Supplementary Table 1. (Continued)

	No. of alleles			Allele frequency			UC vs CD		UC vs control[a]		CD vs control[a]	
HLA allele	UC	CD	Control	UC	CD	Control	OR (95% CI)[b]	*P* value[b]	OR (95% CI)[b]	*P* value[b]	OR (95% CI)[b]	*P* value[b]
DRB1*1101	18	19	41	0.024	0.026	0.023	0.94 (0.49–1.80)	.85				
DRB1*1108	0	0	1	0	0	0.001	—	1				
DRB1*1119	0	1	0	0	0.001	0	0.00 (0.00–38.7)	.50				
DRB1*1123	0	0	1	0	0	0.001	—	1				
DRB1*1201	18	30	71	0.024	0.041	0.039	0.59 (0.32–1.06)	.074				
DRB1*1202	10	7	26	0.013	0.010	0.014	1.42 (0.54–3.76)	.47				
DRB1*1301	2	7	14	0.003	0.010	0.008	0.28 (0.03–1.49)	.11				
DRB1*1302	37	41	97	0.050	0.056	0.054	0.89 (0.56–1.40)	.62				
DRB1*1401	18	37	47	0.024	0.050	0.026	0.47 (0.26–0.83)	.0082				
DRB1*1403	7	12	20	0.009	0.016	0.011	0.57 (0.22–1.47)	.24				
DRB1*1405	15	22	30	0.020	0.030	0.017	0.67 (0.34–1.30)	.23				
DRB1*1406	10	8	21	0.013	0.011	0.012	1.24 (0.49–3.17)	.65				
DRB1*1407	2	2	1	0.003	0.003	0.001	0.99 (0.07–13.7)	1				
DRB1*1429	1	0	1	0.001	0	0.001	—	1				
DRB1*1501	69	32	126	0.093	0.043	0.070	2.26 (1.46–3.48)	1.6E–04	1.37 (1.01–1.86)	.044	0.61 (0.41–0.90)	.013
DRB1*1502	207	44	246	0.279	0.060	0.136	6.09 (4.31–8.59)	3.2E–29	2.46 (1.99–3.03)	9.8E–18	0.40 (0.29–0.56)	4.0E–08
DRB1*1602	6	3	14	0.008	0.004	0.008	1.99 (0.42–12.4)	.51				
HLA–DPB1												
DPB1*0201	114	165	412	0.153	0.222	0.228	0.63 (0.49–0.82)	6.4E–04				
DPB1*0202	28	24	76	0.038	0.032	0.042	1.17 (0.67–2.04)	.58				
DPB1*0301	25	44	62	0.034	0.059	0.034	0.55 (0.33–0.91)	.019				
DPB1*0401	30	30	84	0.040	0.040	0.046	1.00 (0.59–1.67)	.99				
DPB1*0402	53	51	170	0.071	0.069	0.094	1.04 (0.70–1.55)	.85				
DPB1*0501	279	345	698	0.375	0.465	0.386	0.69 (0.56–0.85)	4.4E–04	0.95 (0.80–1.14)	.60	1.38 (1.16–1.64)	.00023
DPB1*0601	5	3	7	0.007	0.004	0.004	1.67 (0.32–10.8)	.73				
DPB1*0901	181	42	226	0.243	0.057	0.125	5.36 (3.76–7.63)	7.1E–24	2.25 (1.81–2.80)	1.2E–13	0.42 (0.30–0.59)	3.1E–07
DPB1*1301	10	14	29	0.013	0.019	0.016	0.71 (0.31–1.61)	.41				
DPB1*1401	11	15	23	0.015	0.020	0.013	0.73 (0.33–1.59)	.42				
DPB1*1701	2	1	2	0.003	0.001	0.001	2.00 (0.10–117.9)	1				
DPB1*1901	6	4	5	0.008	0.005	0.003	1.50 (0.35–7.26)	.75				
DPB1*2501	0	1	0	0	0.001	0	0.00 (0.00–38.9)	.50				
DPB1*3601	0	0	4	0	0	0.002	—	1				
DPB1*3801	0	3	2	0	0.004	0.001	0.00 (0.00–2.41)	.12				
DPB1*4101	0	0	6	0	0	0.003	—	1				
DPB1*4701	0	0	2	0	0	0.001	—	1				

[a]Calculated for the HLA alleles that indicated significant associations between UC cases and CD cases. Based on Bonferroni correction for the number the observed alleles (n = 110), $P < .00045$ was considered to be significant ($\alpha = .05$).
[b]Obtained by the comparison of allele frequencies.

Supplementary Table 2. Case-Case and Case-Control Associations of HLA-Cw*1202-B*5201-DRB1*1502 Haplotype Stratified by Colonic and Noncolonic CD

	Analyzed groups	No. subjects (group 1/group 2)	Frequency (group 1/group 2)	OR (95% CI)	*P* value
Within case analysis	UC vs CD	372/372	0.27/0.054	6.58 (4.60–9.42)	1.1×10^{-33}
	UC vs colonic CD	372/53	0.27/0.10	3.19 (1.67–6.09)	6.4×10^{-5}
	UC vs noncolonic CD	372/315	0.27/0.043	8.36 (5.50–12.72)	8.8×10^{-36}
	Colonic CD vs noncolonic CD	53/315	0.10/0.043	2.62 (1.26–5.48)	.0083
Case-control analysis	UC vs control	372/905	0.27/0.12	2.65 (2.14–3.29)	4.0×10^{-21}
	CD vs control	372/905	0.054/0.12	0.40 (0.28–0.57)	1.1×10^{-7}
	Colonic CD vs control	53/905	0.10/0.12	0.83 (0.44–1.58)	.58
	Noncolonic CD vs control	315/905	0.043/0.12	0.32 (0.21–0.48)	5.2×10^{-9}

Carbon dioxide insufflation compared with air insufflation in double-balloon enteroscopy: a prospective, randomized, double-blind trial

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Background: Few studies have evaluated the degree of pain, the amount of retained gas, and the safety of carbon dioxide (CO_2) insufflation in patients undergoing double-balloon enteroscopy (DBE).

Objective: To clarify the usefulness and safety of CO_2 insufflation during DBE.

Design: Single-center, prospective, randomized, double-blind, controlled trial.

Setting: University hospital.

Patients: Forty eligible patients with small-bowel disease for whom DBE was indicated were randomized to a CO_2 insufflation (CO_2) group or an air insufflation (air) group by means of sealed envelopes.

Intervention: DBE with insufflation of CO_2 or air.

Main Outcome Measurements: Efficacy evaluation was based on the degree of pain as assessed by use of a visual analog scale (VAS) and the amount of residual gas retention within the small and large bowels on radiography. The safety of CO_2 insufflation was evaluated by arterial blood gas analysis.

Results: Significantly fewer patients in the CO_2 group had severe pain of ≥50 mm on the VAS during DBE than in the air group ($P = .02$). Significantly less gas was retained in the small bowel just after and at 3 hours after DBE in the CO_2 group than in the air group ($P = .003$, $P = .01$, respectively). There was significantly less residual gas retention in the large bowel at 3 hours after DBE in the CO_2 group than in the air group ($P = .02$). There was no significant difference in pre-DBE and post-DBE partial pressure of oxygen in the blood (PaO_2) and partial pressure of carbon dioxide in the blood ($PaCO_2$) between groups.

Limitations: Small sample size.

Conclusion: CO_2 insufflation is a safe and useful procedure when performed during DBE. (Gastrointest Endosc 2011;73:743-9.)

Endoscopic examinations are often painful. This tendency is more marked in time-consuming procedures such as colonoscopy, ERCP, and double-balloon enteroscopy (DBE). One of the causes of pain is gas retention within the abdomen from air insufflation. However, carbon dioxide (CO_2) insufflation during endoscopic examination can reduce abdominal pain because CO_2 is rapidly absorbed from the intestine and excreted from the body via pulmonary circula-

Abbreviations: CO_2, carbon dioxide; DBE, double-balloon enteroscopy; PaO_2, partial pressure of oxygen in the blood; $PaCO_2$, partial pressure of carbon dioxide in the blood; SaO_2, arterial oxygenation; VAS, visual analog scale.

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tion. There have been many published studies examining CO_2 insufflation during colonoscopy[1-4] or ERCP.[5]

DBE is widely used as a modality for examination of the small bowel because it enables endoscopists to observe the entire small bowel. However, DBE is usually time-consuming, with patients often experiencing abdominal pain or bloating during the procedure. Such pain can be effectively ameliorated through the use of CO_2 insufflation. Domagk et al[6] reported in their prospective, double-blind trial that the intubation depth of DBE was significantly greater in the CO_2 insufflation group than in the air insufflation group. We previously reported the usefulness of CO_2 insufflation in the practice of endoscopic balloon dilatation.[7] To date, there have been only these 2 reports emphasizing the usefulness of CO_2 insufflation in DBE.

The present trial was conducted with a prospective, randomized, double-blind, controlled design to assess the usefulness of CO_2 insufflation in DBE, focusing on the degree of abdominal pain and the amount of post-DBE residual gas within the intestinal tract. The safety of CO_2 insufflation was evaluated by blood gas analysis monitoring.

Take-home Message

- It is well-known that carbon dioxide (CO_2) insufflation used during colonoscopy is useful for reducing intestinal gas retention as well as for reducing pain. This study indicates that CO_2 insufflation during double-balloon enteroscopy reduces abdominal pain and residual gas retention. Safety assessment based on blood gas analysis shows no risk of systemic CO_2 retention. Accordingly, CO_2 insufflation during double-balloon enteroscopy would seem to be a more useful alternative than routine air insufflation.

PATIENTS AND METHODS

The participants in this study were patients at our hospital who underwent DBE for observation of the small bowel between October 2006 and April 2008. Patients scheduled for endoscopic treatment were excluded. Exclusion criteria were age below 18 years, chronic respiratory disorders, chronic heart failure and New York Heart Association classification of 2 or worse, serum bilirubin levels higher than 2 mg/dL, creatinine levels over 1.5 mg/dL, history of surgical resection of the colon, short bowel syndrome, ileus or subileus, intolerance of preparation, and pregnancy. The protocol for this study was approved by the Fukuoka University Ethics Committee. Each patient was given a full explanation of procedures including DBE, CO_2 or air insufflation, and arterial blood sampling. Their informed consent was confirmed in writing. Forty patients who met the criteria were enrolled in the study. They were randomized to the air insufflation (air) group or the CO_2 insufflation (CO_2) group by means of sealed envelopes that had been prepared by a research assistant and delivered 4 hours before the DBE to a nurse working in the endoscopic unit. Only the nurse was allowed to prepare an insufflator, while the patient and the operator remained unaware of which type of insufflation was being used. A CO_2 gas cylinder was situated next to the endoscopy system throughout the study, and the flow meter gauge was set and then masked with a paper bag by the assisting nurse. CO_2 gas was pumped via a CO_2 regulator (Gas Regulator, Crown, GF2-2503-JT6-F5; Yutaka Engineering, Tokyo, Japan) connected to a CO_2 gas cylinder. The flow rate for CO_2 insufflation was set at 2.0 L/minute.[8] The blinding of the study was maintained until completion of all data analyses. A total of 4 gastroenterologists with at least 10 years of experience took part in this study. EN450P-5 or EN450T-5 (FUJI FILM Medical Co, Tokyo, Japan) was used for the DBE. Patients who underwent DBE performed via the transoral approach had nothing by mouth on the day of DBE. For those undergoing DBE via the transanal approach, 2 L of polyethylene glycol was administered as a preparation on the day of DBE. Before undergoing DBE, every patient received midazolam and buprenorphine hydrochloride for conscious sedation. The operator judged the level of sedation in each patient as follows[5]: grade 0, no sedation given; grade 1, light sedation (patient awake, no clinical impairment); grade 2, moderate sedation (patient awake but drowsy); grade 3, strong sedation (patient somnolent). Arterial oxygenation (SaO_2), blood pressure, and heart rate were monitored during the examination, and appropriate measures were taken in the case of any abnormality. Oxygen inhalation was initiated whenever SaO_2 dropped to below 90%.

Evaluation of abdominal pain

The 100-mm visual analog scale (VAS) was used for evaluation of abdominal pain during the examination as well as just after and at 1, 3, 6, and 24 hours after the examination. VAS scores during and just after the examination were recorded with the score at 1 hour after completion. Patients assessed the degree of abdominal pain along a 100-mm line with the 0-mm point (left end) labeled "no pain" and the 100-mm point (right end) labeled "very severe pain." VAS score data were subjected to analysis with classification by absolute value and degree of abdominal pain. In this study, the cases were grouped for evaluation according to the degree of abdominal pain, that is, mild to moderate pain as 0 to 50 mm and severe pain as 51 to 100 mm on the VAS scale.

Evaluation of residual gas

We assessed post-DBE residual gas retention within the small and large bowels based on plain abdominal radiographic findings. Plain abdominal radiograms were taken with the patient in the supine position before, just after, and at 3 hours after the examination. Residual gas reten-

TABLE 1. Baseline characteristics in CO_2 insufflation and air insufflation groups

	CO_2 group (n = 20)	Air group (n = 20)	*P* value
Sex, male/female	13/7	15/5	.73
Age, mean (± SD), years	42.7 (±17.9)	46.3 (±18.2)	.53
Indications			
Inflammatory bowel disease	13	13	
OGIB	5	6	1
Suspicious small-bowel tumor	2	1	
Intubation route (transoral/transanal)	2/18	3/17	1
Dosages of drugs used for sedation			
Midazolam, mean (± SD), mg	4.6 (±2.1)	5.8 (±3.7)	.21
Buprenorphin HCl, mean (± SD), mg	0.1 (±0.1)	0.2 (±0.1)	.28
Level of sedation			
Grade 0	0	0	
Grade 1	3	4	.94
Grade 2	16	13	
Grade 3	1	3	
Oxygen inhalation, mean (± SD), L/min	1.1 (±1.1)	1.2 (±1.0)	.82

CO_2, Carbon dioxide; *SD*, standard deviation, *OGIB*, obscure GI bleeding.

tion was assessed separately for the small and large bowels as follows[3]: grade 1, trace; grade 2, minimal; grade 3, moderate; grade 4, severe; grade 5, extreme. Two radiologists with at least 10 years' experience, who were unaware of whether air or CO_2 insufflation had been used, read the radiograms and graded this endpoint.

Evaluation of safety

To determine whether CO_2 gas retention might occur in patients undergoing DBE, we performed arterial blood gas analyses on 2 occasions in each case, that is, before and within 15 minutes after the examination. The patients also were assessed for any complications of DBE and CO_2 insufflation.

Statistical analysis

Paired intergroup comparisons of continuous variable data were performed by using the paired *t* test, and unpaired intergroup comparisons of continuous variable data were performed by using the unpaired *t* test. For comparisons of frequency, either the chi-square test or Fisher exact test was used. Statistical analyses were carried out by using the software SPSS Version 16.0 (SPSS, Chicago, Illinois, USA). In all of these statistical analyses, differences were considered statistically significant at $P < .05$.

RESULTS

Forty-one patients who met the inclusion criteria and had none of the exclusion criteria, and who gave written informed consent, were enrolled in this study. One of these patients was excluded because a partial pressure of carbon dioxide in the blood ($PaCO_2$) test done before examination showed a level of 50 mm Hg, which indicated chronic obstructive pulmonary disease. Eventually, 40 patients were evaluated as per protocol; 20 were randomized to the CO_2 group and the other 20 to the air group. There was no significant difference between the CO_2 and air groups with regard to baseline characteristics, including sex, age, indications, insertion route, dosages of drugs used for sedation, level of sedation, amount of oxygen inhalation, or examination time (Table 1).

There was no significant difference in the mean (± SD) small-bowel intubation depth (216.0 ± 199.4 cm in the CO_2 group vs 255.3 ± 183.4 cm in the air group; $P = .52$).

Subjective symptom study

Figure 1 shows changes in VAS scores over time. Absolute VAS scores during the examination tended to be lower in the CO_2 group than in the air group. There was no significant difference in VAS scores at any of the post-DBE assessment time points. When the degree of abdom-

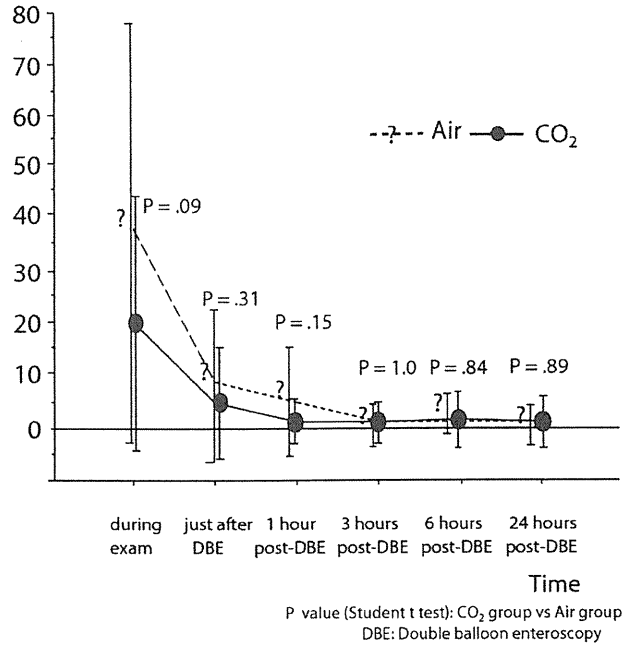

Figure 1. Mean visual analogue scale scores at various observation points during and after examination in the CO_2 and air groups. *P* value (*t* test): CO_2 group versus air group. *CO_2*, carbon dioxide; *DBE*, double-balloon enteroscopy.

TABLE 2. Grading of abdominal pain during DBE in CO_2 and air insufflation groups

Grading, VAS score*	CO_2 group (n = 20)	Air group (n = 20)	*P* value
Mild to moderate	19	12	
Severe	1	8	*P* = .02

DBE, Double-balloon enteroscopy; *CO_2*, carbon dioxide; *VAS*, visual analog scale.
*Mild to moderate, 0 to 50 mm; severe, 51 to 100 mm.

inal pain was assessed by classification into mild-to-moderate pain or severe pain, there were significantly fewer cases with severe pain during DBE in the CO_2 group than in the air group (Table 2; $P = .02$). No significant difference was noted in this respect at any of the post-DBE assessment time points.

Radiographic study

Pre-DBE residual gas retention within both the small and large bowels in the CO_2 group was comparable to that in the air group (Tables 3 and 4). There was significantly less residual gas retention in the small bowel just after and at 3 hours after DBE in the CO_2 group than in the air group ($P = .03$, $P = .01$, respectively). In the CO_2 group, residual gas retention in the small bowel at 3 hours post-DBE did not differ significantly from that noted pre-DBE. In the air group, in contrast, residual gas retention in the small bowel was still significantly greater at 3 hours post-DBE than it had been pre-DBE ($P = .001$). There was significantly less residual gas retention in the large bowel at 3 hours after DBE in the CO_2 group than in the air group ($P = .02$). In the air group, residual gas retention in the large bowel was still significantly greater at 3 hours post-DBE than it had been pre-DBE ($P = .002$).

Blood gas study

Arterial blood sampling was performed safely in all cases. Table 5 shows pre-DBE and post-DBE arterial blood gas values. There were no significant differences in pre-DBE PaO_2, $PaCO_2$, or SaO_2 values. Post-DBE PaO_2 and SaO_2 values did not differ significantly between the CO_2 and air groups. Post-DBE $PaCO_2$ values were significantly higher than the pre-DBE $PaCO_2$ values in both groups ($P < .0001$). However, post-DBE $PaCO_2$ values also did not differ significantly between the CO_2 and air groups. Neither CO_2 narcosis nor any other complications of CO_2 retention occurred in either group.

Other adverse reactions

One patient in the air group who had undergone DBE via the transoral approach developed hyperamylasemia post-DBE. No other complications of DBE were experienced.

DISCUSSION

DBE has become well-established, and its use as a diagnostic procedure for small-bowel disorders has become widespread in recent years.[9] However, this procedure is usually time consuming and, in some instances, the patient has pain. This pain, especially abdominal pain or bloating, is attributable to gas retention within the intestinal tract in most cases. It has been reported that CO_2 insufflation applied during colonoscopy is useful for reducing intestinal gas retention as well as for reducing pain.[1-4] Furthermore, conscious sedation is commonly prescribed to reduce the pain in patients undergoing endoscopic examinations. Bretthauer et al[4] reported the efficacy of moderate conscious sedation in combination with CO_2 insufflation. In the current study, too, all patients underwent conscious sedation. Subjective evaluation of pain during and just after the examination by sedated patients is certainly difficult. It is also very difficult to ask someone else to assess a patient's pain. However, pain associated with the examination is usually maximal during the examination. Therefore, we considered it important to assess the severity of pain during the examination. Actually, the severity of pain as assessed by VAS in the current study was maximal during the examination in both the CO_2 and air groups. This is consistent with the results from other studies that investigated the effect of CO_2 insufflation during total colonoscopy.[2,8] Therefore, as described in the "Methods" section, we asked the patients themselves to assess their pain 1 hour after the DBE procedure. Although

TABLE 3. Frequency of radiograph scores for residual gas within the small bowel before and after DBE

Grade	Before DBE, no. (%)		Just after DBE, no. (%)		3 h after DBE, no. (%)	
	CO_2 group (n = 20)	Air group (n = 20)	CO_2 group (n = 20)	Air group (n = 20)	CO_2 group (n = 20)	Air group (n = 20)
	$P = .36$		$P = .003$		$P = .01$	
1 = Trace	5 (25)	2 (10)	0	0	3 (15)	0
2 = Minimal	12 (60)	16 (80)	9 (45)	0	13 (65)	6 (30)
3 = Moderate	3 (15)	2 (10)	2 (10)	1 (5)	3 (15)	8 (40)
4 = Severe	0	0	5 (25)	7 (35)	1 (5)	6 (30)
5 = Extreme	0	0	4 (20)	12 (60)	0	0
			$P = .67$*			
				$P = .001$†		

DBE, Double-balloon enteroscopy; CO_2, carbon dioxide.
*Before DBE vs after DBE in CO_2 group.
†Before DBE vs after DBE in air group.

TABLE 4. Frequency of radiograph scores for residual gas within the large bowel before and after DBE

Grade	Before DBE, no. (%)		Just after DBE, no. (%)		3 h after DBE, no. (%)	
	CO_2 group (n = 20)	Air group (n = 20)	CO_2 group (n = 20)	Air group (n = 20)	CO_2 group (n = 20)	Air group (n = 20)
	$P = .64$		$P = .23$		$P = .02$	
1 = Trace	1 (5)	1 (5)	1 (5)	0	1 (5)	0
2 = Minimal	12 (60)	9 (45)	5 (25)	2 (10)	10 (50)	2 (10)
3 = Moderate	7 (35)	9 (45)	8 (40)	5 (25)	5 (25)	5 (25)
4 = Severe	0	1 (5)	5 (25)	10 (50)	4 (20)	11 (55)
5 = Extreme	0	0	1 (5)	3 (15)	0	2 (10)
			$P = .21$*			
				$P = .002$†		

DBE, Double-balloon enteroscopy; CO_2, carbon dioxide.
*Before DBE vs after DBE in CO_2 group.
†Before DBE vs after DBE in air group.

we do not think that this method is the best, we used this evaluation method for a number of reasons. Conscious sedation is usually prescribed to patients undergoing DBE. It is impossible to conduct this procedure without sedation, and it is clinically important to evaluate the pain, even in sedated patients. There are several reports in the literature regarding comparison of the severity of pain associated with CO_2/air insufflation during endoscopy.[3-5,8] In fact, in all of these studies, the majority of patients were sedated, and their pain during the examination was also evaluated by VAS or similar tools. Additionally, because the CO_2 group and the air group were comparable to each other with regard to the level of sedation, we concluded that the level of sedation did not influence the comparison of the subjective symptoms between groups. Therefore, we do not think that this evaluation method for the severity of pain was inappropriate.

Patients assessed the degree of pain by means of a VAS, application of which has been cited in recent reports.[2, 4-6] Absolute VAS scores during the examination tended to be lower in the CO_2 group than in the air group. The lack of any significant difference seemed to be attributable to the limited sample size. Because there is great distortion of VAS score data, these data were re-evaluated after the patients were divided into groups based on the degree of abdominal pain, that is, mild to moderate (0-50 mm) or severe (51-100 mm). Based on this evaluation, there were significantly fewer patients who experienced severe pain

TABLE 5. PaO_2, $PaCO_2$, and SaO_2 values before and after DBE

	Before DBE			After DBE		
	CO_2 group (n = 20)	Air group (n = 20)	*P* value	CO_2 group (n = 20)	Air group (n = 20)	*P* value
PaO_2, mean (± SD), mm Hg	91.1 (±11.8)	97.4 (±14.0)	.13	94.3 (±14.1)	98.3 (±14.0)	.55
$PaCO_2$, mean (± SD), mm Hg	40.2 (±5.7)	40.3 (±4.4)	.96	46.7 (±4.7)*	46.9 (±6.4)†	.89
SaO_2, mean (± SD), %	96.8 (±1.0)	97.4 (±1.1)	.12	96.6 (±1.6)	96.7 (±1.6)	.76

PaO_2, partial pressure of oxygen in the blood; *$PaCO_2$*, partial pressure of carbon dioxide in the blood; *SaO_2*, Arterial oxygenation; *DBE*, double-balloon enteroscopy; *CO_2*, carbon dioxide.
*$P < .0001$ (before DBE vs after DBE in CO_2 group).
†$P < .0001$ (before DBE vs after DBE in air group).

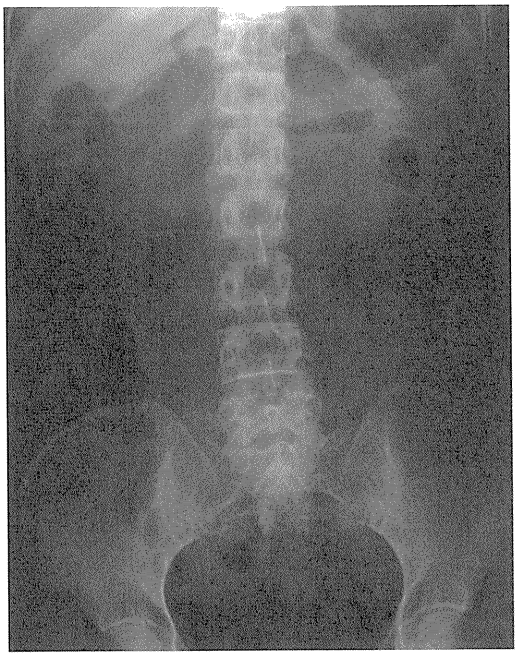

Figure 2. Abdominal radiograph just after double-balloon enteroscopy via the transanal approach with carbon dioxide insufflation. Minimal residual gas retention is visible in the small and large bowels (classified as grade 2).

during DBE in the CO_2 group than in the air group. This significant difference showed that CO_2 insufflation reduced the occurrence of severe pain during DBE.

An investigation into colonoscopy-related residual gas within the intestinal tract has been reported,[3] and the current study was conducted by using the same methods. This is the first report to document the results of intestinal gas retention associated with DBE. Significantly less residual bowel gas retention in both the small and the large bowels was noted in the CO_2 group compared with that in the air group. Residual gas retention in the small and large bowels had diminished to pre-DBE levels by 3 hours after DBE in the CO_2 group. In contrast, in the air group, residual gas retention in the small and large bowels had not decreased even 3 hours post-DBE. These data demonstrate that retained intestinal gas was rapidly absorbed in the CO_2 group in contrast to the air group (Figs. 2 and 3). Insertion of a double-balloon endoscope and endoscopic manipulations are more difficult in the presence of a large amount of residual gas within the intestinal tract.[6] Furthermore, an intraintestinal high pressure status with marked residual gas is assumed to affect the risk of complications, for example, the development of pancreatitis.[10] In view of these points, we consider it a strong advantage to use CO_2 insufflation rather than air insufflation during DBE.

Because systemic CO_2 retention is a potential risk related to CO_2 insufflation, we obtained and analyzed arterial blood gas values before and after DBE. There have been reports of analyses with a $PaCO_2$ monitor before, during, and after DBE,[5] but, as yet, there are no detailed arterial blood gas analysis studies. Although arterial blood gas analysis is a somewhat invasive procedure, arterial blood gas data were judged to be necessary because all patients in the present series were subjected to conscious sedation and thus may have been given oxygen during the study. Post-DBE PaO_2 and SaO_2 did not differ significantly between the CO_2 and the air groups. In both groups, the post-DBE $PaCO_2$ level was significantly increased when compared with the pre-DBE level. However, post-DBE $PaCO_2$ levels did not differ significantly between groups. The post-DBE $PaCO_2$ elevation was considered not to reflect an effect of CO_2 insufflation but rather to be attributable to shallow respiration because of conscious sedation.[4,11] Systemic CO_2 retention is thus not considered to be a risk of CO_2 insufflation.

The present study has some limitations. First, the study population was small. The small sample size might account for the failure to demonstrate statistically significant differences between the CO_2 and air groups in post-DBE VAS scores. Second, the approaches were mainly limited to the transanal route. DBE by the transoral route is usually

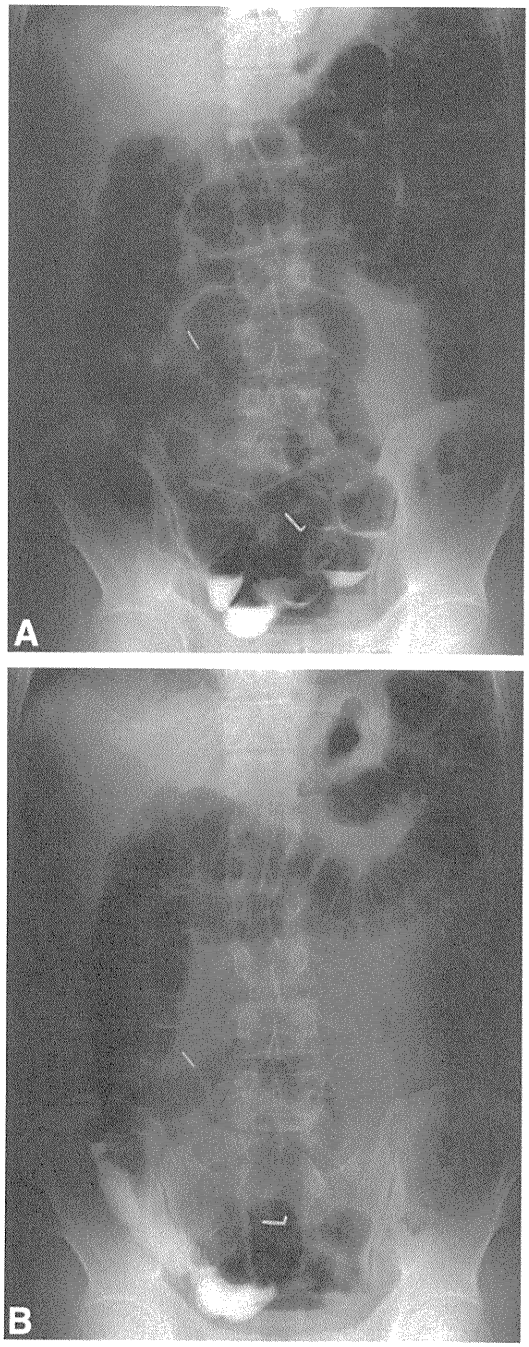

Figure 3. Abdominal radiographs after double-balloon enteroscopy (DBE) via the transanal approach with air insufflation. **A,** Extreme residual gas retention is visible just after DBE in the small and large bowels (classified as grade 5). **B,** Severe residual gas retention is still visible in the small and large bowels 3 hours after DBE (grade 4).

more painful than by the transanal route. The frequent use of the transanal route in the current study may be one of the reasons for the absence of any significant difference in the absolute VAS scores. Third, the participants may have had slightly biased responses. Twenty-six of 40 patients (60%) enrolled in the study had inflammatory disorders; hence, this may have had some impact on the comparison of the small-bowel intubation depth in DBE because of strictures or other factors.

The present data, nevertheless, confirm that CO_2 insufflation can ameliorate severe abdominal pain during DBE and can reduce residual gas retention in the small and large bowels, in contrast to routine air insufflation. Safety assessments have shown that CO_2 insufflation carries no risk of CO_2 retention. We conclude that CO_2 insufflation appears to be equally as safe as air insufflation and may cause less pain. Based on the results of this study, it is considered that CO_2 insufflation may become the standard procedure in DBE.

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