

Retrospective Study

Percutaneous endoscopic gastrostomy under steady pressure automatically controlled endoscopy: First clinical series

Hiroyuki Imaeda, Kiyokazu Nakajima, Naoki Hosoe, Masanori Nakahara, Shinichiro Zushi, Motohiko Kato, Kazuhiro Kashiwagi, Yasushi Matsumoto, Kayoko Kimura, Rieko Nakamura, Norihito Wada, Masahiko Tsujii, Naohisa Yahagi, Toshifumi Hibi, Takanori Kanai, Tetsuo Takehara, Haruhiko Ogata

Hiroyuki Imaeda, Department of General Internal Medicine, Saitama Medical University, Saitama 350-0495, Japan

Kiyokazu Nakajima, Division of Next Generation Endoscopic Intervention, Osaka University, Osaka 565-0871, Japan

Naoki Hosoe, Kazuhiro Kashiwagi, Kayoko Kimura, Rieko Nakamura, Haruhiko Ogata, Center for Diagnostic and Therapeutic Endoscopy, School of Medicine, Keio University, Tokyo 160-8582, Japan

Masanori Nakahara, Shinichiro Zushi, Yasushi Matsumoto, Department of Gastroenterology, Ikeda City Hospital, Osaka 563-8510, Japan

Motohiko Kato, Masahiko Tsujii, Tetsuo Takehara, Department of Gastroenterology and Hepatology, Graduate School of Medicine, Osaka University, Osaka 565-0871, Japan

Norihito Wada, Department of Surgery, School of Medicine, Keio University, Tokyo 160-8582, Japan

Naohisa Yahagi, Division of Research and Development for Minimally Invasive Treatment, Cancer Center, School of Medicine, Keio University, Tokyo 160-8582, Japan

Toshifumi Hibi, Takanori Kanai, Division of Gastroenterology and Hepatology, Department of Internal Medicine, School of Medicine, Keio University, Tokyo 160-8582, Japan

Author contributions: Imaeda H and Nakajima K planed the study design; Hosoe N and Kashiwagi K advised the study design, data analyst and enrollment of patients; Nakahara M, Zushi S, Kato M and Matsumoto Y enrolled the patients; Kimura K and Nakamura R were the endoscopist; Wada N, Tsujii M, Yahagi N, Hibi T, Kanai T, Takehara T and Ogata H supervised the study.

Institutional review board statement: The study protocol was approved by the institutional review board at our institutions.

Informed consent statement: Written informed consent was

obtained from all the patients.

Conflict-of-interest statement: The authors disclosed no financial relationships relevant to this study.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Hiroyuki Imaeda, MD, Department of General Internal Medicine, Saitama Medical University, 38 Morohongo, Moroyama-machi, Iruma-gun, Saitama 350-0495, Japan. imaedahi@yahoo.co.jp
Telephone: +81-49-2761667
Fax: +81-49-2761667

Received: September 11, 2015

Peer-review started: September 16, 2015

First decision: October 21, 2015

Revised: November 8, 2015

Accepted: December 8, 2015

Article in press: December 11, 2015

Published online: February 10, 2016

Abstract

AIM: To elucidate the safety of percutaneous endoscopic gastrostomy (PEG) under steady pressure automatically controlled endoscopy (SPACE) using carbon dioxide (CO₂).

METHODS: Nine patients underwent PEG with a modified introducer method under conscious sedation. A T-tube was attached to the channel of an endoscope connected to an automatic surgical insufflator. The stomach was inflated under the SPACE system. The intragastric pressure was kept between 4–8 mmHg with a flow of CO₂ at 35 L/min. Median procedure time, intragastric pressure, median systolic blood pressure, partial pressure of CO₂, abdominal girth before and immediately after PEG, and free gas and small intestinal gas on abdominal X-ray before and after PEG were recorded.

RESULTS: PEG was completed under stable pneumostomach in all patients, with a median procedural time of 22 min. Median intragastric pressure was 6.9 mmHg and median arterial CO₂ pressure before and after PEG was 42.1 and 45.5 Torr (NS). The median abdominal girth before and after PEG was 68.1 and 69.6 cm (NS). A mild free gas image after PEG was observed in two patients, and faint abdominal gas in the downstream bowel was documented in two patients.

CONCLUSION: SPACE might enable standardized pneumostomach and modified introducer procedure of PEG.

Key words: Percutaneous endoscopic gastrostomy; Steady pressure automatically controlled endoscopy; Carbon dioxide

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: We report the safety of percutaneous endoscopic gastrostomy (PEG) under steady pressure automatically controlled endoscopy (SPACE) using carbon dioxide (CO₂). Nine patients underwent PEG with a modified introducer method under conscious sedation. The stomach was inflated under the SPACE system. PEG was completed under stable pneumostomach in all patients. Median arterial CO₂ pressure before and after PEG was 42.1 and 45.5 Torr (NS). The median abdominal girth before and after PEG was 68.1 and 69.6 cm (NS). A mild free gas image after PEG was observed in two patients. SPACE might enabled standardized pneumostomach which leads to easier and safer PEG procedures.

Imaeda H, Nakajima K, Hosoe N, Nakahara M, Zushi S, Kato M, Kashiwagi K, Matsumoto Y, Kimura K, Nakamura R, Wada N, Tsujii M, Yahagi N, Hibi T, Kanai T, Takehara T, Ogata H. Percutaneous endoscopic gastrostomy under steady pressure automatically controlled endoscopy: First clinical series. *World J Gastrointest Endosc* 2016; 8(3): 186–191 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v8/i3/186.htm> DOI: <http://dx.doi.org/10.4253/wjge.v8.i3.186>

INTRODUCTION

Percutaneous endoscopic gastrostomy (PEG) has been

widely accepted for external feeding since Gauderer *et al*^[1] first reported it in 1980. A conventional on-demand insufflation using atmospheric air through the endoscope has been a gold standard in performing PEG, not only for optimal visualization but also for maintaining pneumostomach to keep puncture sites on the gastric/abdominal walls stabilized. Abdominal distension and pneumoperitoneum often occur after PEG^[2–7]. Carbon dioxide (CO₂) insufflation has been initially reported for colonoscopic electrosurgical polypectomy in the field of gastrointestinal (GI) endoscopy^[8]. CO₂ is now increasingly being used instead of atmospheric air in GI endoscopic procedures since CO₂ is rapidly absorbed *via* the gut lining. Total colonoscopy^[9–13], endoscopic retrograde cholangiopancreatography^[14–17], peroral cholangioscopy^[18], double-balloon enteroscopy^[19], PEG^[20], gastric and colonic endoscopic submucosal dissection (ESD)^[21–25], and upper GI intragastric endoscopy during laparoscopic surgery under CO₂ insufflation^[26] have been reported to be safe and more comfortable compared with air insufflation.

GI endoscopy has been performed under on-demand insufflation by endoscopists through the endoscope itself in a manual manner without pressure monitoring. This practice has been justified because the gastrointestinal tract allows migration of excessive gas into the upstream/downstream bowel. Excessive air supply may result in gaseous regurgitation, vomiting, and abdominal bloating. Steady pressure automatically controlled endoscopy (SPACE) using CO₂, developed by Nakajima *et al*^[27,28], Kato *et al*^[29] and Yamada *et al*^[30] is expected to improve and standardize endoscopic visualization and working space in the GI lumen. Although SPACE has been reported to shorten procedural time and improve the safety of endoscopic intervention^[28–30], CO₂ narcosis is of concern during PEG under sedation, since patients usually suffer from respiratory disease and/or consciousness disturbance. The SPACE system consists of a standard commercially available endoscope overtube (Top Co., Ltd., Tokyo, Japan) and a newly developed detachable leak-proof device with an anti-reflux valve and a Luer lock connection (Leak Cutter; Top)^[28,29]. A commercially available automatic surgical insufflator is then connected to the system. Esophageal ESD under SPACE has been reported to be feasible and safe^[28,29]. Recently, gastric ESD under SPACE has been also reported to be feasible and safe in an preclinical study^[30].

The aim of this study is to elucidate the safety of PEG under the SPACE system. To our knowledge, this is the first clinical study regarding application of SPACE technology in PEG.

MATERIALS AND METHODS

Ten patients undergoing treatment at our institutions were enrolled in the study. Patients who had CO₂ retention due to chronic obstructive pulmonary dysfunction were excluded. One of the ten enrolled patients was excluded because he withdrew his consent after informed consent

Table 1 Clinical characteristic of patients

Clinical characteristics	Data
Male/female	6/3
Mean age	78 (61–89)
Comorbid disease	
Parkinson's disease	4
Cerebrovascular disease	1
Amyotrophic lateral sclerosis	1
Necrotizing fasciitis	1
Disuse syndrome	1
Laryngeal cancer	1

was obtained. Therefore, a total of nine patients, six males and three females, underwent PEG under SPACE. The mean age of patients was 78 years (ranging from 61 to 89). Four patients had Parkinson's disease, one had cerebrovascular disease, one had amyotrophic lateral sclerosis, one had necrotizing fasciitis, one had disuse syndrome, and one had laryngeal cancer (Table 1).

PEG was performed under conscious sedation using intravenous injection of 35 mg pethidine chloride and 0.1–0.2 mg of flunitrazepam or 1–2 mg of midazolam and oxygen inhalation. A T-tube with two junctions (MD-807, Olympus Medical Systems Co. Ltd., Tokyo, Japan) was connected directly to the channel of the flexible gastroscope (GIF-H260, Olympus Medical Systems Co. Ltd., Tokyo, Japan) (Figure 1). One of the junctions was connected to a commercially available automatic surgical insufflator (UHI-3, Olympus Medical Systems Co. Ltd., Tokyo, Japan) that feeds 35 L of CO₂ per minute into the stomach through the channel (Figure 2). The intragastric pressure was kept between 4–8 mmHg. PEG was performed using a modified introducer procedure and a dedicated kit (Direct Ideal PEG kit, Olympus Medical Systems Co. Ltd., Tokyo, Japan). The gastroscope was inserted from the mouth to the esophagus under conventional manual air insufflation. After insertion into the stomach, conventional manual air insufflation was switched to the SPACE system. First, percutaneous gastropexy was conducted at two sites while the stomach was inflated under the SPACE system through the endoscope channel. Second, after puncture using an indwelling needle was performed between the two gastropexy sites, a guide-wire was replaced with the needle. Third, the PEG site was dilated by the dilator through the guide-wire. When the dilator was withdrawn, the CO₂ supply was temporarily stopped, the PEG tube was inserted through the guide-wire, and the CO₂ supply was restarted and checked to ensure it had been located correctly.

Data such as mean procedure time, intragastric pressure, mean systolic blood pressure, partial pressure of CO₂ (PaCO₂), abdominal circumference before and soon after PEG, and change of free gas and small intestinal gas on abdominal X-ray before and immediately after PEG were obtained and prospectively recorded in the database.

**Figure 1** T-tube attached to the endoscopic channel.**Figure 2** Automatic surgical insufflator connected to the T-tube.

The study protocol was in accordance with the tenets of the revised Declaration of Helsinki (1989) and was approved by the institutional review board at our institutions. Written informed consent was obtained from all the patients.

Statistical analysis

Statistical analysis was performed by Fischer's test using SPSS software, version 17 (SPSS Inc., Chicago, IL). For therapeutic performance, sensitivity, specificity, and accuracy are presented as percentages with 95% CIs. All probability values calculated in this analysis were sided, and $P < 0.05$ was considered significant.

RESULTS

The median procedural time was 22 min (14–38 min) (Table 2). It was possible to maintain a good endoscopic visualization and a sufficient pneumostomach to keep puncture sites stabilized during PEG, which was completed easily in all 9 patients. Visualization after intentional suction was regained more quickly than with conventional endoscopy (Video 1). PEG was established exactly in the scheduled puncture sites. Median intragastric pressure was kept at 6.9 mmHg as preset (5–8 mmHg). Median O₂ inhalation was 1.7 L/min (0–3). Median systolic blood pressure before and immediately after PEG was 129.3 mmHg (101–158 mmHg) and 120.6 mmHg (90–145

Table 2 Results of percutaneous endoscopic gastrostomy under steady pressure automatically controlled endoscopy

Clinical outcomes		P value
Median procedural time (min)	22 (14-38)	
Median intragastric pressure (mmHg)	6.9 (5-8)	
Median systolic pressure		
Before PEG (mmHg)	129.3 (101-158)	0.33
Soon after PEG (mmHg)	120.6 (90-145)	
Median PaCO ₂		
Before PEG (Torr)	42.1 (35.2-45.7)	0.10
Soon after PEG (Torr)	45.5 (41.0-54.6)	
Median abdominal girth		
Before PEG (cm)	68.1 (58-85)	0.38
Soon after PEG (cm)	69.6 (60-86)	
Mild free gas after PEG (n)	2	
Mild increase of small intestinal gas after PEG (n)	2	

PEG: Percutaneous endoscopic gastrostomy.

mmHg). There was no significant difference in these data ($P = 0.33$). Median PaCO₂ before and after PEG was 42.1 Torr (35.2-45.7 Torr) and 45.5 Torr (41.0-54.6 Torr). There was a tendency to an elevated median PaCO₂ after PEG compared with prior values ($P = 0.10$); however no CO₂ narcosis was encountered in the series.

The median abdominal girth before and immediately after PEG was 68.1 cm (58-85 cm) and 69.6 cm (60-86 cm), and there was no significant difference ($P = 0.38$). Mild free gas was observed postoperatively in two patients, and small intestinal gas was slightly increased in two patients (Figure 3). All these were subclinical, and no other serious adverse events were encountered in any patients.

DISCUSSION

Several endoscopic procedures under CO₂ insufflation have been reported to be safe and more comfortable compared with air insufflation because CO₂ is absorbed rapidly *via* the gut lining. CO₂ insufflation during PEG reduces risk of pneumoperitoneum and bloating^[8-25]. Technically, it is a key point to maintain pneumostomach stabilized during PEG so that PEG can be fashioned in the scheduled puncture sites.

In our study, although PaCO₂ was subclinically elevated during and after the procedure, there were no adverse events associated with CO₂ insufflation. The insufflation is mandatory in PEG for maintaining a pneumostomach to keep puncture sites stabilized. Nishiwaki *et al.*^[20] reported that PEG under CO₂ insufflation compared with air insufflation was safer and more comfortable because of the lower incidence of pneumoperitoneum, less distension of the small bowel, and no adverse events. Our present data first showed that PEG is safely fashioned under SPACE.

Nakajima *et al.*^[27] reported that a steady-pressure pneumostomach was successfully created and maintained for 100 min on average without clamping the



Figure 3 Free air (indicated by arrows) in abdominal X-ray after percutaneous endoscopic gastrostomy under steady pressure automatically controlled endoscopy.

downstream bowel in laparoscopic intragastric surgery (LIGS). The stomach was insufflated with a UHI-3 surgical insufflation unit connected to a transgastric port at an intragastric pressure of 6-8 mmHg. No adverse events were noted during LIGS, and no postoperative abdominal distention was observed. Nakajima *et al.*^[28] have also reported esophageal ESD under SPACE using a standard endoscopic overtube and a detachable leak-proof valve with a luer-lock connection in an animal model. Moreover, Kato *et al.*^[29] reported on the feasibility and safety of esophageal ESD under SPACE in a clinical study, and Yamada *et al.*^[30] reported on the feasibility and safety of gastric ESD under SPACE in an animal model. In SPACE, endoscopic visualization is automatically obtained once the insufflation pressure and flow rate are set. Visualization after suction is automatically regained more quickly than with conventional endoscopy. The flow capacity of current surgical insufflators is higher than that of manual endoscopic insufflators and is considered responsible for the rapid regaining. UHI-3 can supply 35 L of CO₂ per minute and these flow rates are significantly higher than those of actual endoscopic flow with manual CO₂ insufflation (1.4 L/min). The insufflation process is automatic in SPACE. Air/water button manipulation is no longer necessary, leaving the endoscopist free to focus on the intervention itself. SPACE can prevent excessive CO₂ supply, which may result in gaseous regurgitation, vomiting, and abdominal bloating^[30].

In this study, CO₂ was successfully supplied through the endoscopic channel using a T-tube without an overtube. The intragastric pressure was kept from 5 to 8 mmHg throughout the procedure. PEG under SPACE had no negative effects such as vomiting or abdominal bloating and no impact on vital signs. Mild postprocedural free gas was observed in two patients and abdominal gas was slightly increased in another two patients. There were, however, no adverse events in any patients. Even if CO₂ is leaked into the abdominal cavity through the PEG site, CO₂ can be absorbed quickly *via* the peritoneal lining and abdominal distention will be resolved immediately. Nishiwaki *et al.*^[20] reported that pneumoperitoneum was

not observed in the CO₂ insufflation group. In our study, pneumoperitoneum might have occurred because of the leakage of remnant air in the stomach. Nishiwaki *et al.*^[20] performed a pull method of the PEG procedure, while in our study, a modified introducer method was performed. After the dilator was withdrawn, the PEG tube was inserted during the modified introducer method, and it was possible that intragastric gas (air) might have leaked into the abdominal cavity at this time. Thus we hypothesized that postprocedural pneumoperitoneum might be caused by the difference of the PEG procedure. Yamada *et al.*^[30] reported the potential safety of pneumoperitoneum under SPACE, because intra-gastric pressure was regulated within the preset pressure range to prevent excessive transmural insufflation. Nakajima *et al.*^[28] have reported that the migration of CO₂ over the proximal jejunum does not occur because of a pinch-cock phenomenon and intestinal surface tension. In this pinch-cock phenomenon, the distended upstream bowel (stomach and duodenum) acts as a cock that compresses the downstream bowel, resulting in the prevention of massive gas migration. The surface tension in the collapsed gut lumen may work as another pressure barrier. The insufflated gas volume was sufficiently low in each SPACE, suggesting no major gas migration into the downstream bowel during SPACE. In fact, CO₂ outflow stopped automatically whenever the stomach was insufflated.

Although conscious sedation is necessary during PEG procedure, most patients who undergo PEG have cerebrovascular diseases and aspiration pneumonia, which means they are at high risk for developing respiratory dysfunction. CO₂ narcosis might develop in patients with chronic pulmonary diseases, so they were excluded from this study. There was a tendency to an elevated PaCO₂ median after PEG compared with before PEG, but CO₂ narcosis did not occur in any cases. This elevation might be caused by PEG under SPACE, but it could also be caused by the administration of sedative drugs that suppress the respiratory function.

There were several limitations in this study. First, as this was a pilot study, the sample size was very small. We need to accumulate more clinical data such as a randomized controlled trial between PEG under conventional manual air or CO₂ insufflation and that under SPACE system in near future. There was a tendency to an elevated median PaCO₂ after PEG compared with previous values, indicating that a randomized controlled trial to compare PEG under SPACE and under manual air insufflation is necessary. We examined PaCO₂ only twice: once before and once after PEG. Ideally we should examine the course of PCO₂ during PEG using the monitor of transcutaneous measurement of PCO₂. Most patients cannot complain of abdominal pain or distention because of comorbid diseases such as cerebrovascular disease, so the complaints of all patients cannot be detected. We have to examine the gas volume in the small intestine and the pneumoperitoneum in the abdominal X-ray and/or CT scan. The channel is free during a modified introducer

procedure of PEG, therefore, the SPACE system is available during PEG procedure. The introduction of snares or forceps through the channel affects the SPACE system.

In conclusion, PEG under SPACE might be feasible and safe. SPACE might enable standardized pneumostomach which leads to easier and safer PEG procedures.

COMMENTS

Background

"On-demand" insufflation using atmospheric air has been a gold standard in performing percutaneous endoscopic gastrostomy (PEG), not only for optimal visualization but also for maintaining pneumostomach to keep puncture sites stabilized. However, excessive air insufflation may result in gaseous regurgitation, vomiting, and abdominal bloating.

Research frontiers

PEG under steady pressure automatically controlled endoscopy (SPACE) using carbon dioxide (CO₂) has not been reported.

Innovations and breakthroughs

PEG under SPACE was feasible and safe.

Applications

SPACE enables standardized pneumostomach which leads to easier and safer PEG procedures.

Peer-review

The authors evaluated the safety of PEG under SPACE using CO₂. PEG was completed under stable pneumostomach in all nine patients. Further clinical trials in a randomized controlled study between PEG under conventional manual air or CO₂ insufflation and that under SPACE system will be necessary.

REFERENCES

- 1 **Gauderer MW**, Ponsky JL, Izant RJ. Gastrostomy without laparotomy: a percutaneous endoscopic technique. *J Pediatr Surg* 1980; **15**: 872-875 [PMID: 6780678]
- 2 **Gottfried EB**, Plumser AB, Clair MR. Pneumoperitoneum following percutaneous endoscopic gastrostomy. A prospective study. *Gastrointest Endosc* 1986; **32**: 397-399 [PMID: 3803838]
- 3 **Wojtowycz MM**, Arata JA. Subcutaneous emphysema after percutaneous gastrostomy. *Am J Roentgenol* 1988; **151**: 311-312 [PMID: 3134806]
- 4 **Dulabon GR**, Abrams JE, Rutherford EJ. The incidence and significance of free air after percutaneous endoscopic gastrostomy. *Am Surg* 2002; **68**: 590-593 [PMID: 12079145]
- 5 **Wiesen AJ**, Sideridis K, Fernandes A, Hines J, Indaram A, Weinstein L, Davidoff S, Bank S. True incidence and clinical significance of pneumoperitoneum after PEG placement: a prospective study. *Gastrointest Endosc* 2006; **64**: 886-889 [PMID: 17140892]
- 6 **Schrag SP**, Sharma R, Jaik NP, Seamon MJ, Lukaszczuk JJ, Martin ND, Hoey BA, Stawicki SP. Complications related to percutaneous endoscopic gastrostomy (PEG) tubes. A comprehensive clinical review. *J Gastrointest Liver Dis* 2007; **16**: 407-418 [PMID: 18193123]
- 7 **Blum CA**, Selander C, Ruddy JM, Leon S. The incidence and clinical significance of pneumoperitoneum after percutaneous endoscopic gastrostomy: a review of 722 cases. *Am Surg* 2009; **75**: 39-43 [PMID: 19213395]
- 8 **Rogers BH**. The safety of carbon dioxide insufflation during colonoscopic electrosurgical polypectomy. *Gastrointest Endosc* 1974; **20**: 115-117 [PMID: 4815026]
- 9 **Hussein AM**, Bartram CI, Williams CB. Carbon dioxide insufflation for more comfortable colonoscopy. *Gastrointest*

- Endosc* 1984; **30**: 68-70 [PMID: 6425108]
- 10 **Stevenson GW**, Wilson JA, Wilkinson J, Norman G, Goodacre RL. Pain following colonoscopy: elimination with carbon dioxide. *Gastrointest Endosc* 1992; **38**: 564-567 [PMID: 1397911]
 - 11 **Yamano HO**, Yoshikawa K, Kimura T, Yamamoto E, Harada E, Kudou T, Katou R, Hayashi Y, Satou K. Carbon dioxide insufflation for colonoscopy: evaluation of gas volume, abdominal pain, examination time and transcutaneous partial CO₂ pressure. *J Gastroenterol* 2010; **45**: 1235-1240 [PMID: 20635100 DOI: 10.1007/s00535-010-0286-5]
 - 12 **Uraoka T**, Kato J, Kuriyama M, Hori K, Ishikawa S, Harada K, Takemoto K, Hiraoka S, Fujita H, Horii J, Saito Y, Yamamoto K. CO₂ insufflation for potentially difficult colonoscopies: efficacy when used by less experienced colonoscopists. *World J Gastroenterol* 2009; **15**: 5186-5192 [PMID: 19891018]
 - 13 **Yasumasa K**, Nakajima K, Endo S, Ito T, Matsuda H, Nishida T. Carbon dioxide insufflation attenuates parietal blood flow obstruction in distended colon: potential advantages of carbon dioxide insufflated colonoscopy. *Surg Endosc* 2006; **20**: 587-594 [PMID: 16437273]
 - 14 **Bretthauer M**, Seip B, Aasen S, Kordal M, Hoff G, Aabakken L. Carbon dioxide insufflation for more comfortable endoscopic retrograde cholangiopancreatography: a randomized, controlled, double-blind trial. *Endoscopy* 2007; **39**: 58-64 [PMID: 17252462]
 - 15 **Maple JT**, Keswani RN, Hovis RM, Saddedin EZ, Jonnalagadda S, Azar RR, Hagen C, Thompson DM, Waldbaum L, Edmundowicz SA. Carbon dioxide insufflation during ERCP for reduction of postprocedure pain: a randomized, double-blind, controlled trial. *Gastrointest Endosc* 2009; **70**: 278-283 [PMID: 19523621 DOI: 10.1016/j.gie.2008.12.050]
 - 16 **Dellon ES**, Velayudham A, Clarke BW, Isaacs KL, Gangarosa LM, Galanko JA, Grimm IS. A randomized, controlled, double-blind trial of air insufflation versus carbon dioxide insufflation during ERCP. *Gastrointest Endosc* 2010; **72**: 68-77 [PMID: 20493485 DOI: 10.1016/j.gie.2010.01.041]
 - 17 **Nelson DB**, Freeman ML, Silvis SE, Cass OW, Yakshe PN, Vennes J, Stahnke LL, Herman M, Hodges J. A randomized, controlled trial of transcutaneous carbon dioxide monitoring during ERCP. *Gastrointest Endosc* 2000; **51**: 288-295 [PMID: 10699773]
 - 18 **Ueki T**, Mizuno M, Ota S, Ogawa T, Matsushita H, Uchida D, Numata N, Ueda A, Morimoto Y, Kominami Y, Nanba S, Kurome M, Ohe H, Nakagawa M, Araki Y. Carbon dioxide insufflation is useful for obtaining clear images of the bile duct during peroral cholangioscopy (with video). *Gastrointest Endosc* 2010; **71**: 1046-1051 [PMID: 20438891 DOI: 10.1016/j.gie.2010.01.015]
 - 19 **Domagk D**, Bretthauer M, Lenz P, Aabakken L, Ullerich H, Maaser C, Domschke W, Kucharzik T. Carbon dioxide insufflation improves intubation depth in double-balloon enteroscopy: a randomized, controlled, double-blind trial. *Endoscopy* 2007; **39**: 1064-1067 [PMID: 18072057]
 - 20 **Nishiwaki S**, Araki H, Hayashi M, Takada J, Iwashita M, Tagami A, Hatakeyama H, Hayashi T, Maeda T, Saito K. Inhibitory effects of carbon dioxide insufflation on pneumoperitoneum and bowel distension after percutaneous endoscopic gastrostomy. *World J Gastroenterol* 2012; **18**: 3565-3570 [PMID: 22826621 DOI: 10.3748/wjg.v18.i27.3565]
 - 21 **Maeda Y**, Hirasawa D, Fujita N, Obana T, Sugawara T, Ohira T, Harada Y, Yamagata T, Suzuki K, Koike Y, Kusaka J, Tanaka M, Noda Y. A prospective, randomized, double-blind, controlled trial on the efficacy of carbon dioxide insufflation in gastric endoscopic submucosal dissection. *Endoscopy* 2013; **45**: 335-341 [PMID: 23468193 DOI: 10.1055/s-0032-1326199]
 - 22 **Nonaka S**, Saito Y, Takisawa H, Kim Y, Kikuchi T, Oda I. Safety of carbon dioxide insufflation for upper gastrointestinal tract endoscopic treatment of patients under deep sedation. *Surg Endosc* 2010; **24**: 1638-1645 [PMID: 20108154 DOI: 10.1007/s00464-009-0824-5]
 - 23 **Saito Y**, Uraoka T, Matsuda T, Emura F, Ikehara H, Mashimo Y, Kikuchi T, Kozu T, Saito D. A pilot study to assess the safety and efficacy of carbon dioxide insufflation during colorectal endoscopic submucosal dissection with the patient under conscious sedation. *Gastrointest Endosc* 2007; **65**: 537-542 [PMID: 17321264]
 - 24 **Kikuchi T**, Fu KI, Saito Y, Uraoka T, Fukuzawa M, Fukunaga S, Sakamoto T, Nakajima T, Matsuda T. Transcutaneous monitoring of partial pressure of carbon dioxide during endoscopic submucosal dissection of early colorectal neoplasia with carbon dioxide insufflation: a prospective study. *Surg Endosc* 2010; **24**: 2231-2235 [PMID: 20177925 DOI: 10.1007/s00464-010-0939-8]
 - 25 **Suzuki T**, Minami H, Komatsu T, Masusda R, Kobayashi Y, Sakamoto A, Sato Y, Inoue H, Serada K. Prolonged carbon dioxide insufflation under general anesthesia for endoscopic submucosal dissection. *Endoscopy* 2010; **42**: 1021-1029 [PMID: 21120775 DOI: 10.1055/s-0030-1255969]
 - 26 **Souma Y**, Nakajima K, Takahashi T, Nishimura J, Fujiwara Y, Takiguchi S, Miyata H, Yamasaki M, Doki Y, Nishida T. The role of intraoperative carbon dioxide insufflating upper gastrointestinal endoscopy during laparoscopic surgery. *Surg Endosc* 2009; **23**: 2279-2285 [PMID: 19184210 DOI: 10.1007/s00464-008-0309-y]
 - 27 **Nakajima K**, Nishida T, Milsom JW, Takahashi T, Souma Y, Miyazaki Y, Iijima H, Mori M, Doki Y. Current limitations in endoscopic CO₂ insufflation for NOTES: flow and pressure study. *Gastrointest Endosc* 2010; **72**: 1036-1042 [PMID: 20883992 DOI: 10.1016/j.gie.2010.07.002]
 - 28 **Nakajima K**, Moon JH, Tsutsui S, Miyazaki Y, Yamasaki M, Yamada T, Kato M, Yasuda K, Sumiyama K, Yahagi N, Saida Y, Kondo H, Nishida T, Mori M, Doki Y. Esophageal submucosal dissection under steady pressure automatically controlled endoscopy (SPACE): a randomized preclinical trial. *Endoscopy* 2012; **44**: 1139-1148 [PMID: 22932809 DOI: 10.1055/s-0032-1310093]
 - 29 **Kato M**, Nakajima K, Yamada T, Hirota M, Miyazaki Y, Yamasaki M, Nishida T, Mori M, Doki Y, Tsujii M, Takehara T. Esophageal submucosal dissection under steady pressure automatically controlled endoscopy (SPACE): a clinical feasibility study. *Endoscopy* 2014; **46**: 680-684 [PMID: 24770965 DOI: 10.1055/s-0034-1365465]
 - 30 **Yamada T**, Hirota M, Tsutsui S, Kato M, Takahashi T, Yasuda K, Sumiyama K, Tsujii M, Takehara T, Mori M, Doki Y, Nakajima K. Gastric endoscopic submucosal dissection under steady pressure automatically controlled endoscopy (SPACE): a multicenter randomized preclinical trial. *Surg Endosc* 2015; **29**: 2748-2755 [PMID: 25480619 DOI: 10.1007/s00464-014-4001-0]

P- Reviewer: Casadesus D, Kapetanios D, Trevisani L
S- Editor: Wang JL **L- Editor:** A **E- Editor:** Lu YJ





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>

