23] The quality of each study was evaluated by two investigators (BKG and GB) using the Delphi consensus criteria for RCTs (Table 1).[27]

From all the selected studies, we extracted the baseline study details: the type of study, mean patient age, history of smoking, FEV1 (%), tumor size, resection size, mean procedural size and histological type, and adverse events (Table 2). Six outcomes were measured: procedural length, maximal end-tidal CO_2, maximal post-operative pain, post-procedural hemorrhage, perforation, and overall adverse events (Table 3). Overall adverse events included post-procedural hemorrhage, bowel perforation, aspiration pneumonia, Mallory-Weiss tear, paroxysmal atrial fibrillation, and other adverse events (such as fever, and stricture with dysphagia) (Table 3). The outcomes were calculated with Review Manager (RevMan, version 5.3 for Windows; The Cochrane Collaborations, The Nordic Cochrane Centre, Copenhagen, Denmark, 2014). Analysis was performed by the Mantel-Haenszel test using RevMan. Mean difference (MD) was calculated for continuous variables, whereas the odds ratio (OR) was calculated for categorical variables using a confidence interval (CI) of 95%. Heterogeneity was calculated using I^2. A randomized model was used because low heterogeneity is typically a major problem in small sample size reviews.[28] A p-value of <0.05 was considered significant. Mean values were estimated from the median using a modified Hozo's formula.[26,29] The characteristics of the trials evaluated during the study are presented in Table 4.

RESULTS

A total of 391 patients were included in the four RCTs. The severity of abdominal pain was measured using a 100-mm visual analog scale (VAS).[30] Maximal post-operative pain was significantly lower in the CO_2 insufflation group compared with the air group (MD, -7.41; 95% CI, -13.6–-1.21; p=0.02; Fig. 2). However, procedural time (MD, 5.97; CI, -0.77–12.72; p=0.08; Fig. 3) and maximal end-tidal CO_2 (MD, -0.14; CI, -2.04–1.76; p=0.88; Fig. 4) were not significantly different. A total of 125 adverse events (post-procedural hemorrhage, perforation, aspiration pneumonia, Mallory-Weiss tear, paroxysmal atrial fibrillation, and others) were reported (Table

Table 4. Characteristics of the Trials Reviewed during the Analysis

Study	Year	Design	Sample size	Conclusion of the study	Included in data synthesis
Suzuki et al.[21]	2010	Prospective observational study	100	Partial pressure of carbon dioxide throughout the endoscopic submucosal dissection was within controllable range under general anesthesia and was little enhanced by prolongation of the procedure	No
Takano et al.[11]	2011	Prospective cross-over trial	60	Carbon dioxide is similar in safety compared to air insufflations during endoscopic submucosal dissection under deep sedation	No
Takada et al.[22]	2015	Prospective observational study	322	No significant difference between pulmonary dysfunction and no pulmonary dysfunction group in term of end-tidal carbon dioxide before, during and after the endoscopic submucosal dissection was found	No
Takada et al.[26]	2015	Randomized controlled trial	116	No significant different between two groups in term of adverse effects except for significantly lower incidence of Mallory-Weiss tears in carbon dioxide insufflation group	Yes
Kim et al.[24]	2015	Randomized double-blinded, controlled prospective study	110	Reduction in abdominal pain and analgesic usage significant in carbon dioxide insufflation group compared to air group	Yes
Maeda et al.[25]	2013	Randomized, double blind, controlled prospective trial	102	Significant reduction in the residual gas volume in carbon dioxide group compared to air group, but no difference in abdominal pain or distention	Yes
Tanioka et al.[23]	2008	Randomized controlled trial-abstract	95	Carbon dioxide insufflation is safe and effective in reducing post-procedure pain in endoscopic submucosal dissection under propofol sedation	Yes
Mori et al.[20]	2011	Randomized case control prospective study	44	Balloon occlusion method in endoscopic submucosal dissection reduces harmful influences	No
Nonaka et al.[14]	2010	Randomized prospective study	89	Carbon dioxide is as safe as air insufflation in upper endoscopic submucosal dissection for patients under deep sedation	No

Study or Subgroup	CO2 group Mean	SD	Total	Air insufflation group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Kim et al. (2015)[24]	35.2	30.3	50	48.5	29	52	21.9%	−13.30 [−24.82, −1.78]
Maeda et al. (2013)[25]	1	7.3274	54	4	20.6633	48	47.3%	−3.00 [−9.16, 3.16]
Tanioka et al. (2008)[23]	14.3	20.5	50	24.3	25.3	50	30.8%	−10.00 [−19.03, −0.97]
Total (95% CI)			**154**			**150**	**100.0%**	**−7.41 [−13.61, −1.21]**

Heterogeneity: $Tau^2 = 11.29$; $Chi^2 = 3.15$, df = 2 (P = 0.21); $I^2 = 37\%$
Test for overall effect: Z = 2.34 (P = 0.02)

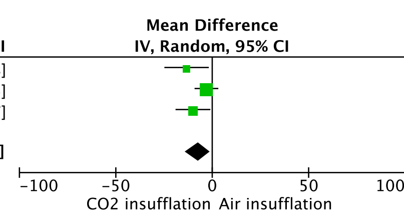

Fig. 2. Forest plot of maximal post-operative pain. CO_2, carbon dioxide; SD, standard deviation; CI, confidence interval.

3). No death was reported in any of the studies. The total number of post-procedural hemorrhages and perforations was 30 and 11, respectively. The difference in post-procedural hemorrhage between the two groups was not significant (OR, 0.51; 95% CI, 0.22–1.19; p=0.12; Fig. 5). Similarly, no significant difference in the rate of perforation was found (OR, 0.39; 95% CI, 0.10–1.57; p=0.19; Fig. 6). Statistical significance was also calculated for overall adverse events. The incidence of overall adverse events was significantly lower in the CO_2 group (OR, 0.51; CI 0.32–0.84; p=0.007; Fig. 7). The study by Takada et al. uniquely reported Mallory-Weiss tear as a separate category, and its occurrence was significantly lower in the CO_2 group compared to the air insufflation group (p=0.013).[26]

	CO2 insufflation			Air insufflation				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Kim et al. (2015)[24]	48.8	26.9	50	48.6	31.1	52	35.8%	0.20 [−11.07, 11.47]
Maeda et al. (2013)[25]	69.4	27.6	54	62.1	28.9	48	37.6%	7.30 [−3.70, 18.30]
Takada et al. (2015)[26]	76.83	44	36	65.08	32.5	51	15.9%	11.75 [−5.17, 28.67]
Tanioka et al. (2008)[23]	119	58	50	107	46	50	10.8%	12.00 [−8.52, 32.52]
Total (95% CI)			**190**			**201**	**100.0%**	**5.97 [−0.77, 12.72]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.84$, df = 3 (P = 0.61); $I^2 = 0\%$
Test for overall effect: Z = 1.74 (P = 0.08)

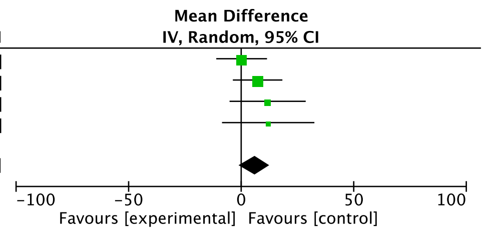

Fig. 3. Forest plot of procedure time. CO_2, carbon dioxide; SD, standard deviation; CI, confidence interval.

	CO2 insufflation			Air insufflation				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Maeda et al. (2013)[25]	40.6	4.3	54	41.5	4.4	48	38.8%	−0.90 [−2.59, 0.79]
Takada et al. (2015)[26]	53.8	6.25	36	51.51	6	51	27.0%	2.29 [−0.33, 4.91]
Tanioka et al. (2008)[23]	48.8	4.8	50	50	5.5	50	34.2%	−1.20 [−3.22, 0.82]
Total (95% CI)			**140**			**149**	**100.0%**	**−0.14 [−2.04, 1.76]**

Heterogeneity: $Tau^2 = 1.67$; $Chi^2 = 4.97$, df = 2 (P = 0.08); $I^2 = 60\%$
Test for overall effect: Z = 0.14 (P = 0.88)

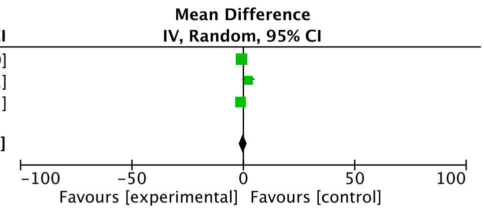

Fig. 4. Forest plot of end-tidal carbon dioxide (CO_2). SD, standard deviation; CI, confidence interval.

	CO2 insufflation		Air insufflation			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Kim et al. (2015)[24]	9	50	15	52	82.4%	0.54 [0.21, 1.38]
Maeda et al. (2013)[25]	1	54	1	48	9.3%	0.89 [0.05, 14.58]
Takada et al. (2015)[26]	0	36	4	51	8.3%	0.14 [0.01, 2.77]
Tanioka et al. (2008)[23]	1	50	4	50		Not estimable
Total (95% CI)		**140**		**151**	**100.0%**	**0.51 [0.22, 1.19]**
Total events	10		20			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.89$, df = 2 (P = 0.64); $I^2 = 0\%$
Test for overall effect: Z = 1.56 (P = 0.12)

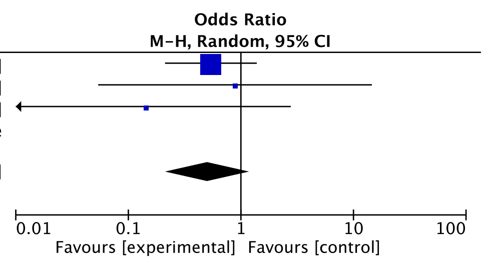

Fig. 5. Forest plot of post-operative hemorrhage. CO_2, carbon dioxide; CI, confidence interval.

	CO2 insufflation		Air insufflation			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Kim et al. (2015)[24]	0	50	0	52		Not estimable
Maeda et al. (2013)[25]	1	54	3	48	36.6%	0.28 [0.03, 2.82]
Takada et al. (2015)[26]	1	36	1	51	24.5%	1.43 [0.09, 23.62]
Tanioka et al. (2008)[23]	1	50	4	50	38.9%	0.23 [0.03, 2.18]
Total (95% CI)		**190**		**201**	**100.0%**	**0.39 [0.10, 1.57]**
Total events	3		8			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.10$, df = 2 (P = 0.58); $I^2 = 0\%$
Test for overall effect: Z = 1.32 (P = 0.19)

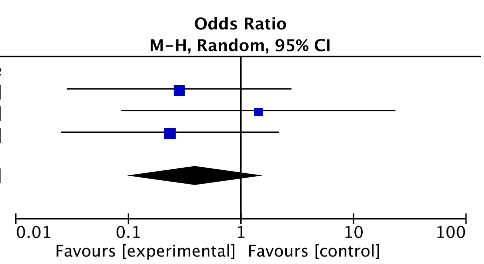

Fig. 6. Forest plot of perforation rate. CO_2, carbon dioxide; CI, confidence interval.

DISCUSSION

As in any endoscopic procedure, adequate gastric distention is required for the safe advancement of the scope and adequate visualization of the mucosa during ESD. Although it is universally available, ambient air is poorly absorbed by the GI tract, causing excessive post-operative distention of the bowel lumen and consequent pain and discomfort.[31] On the contrary, CO_2 is absorbed approximately 160 times faster than nitrogen (a major gaseous ingredient of ambient air) into gut mucosa and is rapidly exhaled through the lungs, resulting in reduced gut distention. This leads to significantly less post-procedural pain and discomfort, and improved recovery times, which has been proven in multiple previous studies on GI endoscopy.[13,15,31-34] To the best of our knowledge, this is the first review comparing CO_2 to air insufflation in gastric ESD. Our analysis of 391 patients showed significantly less post-operative pain in the CO_2 insufflation group, which is attributable to the shorter duration of bowel distention. Pain associated with the procedure was analyzed in three of the four trials.[23-25] Kim et al. and Tanioka et al. showed that there were significantly lower mean pain scores in the CO_2 group compared with the air insufflation group (p=0.028 and p=0.04, respectively).[23,24] As a result, patients in

Study or Subgroup	CO2 insufflation Events	CO2 insufflation Total	Air insufflation Events	Air insufflation Total	Weight	Odds Ratio M-H, Random, 95% CI
Kim et al. (2015)[24]	9	50	15	52	26.8%	0.54 [0.21, 1.38]
Maeda et al. (2013)[25]	26	54	30	48	37.6%	0.56 [0.25, 1.23]
Takada et al. (2015)[26]	13	36	27	51	30.8%	0.50 [0.21, 1.20]
Tanioka et al. (2008)[23]	1	50	4	50	4.8%	0.23 [0.03, 2.18]
Total (95% CI)		**190**		**201**	**100.0%**	**0.51 [0.32, 0.84]**
Total events	49		76			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.53$, df = 3 (P = 0.91); $I^2 = 0\%$
Test for overall effect: Z = 2.69 (P = 0.007)

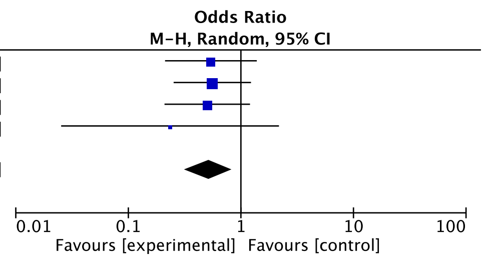

Fig. 7. Forest plot of overall adverse event. CO_2, carbon dioxide; CI, confidence interval.

the air insufflation group requested more analgesics for pain control. This finding has been corroborated by other studies and meta-analyses done on sigmoidoscopy, colonoscopy, double-balloon enteroscopy, and endoscopic retrograde cholangiopancreatography.[12,13,15,31,33-39] However, the study by Maeda et al.[25] showed no significant difference in pain levels between the two groups. We believe this is due to the strong analgesic effect of pentazocine, which was used in both groups in that study. Otherwise, significant discomfort can be expected in the air insufflation group, in which a mean of 1,037 mL of residual gas in the GI tract was observed post-operatively compared with that of 643 mL in the CO_2 group ($p<0.001$).

The other important consideration in this study was the procedure time, which was not significantly different between the two groups. The implications of this finding are three-fold. First, it shows that the type of gas used does not influence the length of the procedure. Second, the endoscopists in both groups were equally skilled. This finding is substantiated by the fact that all the procedures were performed by endoscopists with years of experience in therapeutic GI endoscopy at high-volume tertiary care centers. Third, the comparison of end-tidal CO_2 between the two groups increases in reliability as a result. The end-tidal CO_2 increased significantly from baseline in both groups in the study by Takada et al.;[26] however, our study failed to show a difference in maximal end-tidal CO_2 between the two groups. This result is in accordance with previous data on the safety of CO_2 in various GI endoscopic procedures.[14,40,41] However, most of those studies did not include patients with significant pulmonary dysfunction. On the other hand, some other studies conducted on patients with pulmonary dysfunction also failed to show significant CO_2 retention, acidosis, or narcosis, and CO_2 was found to be safe in terms of adverse event risks and hospital stay. In those studies, the only significant correlation that was found was between the length of the procedure and an elevation in end-tidal CO_2.[22] In fact, CO_2 insufflation has been found to be safe even in patients with obstructive ventilatory disturbances in various gastric and non-gastric ESD studies.[11,42] Moreover, end-tidal CO_2 remained within acceptable limits even in the context of prolonged procedure time in those studies.[21,40] In general, there is a paucity of data demonstrating CO_2 retention in patients with pulmonary dysfunction in ESD.

In terms of adverse events, the rate of procedure-related hemorrhage and bowel perforation did not reach a statistically significant level between the two groups since only four trials were included in the study. Additionally, all studies were conducted in high-volume medical centers by experts in their field, which naturally led to a lower rate of adverse events. However, the overall adverse event rate was significantly lower in the CO_2 insufflation group. In the study by Takada et al.,[26] CO_2 insufflation was shown to confer the benefit of reducing the risk of Mallory-Weiss tears ($p=0.013$). Again, this is due to the more rapid absorption of CO_2 compared with air, which resulted in a significantly lower overall adverse event rate in the CO_2 group in our study. Although no life-threatening adverse events were reported in our study, air insufflation is known to cause adverse events such as perforation, tension pneumothorax, air embolism, mediastinal emphysema, and abdominal compartment syndrome during endoscopic procedures.[43-46] CO_2 insufflation would be advantageous in such situations, as it is more rapidly absorbed into the blood and cleared by the lungs. Our study had a few limitations. The main limiting factor of our study is the low number of included studies due to the small number of published RCTs. Additionally, the studies did not include patients with significant pulmonary dysfunction.

In conclusion, CO_2 insufflation appears to be safe and effective for gastric ESD. It significantly decreases post-procedural pain and discomfort and neither prolongs the procedure time, nor significantly increases end-tidal CO_2. Lastly, fewer overall adverse events were observed in the CO_2 insufflation group during ESD.

Conflicts of Interest

The authors have no financial conflicts of interest.

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