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

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Abstract

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

Percutaneous endoscopic gastrostomy (PEG) has been widely accepted for external feeding since Gauderer et al. 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. Carbon dioxide (CO₂) insufflation has been initially reported for colonoscopic electrosurgical polyectomy in the field of gastrointestinal (GI) endoscopy. 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, endoscopic retrograde cholangiopancreatography, peroral cholangioscopy, double-balloon enteroscopy, PEG, gastric and colonic endoscopic submucosal dissection (ESD), and upper GI intragastric endoscopy during laparoscopic surgery under CO₂ insufflation 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. and Yamada et al. 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, 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. A commercially available automatic surgical insufflator is then connected to the system. Esophageal ESD under SPACE has been reported to be feasible and safe. Recently, gastric ESD under SPACE has been also reported to be feasible and safe in a preclinical study.

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.

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 procedural 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

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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 fascitis, 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, intraoperative 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.

### 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 fascitis     | 1    |
| Disuse syndrome          | 1    |
| Laryngeal cancer         | 1    |

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 intraoperative 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 WJGE | www.wjgnet.com February 10, 2016 | Volume 8 | Issue 3 |
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) |
| Soon after PEG (mmHg)                    | 120.6 (90-145) |
| PaCO₂ Before PEG (Torr)                  | 42.1 (35.2-45.7) |
| Soon after PEG (Torr)                    | 45.5 (41.0-54.6) |
| Median abdominal girth                   |         |
| Before PEG (cm)                          | 68.1 (58-85) |
| Soon after PEG (cm)                      | 69.6 (60-86) |
| Mild free gas after PEG (cm)             | 2       |
| Mild increase of small intestinal gas    | 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 pneumoperitonium and bloating. 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.⁸ 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 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 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 bloating²⁴.

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 CO\textsubscript{2} insufflation group. In our study, pneumoperitoneum might have occurred because of the leakage of remnant air in the stomach. Nishiwaki \textit{et al.}\textsuperscript{[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 \textit{et al.}\textsuperscript{[21]} 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 \textit{et al.}\textsuperscript{[22]} have reported that the migration of CO\textsubscript{2} 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, CO\textsubscript{2} 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. CO\textsubscript{2} narcosis might develop in patients with chronic pulmonary diseases, so they were excluded from this study. There was a tendency to an elevated PaCO\textsubscript{2} median after PEG compared with before PEG, but CO\textsubscript{2} 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 CO\textsubscript{2} insufflation and that under SPACE system in near future. There was a tendency to an elevated median PaCO\textsubscript{2} 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 PaCO\textsubscript{2} only twice: once before and once after PEG. Ideally we should examine the course of PCO\textsubscript{2} during PEG using the monitor of transcutaneous measurement of PCO\textsubscript{2}. 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 (CO\textsubscript{2}) 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 CO\textsubscript{2}. 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 CO\textsubscript{2} insufflation and that under SPACE system will be necessary.

**REFERENCES**

1. Gauderer MW, Ponsky JL, Izant RJ. Gastrostomy without laparotomy: a percutaneous endoscopic technique. \textit{J Pediatr Surg} 1980; 15: 872-875 [PMID: 6780678]
2. Gottfried EB, Plumser AB, Clair MR. Pneumoperitoneum following percutaneous endoscopic gastrostomy. A prospective study. \textit{Gastroint Endosc} 1986; 32: 397-399 [PMID: 3803838]
3. Wojtowycz MM, Arata JA. Subcutaneous emphysema after percutaneous gastrostomy. \textit{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. \textit{Am Surg} 2002; 68: 590-593 [PMID: 12079145]
5. Wiesen AJ, Sideridis K, Fernandes A, Hines J, Indaram A, Weinland L, Davidoff S, Bank S. True incidence and clinical significance of pneumoperitoneum after PEG placement: a prospective study. \textit{Gastroint Endosc} 2006; 64: 886-889 [PMID: 17140892]
6. Schrag SP, Sharma R, Jaik NP, Seamon MJ, Lukaszczyzk JJ, Martin ND, Hoey BA, Stawicki SP. Complications related to percutaneous endoscopic gastrostomy (PEG) tubes. A comprehensive clinical review. \textit{J Gastrointestin 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. \textit{Am Surg} 2009; 75: 39-43 [PMID: 19213395]
8. Rogers BH. The safety of carbon dioxide insufflation during colonoscopic electro surgical polypectomy. \textit{Gastroint Endosc} 1974; 20: 115-117 [PMID: 4815026]
9. Hussein AM, Bartram CI, Williams CB. Carbon dioxide insufflation for more comfortable colonoscopy. \textit{Gastrointest
Carbon dioxide insufflation for more comfortable endoscopic retrograde cholangiopancreatography: a randomized, controlled, double-blind trial. *Gastrointest Endosc* 2010; 72: 278-283 [PMID: 19523621 DOI: 10.1016/j.gie.2008.12.050]

Dellon ES, Velayudham A, Clarke BW, Isaac KL, Gargarosa 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]

Nelson DB, Freeman ML, Silvis SE, Cass OW, Yaksh 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]

Ueki T, Mizuno M, Ota S, Ogawa T, Matsushita H, Uchida D, Numata N, Ueda A, Morimoto Y, Kominami Y, Nanba S, Kurome K, 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]

Domagk G, Brethauer M, Lene P, Aabakken L, Ullrich H, Maaser C, Domschke W, Kucharzik T. Carbon dioxide insufflation improves intubation depth in double-balloon endoscopy: a randomized, controlled, double-blind trial. *Endoscopy* 2007; 39: 1064-1067 [PMID: 18072057]

Nishiwaki S, Araki H, Hayashi M, Takada J, Iw Ashley M, Tagami A, Hatakeyama H, Hayashi T, Maeda T, Saito K. Inhibitory effects of carbon dioxide insufflation on neopomptereon and bowel distension after percutaneous endoscopic gastrostomy. *World J Gastroenterol* 2012; 18: 3565-3570 [PMID: 22826621 DOI: 10.3748/wjg.v18.i27.3565]
