



Title	Carbon dioxide insufflation during endoscopic retrograde cholangiopancreatography reduces bowel gas volume but does not affect visual analogue scale scores of suffering: a prospective, double-blind, randomized, controlled trial
Author(s)	Kuwatani, Masaki; Kawakami, Hiroshi; Hayashi, Tsuyoshi; Ishiwatari, Hirotohi; Kudo, Taiki; Yamato, Hiroaki; Ehira, Nobuyuki; Haba, Shin; Eto, Kazunori; Kato, Mototsugu; Asaka, Masahiro
Citation	Surgical Endoscopy, 25(12), 3784-3790 https://doi.org/10.1007/s00464-011-1789-8
Issue Date	2011-12
Doc URL	http://hdl.handle.net/2115/50764
Rights	The original publication is available at www.springerlink.com
Type	article (author version)
File Information	SE25-12_3784-3790.pdf



[Instructions for use](#)

Carbon dioxide insufflation during endoscopic retrograde cholangiopancreatography reduces bowel gas volume, but does not affect visual analogue scale scores of suffering: a prospective, double-blind randomized controlled trial

Running head: Carbon dioxide insufflation during ERCP

Masaki Kuwatani¹, M.D., Ph.D., Hiroshi Kawakami¹, M.D., Ph.D., Tsuyoshi Hayashi², M.D., Ph.D., Hirotoishi Ishiwatari², M.D., Ph.D., Taiki Kudo¹, M.D., Hiroaki Yamato¹, M.D., Nobuyuki Ehira¹, M.D., Shin Haba¹, M.D., Kazunori Eto¹, M.D., Mototsugu Kato¹, M.D., Ph.D., Masahiro Asaka¹, M.D., Ph.D.

¹Department of Gastroenterology, Hokkaido University Graduate School of Medicine, North 15, West 7, Kita-ku, Sapporo 060-8638, Japan

²Fourth Department of Internal Medicine, Sapporo Medical University School of Medicine, South 1, West 16, Chuo-ku, Sapporo 060-8556, Japan

Supported by a Japanese Foundation for Research and Promotion of Endoscopy Grant.

Address correspondence to: Hiroshi Kawakami, M.D., Ph.D., Department of Gastroenterology, Hokkaido University Graduate School of Medicine, North 15, West 7, Kita-ku, Sapporo 060-8638, Japan

E-mail: hiropon@med.hokudai.ac.jp

Tel: +81-11-716-1161 (ext. 5918); Fax: +81-11-706-7867

Abstract

Background Endoscopic retrograde cholangiopancreatography (ERCP) and related procedures can cause abdominal pain and discomfort. Two clinical trials have indicated, using the visual analogue scale (VAS) score, that CO₂ insufflation during ERCP ameliorates the suffering of patients without complications, as compared with air insufflation. However, differences in patient suffering between CO₂ and air insufflation after ERCP under deep conscious sedation have not been reported. We focused on the gas volume score (GVS) as an objective indicator of gas volume, and designed a multicenter, prospective, double-blind randomized controlled study with CO₂ and air insufflation during ERCP.

Methods Between March 2010 and August 2010, 80 patients who required ERCP were enrolled and evenly randomized to receive CO₂ insufflation (CO₂ group) or air insufflation (air group). ERCP and related procedures were performed under deep conscious sedation with fentanyl citrate or pethidine and midazolam or diazepam. The GVS was evaluated as the primary endpoint in addition to the VAS score as the secondary endpoint.

Results The GVS after ERCP and related procedures in the CO₂ group was significantly lower than that in the air group (0.14 ± 0.06 vs. 0.31 ± 0.11 , $p < 0.01$), as well as the increase in the rate of GVS ($[\text{GVS after} - \text{GVS before}] / [\text{GVS before ERCP and related procedures}] \times 100$) (3.8 ± 5.9 vs. $21.0 \pm 11.1\%$, $p < 0.01$). VAS scores 3 and 24 hours after ERCP and related procedures were comparable between the CO₂ and air groups for abdominal pain, abdominal distension, and nausea. Additionally, VAS scores were not correlated with the GVS.

Conclusions CO₂ insufflation during ERCP reduces GVS (bowel gas volume), but not

the VAS score of suffering, as compared with air insufflation. Deep and sufficient sedation during ERCP and related procedures is important for the palliation of patients' pain and discomfort.

Keywords: carbon dioxide insufflation, air insufflation, conscious sedation, endoscopic retrograde cholangiopancreatography, gas volume

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) and related procedures are important in the examination and treatment of pancreatobiliary diseases because ERCP provides critical information and care options that ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) cannot provide. The time requirements of ERCP and related procedures can vary, and long procedures can cause abdominal pain, distension, and nausea in patients, which lead to a burden on both patients and doctors.

The utility and safety of carbon dioxide (CO₂) insufflation instead of air insufflation during endoscopic examinations and procedures was first verified in the performance of colonoscopies [1, 2], and clinical trials have indicated that CO₂ insufflation during colonoscopy ameliorates the suffering of patients with no associated complications, as compared with air insufflation. Two reports on the effects of CO₂ insufflation during ERCP revealed that the frequency of abdominal pain and distension after ERCP in the CO₂ group was lower than that in the air group, and that the frequency of complications in both groups was comparable [3, 4]. However, differences in abdominal pain and discomfort between patients undergoing ERCP with CO₂ insufflation and room air under deep conscious sedation with opioid drugs and diazepam have not been evaluated. Furthermore, visual analogue scale (VAS) scores obtained from patients after ERCP, which was the primary end point in the 2 previous reports [3, 4], lack objectivity because patients' susceptibility to pain and discomfort from the same stimulation vary, and scoring by patients themselves is not absolute for quantification. We speculated that the increase in the gastrointestinal gas volume in patients after ERCP and related procedures would result in an increase in the severity of abdominal pain, distension, and

nausea. In addition, we determined that the quantification of gastrointestinal gas volume would lead to a more accurate evaluation of the symptoms mentioned above. Therefore, we focused on the gas volume score (GVS) reported by Koide et al. [5] as an objective indicator of gas volume, and designed the present study as a multicenter, prospective, double-blind randomized controlled study. The effects of CO₂ and air insufflation during ERCP were analyzed using GVS as the primary end point in addition to the VAS score as the secondary end point.

Materials and methods

Study design

This study was conducted as a prospective, multicenter, double-blind randomized controlled trial. Patients were assigned to 2 groups, namely a CO₂ group and an air group. The study protocol was approved by the institutional review boards of each participating institution (Hokkaido University Hospital, clinical research approval number 009-0216; Sapporo Medical University School Hospital, clinical research approval number 21-118).

Patients

Between March 2010 and August 2010, all consecutive patients with pancreatobiliary disease or disorders requiring ERCP for workup or treatment who presented to our department at Hokkaido University Hospital or Sapporo Medical University Hospital were screened for recruitment. The exclusion criteria for patients were as follows: 1) refusal to provide informed consent; 2) poor general status (performance status 4: completely disabled, cannot carry out any self-care, and totally confined to the bed); 3) under 20 years old; 4) inaccessibility of the papilla of Vater for endoscopic examination; 5) acute pancreatitis; 6) chronic pancreatitis with acute exacerbation; 7) severe heart dysfunction; 8) chronic obstructive pulmonary disease; 9) pregnancy; 10) stricture of the digestive tract; 11) abdominal pain before ERCP; 12) use of sedative drugs (within 12 h) before ERCP; and 13) judged inappropriate by a doctor. A total of 80 patients were included in the study, and written informed consent was obtained from all patients. The patients enrolled in the study were admitted to the 2 university hospitals mentioned above, and they underwent ERCP and related procedures.

Randomization and blinding of the study

Enrolled patients were evenly randomized between the CO₂ insufflation group (CO₂ group, n = 40) and the air insufflation group (air group, n = 40) by using a computer-generated sequence just before ERCP. A clinical engineer set the gas insufflation system to CO₂ or air according to the result of randomization. CO₂ was administered using a commercially available CO₂ regulator designed for use in endoscopic procedures (Olympus Medical Systems, Tokyo, Japan). The patients, endoscopists, assistants, and X-ray image and VAS score analysts were all blinded with regard to the type of gas used. Unblinding was prevented by concealing the lumps indicating actuation of the CO₂ device and the air inlet button on the endoscopy rack using thick paper screens.

ERCP

ERCP and related procedures were performed as previously reported [6] under deep conscious sedation with fentanyl citrate or pethidine and midazolam or diazepam. The operator and assistants determined the level of sedation in each patient and increased the doses of the sedative drugs until deep sedation was achieved, as indicated by the somnolent condition of the patient. Administration of antispastic drugs, scopolamine butylbromide or glucagon, and oxygen supply by nasal tube (2–3 L/min) were also appropriately performed. Bile duct or main pancreatic duct (MPD) cannulation were performed using wire-guided cannulation (WGC) with a triple-lumen papillotome (CleverCut3V, Olympus) or ERCP catheter (Article-No.0130211; MTW Endoskopie,

Wesel, Germany) with a guide wire (VisiGlide™; 0.025-inch, Olympus) as previously reported [7]. If cannulation by WGC was not possible, alternative cannulation methods were used. ERCP was performed after successful deep cannulation of the bile duct or MPD, and each patient underwent specific procedures such as biopsy of the bile duct and biliary stenting as indicated.

Clinical assessments and end points

Patients were routinely monitored by pulse oximeter (SpO₂) to measure oxygen saturation; pulse rate and arterial blood pressure were recorded using a bedside monitor (BSM-2301; Nihon Kohden Corporation, Tokyo, Japan); and the total dose of sedative drugs during ERCP was routinely recorded. Hypoxia was defined as a decrease in SpO₂ to $\leq 90\%$. Hypotension was defined as a decrease in systolic blood pressure to < 80 mm Hg. Direct measurement of arterial pCO₂ or transcutaneous pCO₂ measurements were not performed, on the basis of the results of previous studies showing that CO₂ insufflation during ERCP or colonoscopy does not lead to an increase in pCO₂ [1-4, 8].

Accidents were classified using the Cotton classification [9]. On the basis of a consensus meeting held in 1991, the diagnostic criteria for post-ERCP pancreatitis are abdominal pain lasting > 24 hours after ERCP and hyperamylasemia (> 3 times the upper limit of the normal range). The Cotton classification was used for the assessment of severity, but on the basis of the medical circumstances in Japan, the time leading up to food consumption was used as an indicator of the severity rather than the duration of hospitalization [7].

Bowel gas volume was quantified using abdominal X-ray photographs as follows. Plain abdominal radiographs in the supine position taken just before and 5 minutes after

ERCP were digitized and transmitted to a computer. After the region of bowel gas was identified, its outline was traced on the monitor and distinguished from other areas by image adjustment (contrast enhancement). The total quantity of bowel gas was determined by counting the pixel value of the resulting images. ImageJ version 1.43, which was developed by Dr. Wayne Rasband and colleagues at the National Institutes of Health (<http://rsb.info.nih.gov/ij/>), was used to measure the pixel value. The measurements of bowel gas were standardized using physical parameters by calculating the ratio of the quantity of bowel gas to the pixel value in a region surrounded by a horizontal line tangential to the upper margin of the pubic bone, a horizontal line tangential to the uppermost diaphragm, and the most lateral line tangential to the right and left costal arches, which was defined as the GVS as previously reported [5] (Fig. 1). The GVS was set as the primary end point. Furthermore, the increase in the rate of GVS ($[GVS \text{ after} - GVS \text{ before}] / [GVS \text{ before ERCP and related procedures}] \times 100$) was also calculated to remove the potential bias generated by the gas volume before ERCP and related procedures.

A 10-point visual analogue scale (VAS) was used as the secondary end point in this study to quantify abdominal pain and discomfort (distension and nausea) experienced during ERCP and 3 and 24 hours after ERCP and related procedures, as described in recent studies [3, 4, 8]. A sheet describing the VAS was handed out to each participant after the procedure, to be filled out the next day and collected.

In addition, ERCP and related procedures performed within 30 minutes and >30 minutes were defined as short and long time procedures, respectively.

Sample size

Sample size was determined by power calculation. On the basis of previous data (not shown), the room air group was speculated to have an approximately 1.5-fold to 2-fold higher mean abdominal gas volume in the X-ray images just after ERCP compared with the CO₂ group. To detect this difference with a power of 0.8 and an alpha of 0.05, complete data were required for at least 36 patients per group. Therefore, assuming the dropout of 10% of the enrolled patients, the present recruitment goal was a total of 80 patients.

Statistical analysis

Categorical data were examined using the χ^2 test. The Mann-Whitney *U* test or *t* test were used for comparison of quantitative data. Spearman correlation analysis was performed for the test of correlations. These tests were performed with Microsoft Excel software (Redmond, WA), and the results were regarded as significant if $p < 0.05$.

This study is registered in the University Hospital Medical Information Network (UMIN ID: UMIN000003062).

Results

A total of 80 patients who required ERCP were enrolled in the study after the application of exclusion criteria as described above. ERCP and its related procedures were performed by CO₂ or air insufflation on the basis of the randomization of patients (Fig. 2). Table 1 shows the characteristics of the 80 patients. There were no significant differences in patient number, age, sex, and disease between the CO₂ and the air groups.

The GVS was first estimated as the primary and objective end point. Table 2 shows the GVS values of both the CO₂ and air groups. The GVS before ERCP and related procedures did not show significant differences between the 2 groups (0.11 ± 0.04 vs. 0.10 ± 0.05). However, the GVS after ERCP and related procedures in the CO₂ group was significantly lower than that in the air group (0.14 ± 0.06 vs. 0.31 ± 0.11 , $p < 0.01$). The increase in the rate of GVS (%) in the CO₂ group was also significantly lower than that in the air group (3.8 ± 5.9 vs. $21.0 \pm 11.1\%$, $p < 0.01$). The total time of the procedure, which appeared to affect GVS values, was similar between both groups (2700 ± 1485 vs. 2582 ± 1345 s). The relationship between the length of the procedure and GVS was also analyzed (Table 3). In patients with short procedure times (within 30 min), GVS significantly differed between the CO₂ and air groups ($p < 0.01$), while in patients with long procedure times (>30 min), the result was the same. The GVS values among patients within the CO₂ group and the air group were similar between the short and long procedures.

The VAS scores for abdominal pain, distension, and nausea were next evaluated after ERCP and related procedures as the secondary end point. As shown in Table 4, VAS scores 3 and 24 hours after ERCP and related procedures were not significantly different between the CO₂ and air groups with regard to abdominal pain (3 h, 1.4 ± 2.0

vs. 0.9 ± 2.0 ; 24 h, 0.9 ± 1.8 vs. 0.5 ± 1.3), abdominal distension (3 h, 0.6 ± 1.2 vs. 0.6 ± 1.1 ; 24 h, 0.6 ± 1.6 vs. 0.4 ± 1.1), and nausea (3 h, 0.2 ± 0.8 vs. 0.2 ± 0.9 ; 24 h, 0.2 ± 0.9 vs. 0.1 ± 0.3). Unexpectedly, the VAS scores for abdominal pain, distension, and nausea were not correlated with the GVS values (Spearman's correlation coefficient: 3 h, 0.01, 0.03, and 0.16; 24 h, 0.05, 0.01, and 0.17, respectively).

Furthermore, the effect of CO₂ and air insufflation on the doses of sedative and antispastic drugs administered during the procedures (Table 4) was also assessed. The sedative drugs fentanyl citrate (100–200 µg) or pethidine (17.5–35 mg) and midazolam (2–15 mg) or diazepam (1–3 mg) were used. There were no significant differences among the groups in the drug doses except for pethidine ($p < 0.03$). Similar results were also obtained with antispastic drugs (scopolamine butylbromide [20–40 mg] and glucagon [1–3 mg]).

Arterial oxygen saturation levels were measured in all patients by using a pulse oximeter (SpO₂) to assess the effect of CO₂ or air insufflation before, during, and 3 and 24 hours after ERCP and related procedures. In both the CO₂ and air groups, SpO₂ did not change before and after the procedures (CO₂ group: before, $97.8 \pm 1.3\%$; 3 h after, $97.1 \pm 1.4\%$; 24 h after, $97.2 \pm 1.4\%$; air group: before, $97.7 \pm 1.3\%$; 3 h after, $96.6 \pm 1.3\%$; 24 h after, $97.0 \pm 1.2\%$) (Fig. 3). The routine administration of oxygen during the procedure by nasal tube (2–3 L/min) did not cause changes in SpO₂ in either the CO₂ or air group.

Complications associated with the procedure are shown in Table 5. The total number of complications was the same in both the CO₂ and air groups (4 vs. 4). Post-ERCP pancreatitis (PEP) was the most frequent complication in both groups (4 cases vs. 3 cases). PEP was mild or moderate in all cases (mild in 2 and moderate in 5 cases) and it

was cured by conservative therapies. Other complications included retroperitoneal perforation in one case in the air group who was also cured by noninvasive therapies.

Discussion

The utility of CO₂ insufflation during ERCP has been described in previous reports, which demonstrated a reduction in abdominal pain and discomfort in patients undergoing ERCP with CO₂ insufflation compared with those treated by air insufflation [3, 4]. This result was also reported for colonoscopy patients [1, 2]. However, a different study reported that there were no advantages of CO₂ insufflation during ERCP in terms of a reduction in symptoms [8]. The studies that reported the advantages of CO₂ insufflation during endoscopy used VAS scores for abdominal pain and discomfort as indicators of patient suffering after endoscopy [1-4]. However, differences in VAS scores (for abdominal pain and discomfort) between patients treated with CO₂ and air insufflation after ERCP under deep conscious sedation in Japan have not been reported. In addition, the VAS score itself is not an absolute indicator. On the other hand, Koide et al. [5] reported that the GVS is reproducible and very objective.

First, we validated the availability of the GVS as a new surrogate and objective marker of patients' stress after ERCP. GVS values revealed that remnant gastrointestinal gas volume after ERCP was significantly lower in the CO₂ group than that in the air group regardless of the length of the procedure (Table 2, 3). It was quantitatively demonstrated that less gastrointestinal gas volume in the CO₂ insufflation group in the two previous reports on ERCP [3, 4] led to a reduction in patients' suffering. However, because the results of the present study show that there is no correlation between the GVS and VAS scores, GVS is not considered a useful marker of patient suffering after ERCP under deep conscious sedation. This difference between the present and previous results could be attributed to differences in the degree of conscious sedation (deep vs. moderate) and the speed of recovery of consciousness (late

vs. early) [3, 4]. Under conditions of no, mild, or moderate conscious sedation, we hypothesize that the GVS and VAS scores would be strongly correlated for endoscopy including ERCP [1-4], and the superiority of CO₂ insufflation would be more objectively and quantitatively verified by the GVS under these conditions.

The VAS score as a method for the evaluation of patient suffering after ERCP with CO₂ or air insufflation under deep conscious sedation was also assessed. Patients and blood samples are commonly evaluated 3 and 24 hours after ERCP to identify the presence or absence of complications. It is therefore relatively simple to record VAS scores at these 2 times. In addition, on the basis of our experience, patients with abdominal pain, distension, or nausea after ERCP usually complain of symptoms within 3 hours after ERCP or the next day. On the basis of these 2 reasons, VAS scores were checked at 3 and 24 hours after ERCP in the present study. This was, however, considered a limitation and bias of our study, the results of which showed that VAS scores 3 and 24 hours after ERCP were not statistically different between the 2 insufflation groups (Table 4). Although the VAS score of abdominal pain in the CO₂ group was slightly higher than in the air group, this was likely caused by the higher frequency of moderate pancreatitis after ERCP (4 vs. 1 case) and pancreatic cancer with perineural invasion (3 vs. 0 case) in the CO₂ group than in the air group (data not shown). Unexpectedly, the VAS scores in both insufflation groups were consistently low. The half-lives of the sedative drugs fentanyl citrate, pethidine, midazolam, and diazepam are 3.6, 3.5, 2.5, and 34.9 hours, respectively. The assessment of VAS scores 3 hours after ERCP under deep conscious sedation is therefore difficult. In addition, although the assessment of VAS scores is possible at 24 hours after ERCP, at this time the bowel has usually started to move and both CO₂ and air in the bowel have already

been excreted or absorbed. The results of the present study show that deep conscious sedation during ERCP has a similar effect on the alleviation of patient suffering after ERCP as well as CO₂ insufflation to that under mild conscious sedation, although the comparative study between mild or moderate versus deep conscious sedation is mandatory.

With regard to the level of sedation during ERCP, moderate sedation with opioid (pethidine) plus benzodiazepines or propofol alone is generally recommended in the United States [10] and Europe [11]. Recent reports have demonstrated that under air insufflation, deep sedation with propofol alone or propofol plus sedatives during ERCP show better results for patients and endoscopists than moderate sedation [12, 13, 14]. This indicates that strong sedation during ERCP is beneficial not only to alleviate pain in patients but also to reduce endoscopists' stress regardless of the type of gas used for insufflation. However, because a distended bowel can frequently limit or prevent the flexibility and controllability of the endoscope, CO₂ insufflation during ERCP is preferable to air insufflation to reduce stomach and duodenal distension. Furthermore, another advantage of CO₂ insufflation during ERCP is that a reduction in GVS, in other words, less bowel gas during fluoroscopy, greatly improves the resolution of cholangiograms or pancreatograms.

The frequency of complications associated with ERCP and related procedures in the present study (10%) was similar to that previously reported (5–10%) [15] and it was comparable among the groups in this study. However, CO₂ insufflation would be required in cases of perforation of the duodenum following difficult endoscopic sphincterotomy (ES) or papillectomy, or in patients with choledocholithiasis after ES undergoing endoscopic treatment. This assumption is based on good absorption of CO₂

and previous reports of air embolism during ERCP [16, 17].

In conclusion, CO₂ insufflation during ERCP reduces GVS (bowel gas volume), but not the VAS score of suffering, as compared with air insufflation. In addition, deep and sufficient sedation during ERCP and related procedures is important for palliation of pain and discomfort of patients.

Acknowledgments

This study was supported by a Japanese Foundation for Research and Promotion of Endoscopy Grant.

Conflict of interest statement

Drs. Masaki Kuwatani, Hiroshi Kawakami, Tsuyoshi Hayashi, Hirotoshi Ishiwatari, Taiki Kudo, Hiroaki Yamato, Nobuyuki Ehira, Shin Haba, Kazunori Eto, Mototsugu Kato, and Masahiro Asaka have no conflicts of interest or financial ties to disclose.

References

1. Stevenson GW, Wilson JA, Wilkinson J, Norman G, Goodacre RL (1992) Pain following colonoscopy: elimination with carbon dioxide. *Gastrointest Endosc* 38: 564-567
2. Dellon ES, Hawk JS, Grimm IS, Shaheen NJ (2009) The use of carbon dioxide for insufflation during GI endoscopy: a systematic review. *Gastrointest Endosc* 69: 843-849
3. Bretthauer M, Seip B, Aasen S, Kordal M, Hoff G, Aabakken L (2007) Carbon dioxide insufflation for more comfortable endoscopic retrograde cholangiopancreatography: a randomized, controlled, double-blind trial. *Endoscopy* 39: 58-64
4. Maple JT, Keswani RN, Hovis RM, Saddedin EZ, Jonnalagadda S, Azar RR, Hagen C, Thompson DM, Waldbaum L, Edmundowicz SA (2009) Carbon dioxide insufflation during ERCP for reduction of postprocedure pain: a randomized, double-blind, controlled trial. *Gastrointest Endosc* 70 :278-283
5. Koide A, Yamaguchi T, Odaka T, Koyama H, Tsuyuguchi T, Kitahara H, Ohto M, Saisho H (2000) Quantitative analysis of bowel gas using plain abdominal radiograph in patients with irritable bowel syndrome. *Am J Gastroenterol* 95:1735-1741
6. Kawakami H, Kuwatani M, Etoh K, Haba S, Yamato H, Shinada K, Nakanishi Y, Tanaka E, Hirano S, Kondo S, Kubota K, Asaka M (2009) Endoscopic retrograde cholangiography versus peroral cholangioscopy to evaluate intraepithelial tumor spread in biliary cancer. *Endoscopy* 41:959-964
7. Kawakami H, Maguchi H, Hayashi T, Yanagawa N, Chiba A, Hisai H, Amizuka H

- (2009) A prospective randomized controlled multicenter trial of duodenoscopes with 5 degrees and 15 degrees backward-oblique angle using wire-guided cannulation: effects on selective cannulation of the common bile duct in endoscopic retrograde cholangiopancreatography. *J Gastroenterol* 44:1140-1146
8. Dellon ES, Velayudham A, Clarke BW, Isaacs KL, Gangarosa LM, Galanko JA, Grimm IS (2010) A randomized, controlled, double-blind trial of air insufflation versus carbon dioxide insufflation during ERCP. *Gastrointest Endosc* 72:68-77
 9. Cotton PB, Lehman G, Vennes J, Geenen JE, Russell RC, Meyers WC, Liguory C, Nickl N (1991) Endoscopic sphincterotomy complications and their management: an attempt at consensus. *Gastrointest Endosc* 37:383-393
 10. American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists (2002) Practice guidelines for sedation and analgesia by non-anesthesiologists. *Anesthesiology* 96:1004-1017
 11. Riphaut A, Wehrmann T, Weber B, Arnold J, Beilenhoff U, Bitter H, Delius SV, Domagk D, Ehlers AF, Faiss S, Hartmann D, Heinrichs W, Hermans ML, Hofmann C, S. Smitten ID, Jung M, Kähler G, Kraus M, Martin J, Meining A, Radke J, Rösch T, Seifert H, Sieg A, Wigglinghaus B, Kopp I (2009) S3 Guideline: Sedation for gastrointestinal endoscopy 2008. *Endoscopy*, DOI:10.1055/s-0029-1215035, August 14, 2009
 12. Paspatis GA, Manolaraki MM, Vardas E, Theodoropoulou A, Chlouverakis G (2008) Deep sedation for endoscopic retrograde cholangiopancreatography: intravenous propofol alone versus intravenous propofol with oral midazolam premedication. *Endoscopy* 2008; 40: 308-313
 13. Riphaut A, Stergiou N, Wehrmann T (2005) Sedation with propofol for routine

- ERCP in high-risk octogenarians: a randomized, controlled study. *Am J Gastroenterol* 100: 1957-1963
14. Ong WC, Santosh D, Lakhtakia S, Reddy DN (2007) A randomized controlled trial on use of propofol alone versus propofol with midazolam, ketamine, and pentazocine “sedato-analgesic cocktail” for sedation during ERCP. *Endoscopy* 39: 807-812
 15. Freeman ML (2002) Adverse outcomes of ERCP. *Gastrointest Endosc* 56:S273-S282
 16. Finsterer J, Stöllberger C, Bastovansky A (2010) Cardiac and cerebral air embolism from endoscopic retrograde cholangio-pancreatography. *Eur J Gastroenterol Hepatol* 22:1157-1162
 17. van Boxel GI, Hommers CE, Dash I, Goodman AJ, Green J, Orme RM (2010) Myocardial and cerebral infarction due to massive air embolism following endoscopic retrograde cholangiopancreatography (ERCP). *Endoscopy* 42 Suppl 2:E80-1

Figure legends

Figure 1.

Calculation of the gas volume score (GVS) using plain abdominal X-ray images of a representative patient (A). The bowel gas (B) area was determined and is indicated by the black region. The GVS is expressed as the black area in (B) divided by the total of the black and white areas (the values were 390,177/3,145,728 pixels.). The GVS in the example shown was 0.124.

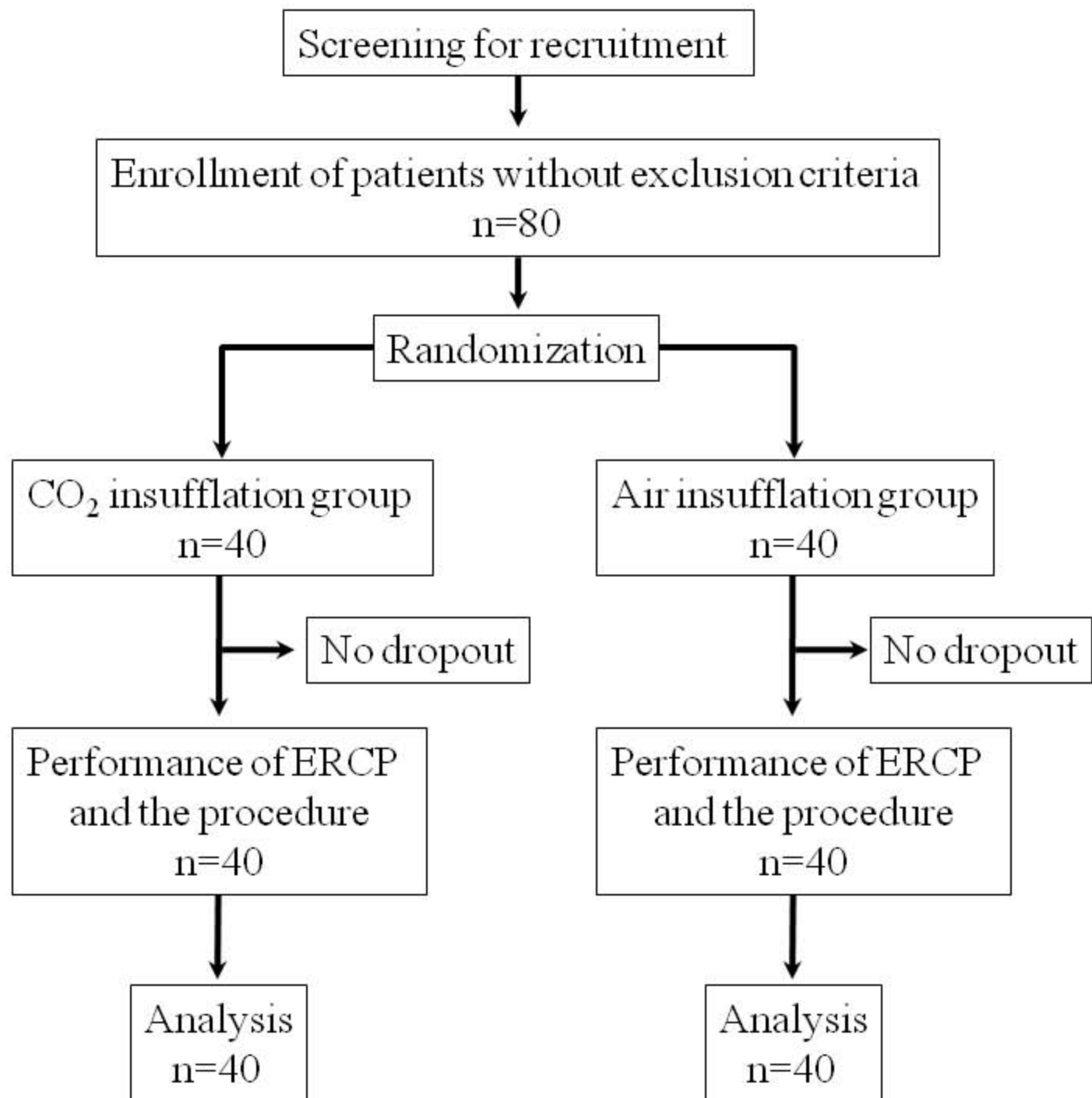
Figure 2.

Flow diagram of the study participants.

Figure 3.

Time course of arterial oxygen saturation levels by pulse oximeter (SpO₂). There was no significant difference between the CO₂ and the air groups at any time point by *t* test.





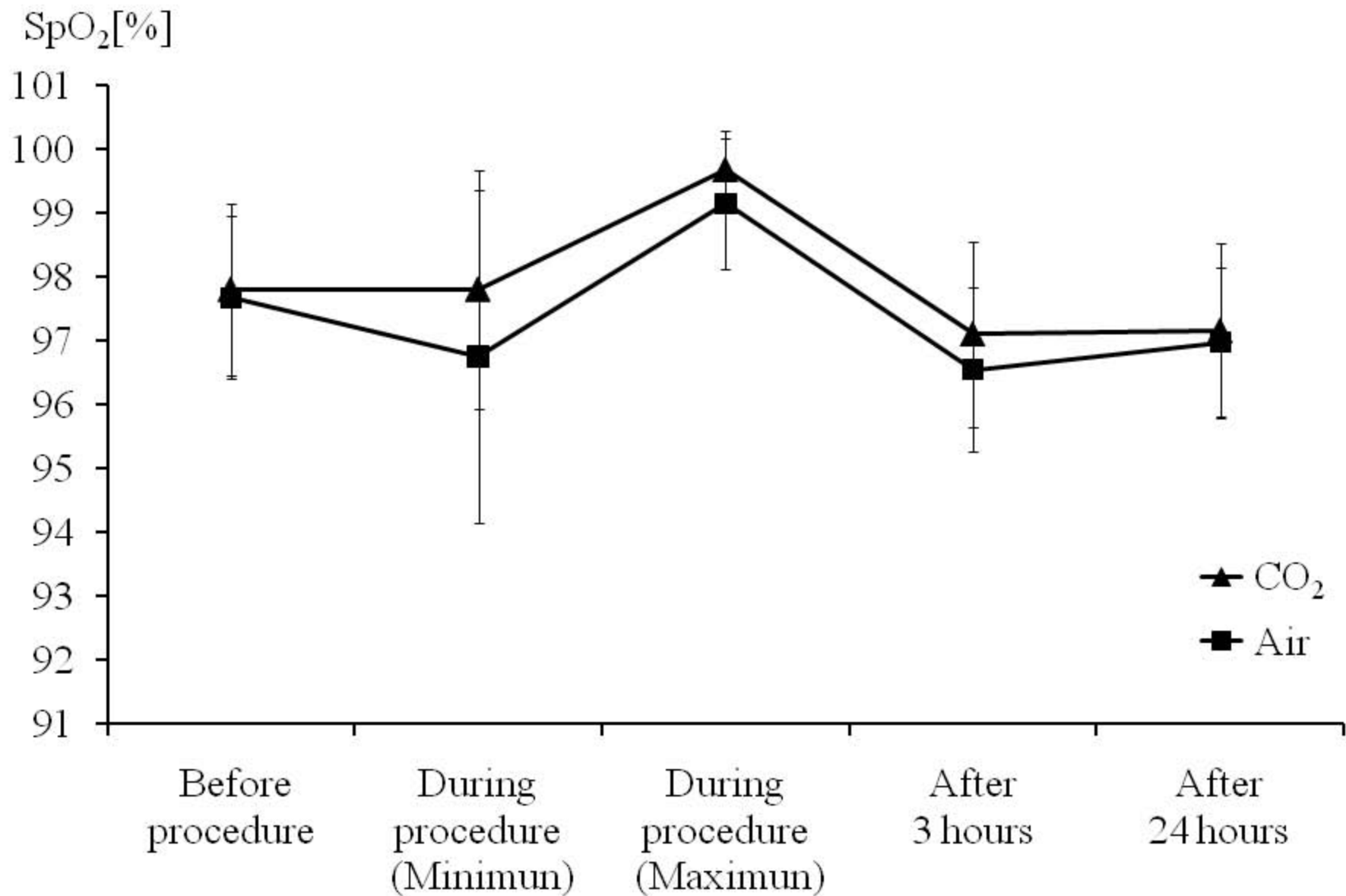


Table 1 Characteristics of the patients

	CO ₂ group	Air group	
Number	40	40	
Age, mean±SD	66.1±9.8	68.7±10.9	NS
Sex, Male/Female	25/15	24/16	NS
Disease			
Cholangiocarcinoma	11	6	NS
Pancreatic cancer	6	7	
GB cancer	1	6	
Papilla tumor	2	1	
BD or GB stone	6	5	
Cholangitis	1	3	
Benign BD stricture	3	5	
Pancreatitis	5	2	
Others	5	5	

SD, standard deviation; GB, gallbladder; BD, bile duct; NS, not significant.

Table 2 Gas volume score (GVS) and total time of the procedures

	CO ₂ group (n=40)	Air group (n=40)	<i>p</i> value
GVS			
Before procedure	0.11±0.04	0.10±0.05	NS
After procedure	0.14±0.06	0.31±0.11	< 0.01
Increased rate of GVS (%)	3.8±5.9	21.0±11.1	< 0.01
Total time of procedure (second)	2700±1485	2582±1345	NS

Values in the central two columns indicate mean ± standard deviation. NS, not significant.

Table 3 Gas volume score (GVS) in each group classified by total time of the procedure

	CO ₂ group (n=40)	Air group (n=40)	<i>p</i> value
GVS (Short time procedure)	(n=14)	(n=13)	
Before procedure	0.12±0.05	0.11±0.07	NS
After procedure	0.14±0.06	0.32±0.10	< 0.01
Increased rate of GVS (%)	2.0±4.6	21.0±12.3	< 0.01
GVS (Long time procedure)	(n=26)	(n=27)	
Before procedure	0.10±0.03	0.10±0.04	NS
After procedure	0.14±0.06	0.31±0.11	< 0.01
Increased rate of GVS (%)	4.8±6.3	21.0±10.8	< 0.01

Values in the central two columns indicate mean ± standard deviation. NS, not significant.

Short time procedure indicates that within 30 minutes.

Long time procedure indicates that over 30 minutes.

Table 4 VAS score and doses of sedative and antispastic drugs

	CO ₂ group	Air group	<i>p</i> value
10-point VAS score			
3 hours after procedure			
Abdominal pain	1.4±2.0	0.9±2.0	NS
Abdominal distension	0.6±1.2	0.6±1.1	NS
Nausea	0.2±0.8	0.2±0.9	NS
24 hours after procedure			
Abdominal pain	1.1±1.9	0.5±1.3	NS
Abdominal distension	0.6±1.6	0.4±1.1	NS
Nausea	0.2±0.9	0.1±0.3	NS
Sedative drugs			
Fentanyl citrate (µg) (n=21)	115.2±48.9	130.0±53.5	NS
Pethidine (mg) (n=19)	54.4±24.5	38.5±11.1	<i>p</i> =0.03
Midazolam (mg) (n=21)	7.3±3.6	8.4±3.7	NS
Diazepam (mg) (n=19)	2.0±0.8	2.0±0.0	NS
Antispastic drugs			
Scopolamine butylbromide (mg) (n=32)	23.0±6.6	20.6±2.4	NS
Glucagon (mg) (n=48)	1.2±0.4	1.1±0.2	NS

Values in the central two columns indicate mean ± standard deviation. NS, not significant.

Table 5 Complications associated with the procedures

	CO ₂ group (n=40)	Air group (n=40)	p value
Total number of complications	4	4	NS
Acute pancreatitis	4 ^a	3 ^b	NS
Retroperitoneal perforation	0	1 ^c	NS
Hypoxia ^d	0	0	NS
Hypotension ^e	0	0	NS

Values in the central two columns indicate mean \pm standard deviation. NS, not significant.

^aTwo cases underwent pancreatography. One case had anomalous arrangement of the pancreaticobiliary ducts.

^bTwo cases underwent precutting with a needle knife.

^cThe case who was also included in 3b cases underwent precutting with a needle knife.

^dHypoxia was defined as a decrease in SpO₂ to $\leq 90\%$.

^eHypotension was defined as a decrease in systolic blood pressure to <80 mmHg.