ORIGINAL ARTICLE: Clinical Endoscopy

The use of carbon dioxide for insufflation during GI endoscopy: a systematic review CME

Evan S. Dellon, MD, MPH, James S. Hawk, MD, Ian S. Grimm, MD, Nicholas J. Shaheen, MD, MPH

Chapel Hill, North Carolina, USA

Background: Insufflation of the lumen is required for visualization during GI endoscopy. Carbon dioxide (CO_2) has been proposed as an alternative to room air for insufflation.

Objectives: To assess the safety and efficacy of CO_2 insufflation for endoscopy.

Design: Systematic review that focuses on evidence from randomized controlled trials (RCT).

Methods: Two investigators independently searched MEDLINE from 1950 to February 13, 2008, to identify all articles that reported the use of CO_2 in a GI endoscopy application. Bibliographies of relevant articles were also hand searched to identify other pertinent reports. Data from RCTs, as well as from nonrandomized studies, were extracted.

Results: Nine RCTs were identified that compared CO_2 and air insufflation for GI endoscopy. Fifteen other nonrandomized studies or reports were also reviewed. In the 8 RCTs in which postprocedural pain was assessed, pain was lower in the CO_2 insufflation group compared with the air group. Two RCTs found decreased flatus in the CO_2 group compared with the air group, and 3 RCTs showed there was decreased bowel distention on abdominal radiography in the CO_2 group compared with the air group. Also, in all 9 RCTs and 6 additional studies in which safety was assessed, there was no CO_2 retention and no adverse pulmonary events related to CO_2 insufflation.

Limitations: Because of study heterogeneity, meta-analytic techniques could not be used.

Conclusions: Consistent RCT evidence indicates that CO_2 insufflation is associated with decreased postprocedural pain, flatus, and bowel distention. CO_2 insufflation also appears to be safe in patients without severe underlying pulmonary disease. (Gastrointest Endosc 2009;69:843-9.)

GI endoscopy, which includes EGD, flexible sigmoidoscopy, colonoscopy, ERCP, and, more recently, double-balloon enteroscopy (DBE), is the cornerstone of diagnostic and therapeutic modalities in gastroenterology. For example, approximately 14 million colonoscopies were performed in the United States in 2002, either to screen for colorectal cancer or to evaluate lower-GI–tract symptoms and pathology; many more colonoscopies are performed worldwide.[1] To achieve optimal visualization of any part of the GI tract once an endoscope has been inserted, it is necessary to insufflate a gas, which distends the lumen and allows the mucosa to be examined. Regardless of the type of endoscope used, it is common practice both in the United States and throughout the world to use ambient atmospheric air, also termed "room air," to insufflate the lumen.[2-4] This is a convenient, abundant, and free source of gas.

More than 3 decades ago, however, Rogers[5] performed a small study that evaluated the safety of insufflating carbon dioxide (CO_2) during colonoscopy, and, since then, a series of investigations examined its use in a variety of endoscopic applications.[2-4,6-16] The rationale for using CO_2 is that it is rapidly absorbed from the bowel, whereas room air is not,[3,17,18] which allows the bowel to decompress more rapidly and potentially decreases

Abbreviations: CO_2, carbon dioxide; DBE, double-balloon enteroscopy; $ETCO_2$, End-tidal carbon-dioxide level; pCO_2, partial pressure of carbon dioxide; RCT, randomized controlled trial.

DISCLOSURE: *All authors disclosed no financial relationships relevant to this publication. This work was funded in part by the National Institutes of Health training grant T32 DK007634.*

See CME section; p 914.

0016-5107/$36.00
doi:10.1016/j.gie.2008.05.067

intraprocedural and postprocedural pain, sedation medication requirements, procedure time, and recovery time. Nevertheless, CO_2 insufflation has not been widely adopted. The reasons for this are not well studied, but potential explanations could include concerns about safety or efficacy, cost, and the requirement of specialized equipment.

There may be a discordance between the results of research studies in this field and their adoption into clinical practice. Therefore, the purpose of this study was to perform a systematic review of the literature to assess the safety and efficacy of CO_2 insufflation for endoscopic purposes, focusing in particular on rigorously conducted randomized controlled trials.

Capsule Summary

What is already known on this topic

- Carbon dioxide (CO_2) insufflation during endoscopy may allow the bowel to decompress more rapidly and potentially decrease procedural pain, sedation requirements, and procedure and recovery times.

What this study adds to our knowledge

- In a systematic review of the safety and efficacy of CO_2 versus room air for insufflation, 8 randomized controlled trials (RCTs) found postprocedural pain was lower in the CO_2 group. Additionally, 2 RCTs found decreased flatus in the CO_2 group, and 3 RCTs found decreased bowel distention on abdominal radiography in the CO_2 group.
- In 9 RCTs and 6 other studies in which safety was assessed, CO_2 was not retained and no adverse pulmonary events related to CO_2 insufflation were seen.

MATERIALS AND METHODS

Methods

Two investigators (E.S.D., J.S.H.) independently performed a search of the medical literature from 1950 through February 13, 2008, as indexed by MEDLINE by using the PubMed search engine (www.pubmed.gov). To capture all potentially relevant articles with the highest degree of sensitivity, the search terms were intentionally broad. We used ''carbon dioxide and (endoscopy or colonoscopy).'' Attempts to narrow the search strategy, for example, by excluding terms such as ''laparoscopy'' or ''pneumoperitoneum,'' proved overly restrictive. We also hand searched the bibliographies of relevant articles to identify additional pertinent reports.

The abstracts of this initial search were then independently reviewed by 2 investigators (E.S.D., J.S.H.) to determine if they were eligible for inclusion for a full article review. If there was disagreement about whether to include an abstract, the full article was reviewed. We included all articles that reported use of CO_2 in an endoscopic application, such as EGD, colonoscopy, flexible sigmoidoscopy, ERCP, and enteroscopy, and further subdivided them into 2 main categories: randomized clinical trials (RCT) and other studies. Both human and animal reports were accepted, as were reports of intraoperative endoscopy. We excluded articles concerning laparoscopic surgery, other non-GI endoscopic surgery, pneumoperitoneum, bronchoscopy, thorascopy, hysteroscopy, cystoscopy, and other nonapplicable topics that addressed nonhuman and basic science subjects. Both investigators independently extracted data into evidence tables, compared the data, and resolved any discrepancies by consensus. Extracted data included the following: study type, endoscopy type, compliance with the CONSORT statement,[19] masking protocol, placebo use, number of centers, number of patients, inclusion and/or exclusion criteria, patient demographics, all outcomes, all safety data, and the method of CO_2 insufflation.

Given the wide range and heterogeneity of studies, meta-analytic techniques could not be applied to the data in a valid fashion.[20] For example, in the identified publications, there were 4 different endoscopic modalities, different patient inclusion and exclusion criteria, different primary and secondary end points, and different methodologies for determining these end points. Therefore, descriptive statistics were used to summarize findings. The methodology for this systematic review conformed to accepted guidelines.[20,21] This study was funded, in part, by a T32 training grant from the National Institutes of Health; there was no other financial or commercial support of this study.

RESULTS

Search strategy

The initial search strategy yielded 2221 publications (Fig. 1). The vast majority of these (2197) were excluded because they were off topic, which was because of the intentionally broad initial search criteria. The remaining 24 publications were reviewed in full. Of these, 9 were randomized controlled clinical trials from which data were extracted (6 studied colonoscopy,[3,7,9-12] and 1 each studied flexible sigmoidoscopy,[8] ERCP,[4] and DBE[14]). Data from these trials are presented in Table 1. All studies but one were double blind, all studies included a placebo group in which air was insufflated, and all studies but 2 were single-center studies; a variety of CO_2 insufflation strategies were used. The other 15 articles included letters and editorials,[22-26] animal studies,[17,18] and case series, case control studies, or other nonrandomized clinical studies.[2,5,6,13,15,16,27,28]

For the 9 randomized studies, we were able to evaluate outcomes of pain, flatus, and bowel-gas distention. For these studies and 6 others,[2,5,6,15,16,23] we were able to evaluate data concerning the safety of CO_2 insufflation.

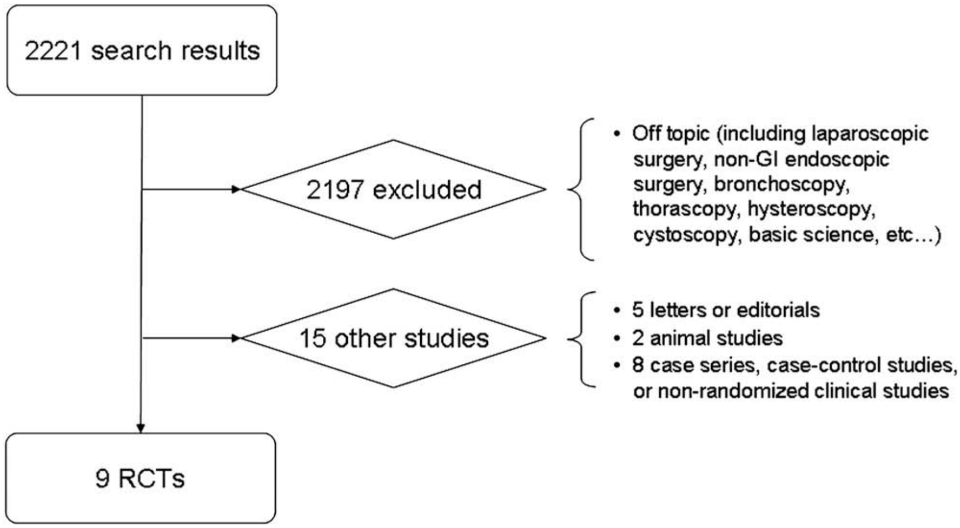

Figure 1. Results of searching the MEDLINE-linked medical literature with the search terms: ''carbon dioxide and (endoscopy or colonoscopy),'' as well as a hand search of the bibliographies of selected articles.

Effect of CO_2 insufflation on procedural and postprocedural abdominal pain

In the 8 RCTs that assessed pain related to the endoscopic procedure,[3,4,7-9,11,12,14] all showed decreased pain in the CO_2 insufflation group in comparison with the air insufflation group (Table 2). Pain was assessed in a variety of ways, including visual analog and 5-point and 10-point Likert scales, and at a variety of time points, including before the procedure, during the procedure, and 10 minutes, 1 hour, 6 hours, and 24 hours after the procedure, which made summary statistics impossible. Five studies, however, reported the proportion of patients who reported no pain at 3 time points (1, 6, and 24 hours) after the procedure.[3,4,8,9,12] For both the 1-hour and 6-hour postprocedure times, the CO_2 group had a higher proportion of pain-free patients (63%-93% at 1 hour, 64%-91% at 6 hours) compared with the air group (17%-64% at 1 hour, 28%-69% at 6 hours). At the 24-hour time point, the proportions were more comparable (64%-95% in the CO_2 group, 38%-82% in the air group). Results were consistent across the colonoscopy, flexible sigmoidoscopy, ERCP, and DBE modalities.

Effect of CO_2 insufflation on flatus

Two studies of colonoscopy (Table 2) assessed the quantity of flatus passed after the procedure, at 1, 6, and 24 hours when using a 5-point scale (none, a little, moderate, a lot, extreme).[7,9] In the first study, there was less flatus reported in the CO_2 group at all time points.[7] For example, 1 hour after the procedure, 92% of the CO_2 group reported passing no gas compared with 46% of the air group. At 6 hours, these proportions were 83% and 4%, respectively, and, at 24 hours, they were 60% and 12%. In the second study, less flatus was reported in the CO_2 group at the 1-hour and 6-hour time points but not at the 24-hour assessment.[9]

Effect of CO_2 insufflation on bowel-gas distention

Three studies (Table 2) assessed the degree of bowel distention on abdominal radiography caused by gas insufflation.[4,7,9] Two studies of colonoscopy used a 5-point Likert scale to characterize the amount of residual gas in the small and large intestine at 1 hour after the procedure.[7,9] These studies found significant less gas in both sites in the CO_2 group compared with the air group. The other study of ERCP used a 4-point grading scale to assess bowel distention 5 minutes after the procedure.[4] In the CO_2 group, 29% had a normal appearance and 13% had severe distention; in the air group, 7% had a normal appearance and 29% had severe distention.

Safety of CO_2 insufflation

All of the RCTs (Table 2) and 6 of the other studies (Table 3) had data related to the safety of administering CO_2. In sum, no adverse respiratory complications or episodes of suppressed ventilation were reported, although most studies excluded patients with severe respiratory compromise or chronic obstructive pulmonary disease with known CO_2 retention.

In the earliest report of CO_2 insufflation, 7 of 10 patients had arterial blood gas evaluation before and after colonoscopy.[5] The average pH was unchanged (7.46 before and 7.45 after colonoscopy), and the average partial pressure of carbon dioxide (pCO_2) was minimally increased but still within the normal reference range (37.3 mm Hg before and 40.6 mm Hg after colonoscopy). Two recent colonoscopy RCTs evaluated end-tidal CO_2 ($ETCO_2$) levels as a primary outcome.[3,12] In the first study, $ETCO_2$ actually decreased in both the CO_2 and air groups, although it fell less appreciably in the CO_2 group compared with the air group.[3] In the second study, no differences in $ETCO_2$ levels were noted between the CO_2 and

TABLE 1. Randomized controlled trials of CO_2 for insufflation in GI endoscopy

Study	Y	Blinding	Placebo	No. centers	CO_2 delivery system
Colonoscopy					
Bretthauer et al[12]	2005	Double	Air	1	Olympus ECR
Bretthauer et al[10]	2003	Double	Air	1	Olympus ECR
Church and Delaney[11]	2003	Single*	Air	1	CO_2 cylinder to specialized water bottle
Sumanac et al[9]	2002	Double	Air	1	Olympus ECR
Bretthauer et al[3]	2002	Double	Air	1	Olympus ECR
Stevenson et al[7]	1992	Double	Air	1	CO_2 cylinder to toggle switch
Flexible sigmoidoscopy†					
Bretthauer et al[8]	2002	Double	Air	1	Olympus ECR
ERCP					
Bretthauer et al[4]	2007	Double	Air	2‡	Olympus ECR
DBE					
Domagk et al[14]	2007	Double	Air	2‡	E-Z-EM Inc CO_2-EFFICIENT

*Patients were not aware of the insufflation gas.
†This was the only RCT to conform to the CONSORT statement guidelines.
‡The majority of patients were recruited from 1 center in each of these trials.

the air groups, although there was a slight increase in $ETCO_2$ for sedated patients compared with unsedated patients, regardless of the type of gas used for insufflation.

A study of submucosal endoscopic dissection during colonoscopy found a small increase in the arterial pCO_2 with CO_2 insufflation (mean rise 4.5 mm Hg), although the mean procedure length was 90 minutes.[16] A study of intraoperative colonoscopy with CO_2 insufflation in patients undergoing laparoscopy found a small increase of $ETCO_2$, with total values remaining in the normal range and with CO_2 pneumoperitoneum already established.[13]

Effect of CO_2 insufflation on other outcomes

Because of the heterogeneity of the studies published, a number of additional outcomes of interest can be reviewed. In a colonoscopy RCT, no difference in insufflated gas volumes was found between the CO_2 and air groups.[10] Lower sedation doses were reported for procedures with CO_2 insufflation compared with air for colonoscopy[16] as well as DBE.[14] There was a trend toward faster cecal intubation times in 1 colonoscopy RCT,[10] but there were no differences in procedure times reported for the flexible sigmoidoscopy RCT.[8] The use of CO_2 during colonoscopy also allowed for successful performance of barium enema in the case of incomplete colonoscopy,[2] and CO_2 insufflation for CT colonoscopy is also tolerated after incomplete conventional colonoscopy.[29] During DBE, deeper insertion depths[14] and higher procedure completion rates[15] were noted with CO_2 insufflation compared with air. No studies have yet been performed by using the single-balloon enteroscope. Also, an assessment of patient satisfaction (10-point scale) with colonoscopy showed no difference between the CO_2 and air groups, with the large majority of patients reporting that they were ''highly'' satisfied with the procedure, regardless of the type of gas used for insufflation.[11]

DISCUSSION

GI endoscopic procedures are widely performed for diagnostic and therapeutic purposes, and visualization of the mucosa relies on insufflating gas to distend the lumen of the GI tract. In the United States, ''room air'' is typically used for insufflation.[2-4] However, because ambient air is not well absorbed and must either be suctioned before the end of the procedure or passed from the GI tract as flatus, there is the potential for residual air to cause bowel distention and abdominal pain. CO_2 has the benefit of being rapidly absorbed from the intestinal lumen into the blood stream, then eliminated from the body via respiration.[3,17,18] The purpose of this systematic review was to assess data regarding the safety and efficacy of CO_2 insufflation during all types of GI endoscopy, with a focus on RCTs.

The overall results are striking, especially in light of the heterogeneity of the studies reviewed and the inability to use formal meta-analytic techniques. First, across all endoscopy types studied in a randomized fashion to date (colonoscopy, flexible sigmoidoscopy, ERCP, and DBE), and regardless of the way pain was quantified, there was

TABLE 2. Results from RCTs of CO_2 for insufflation in GI endoscopy

		No. patients*		Subjective results†			% Patients pain-free after the procedure						
							1 h		6 h		24 h		
Study	Y	Air	CO_2	Pain	Flatus	Bowel gas	Air	CO_2	Air	CO_2	Air	CO_2	Safety data
Colonoscopy studies													
Bretthauer et al[12]	2005	52	51	↓	n/r	n/r	17	63	40	70	52	70	No difference in $ETCO_2$ levels between groups
Bretthauer et al[10]	2003	123	126	n/r	n/r	n/r	n/r	n/r	n/r	n/r	n/r	n/r	Same amount of gas insufflated in each group
Church and Delaney[11]	2003	123	124	↓	n/r	n/r	n/r‡	n/r‡	n/r	n/r	n/r	n/r	No adverse respiratory complications reported
Sumanac et al[9]	2002	49	51	↓	↓	↓	55	93	69	91	82	85	No adverse respiratory complications reported
Bretthauer et al[3]	2002	121	119	↓	n/r	n/r	55	90	60	90	80	90	No adverse respiratory complications reported
Stevenson et al[7]	1992	27	29	↓	↓	↓	n/a	n/a	50	90	56	95	No adverse respiratory complications reported
Flexible sigmoidoscopy study													
Bretthauer et al[8]	2002	97	105	↓	n/r	n/r	64	84	64	78	90	90	No adverse respiratory complications reported
ERCP study													
Bretthauer et al[4]	2007	58	58	↓	n/r	↓	24	66	28	64	38	64	No difference in transdermal pCO_2 levels between groups
DBE study													
Domagk et al[14]	2007	48	52	↓	n/r	n/r	n/r	n/r	n/r	n/r	n/r	n/r	No adverse respiratory complications reported

n/r, Not reported.
*Number of patients analyzed per group in each study.
†The down arrow "↓" represents less pain, flatus, or bowel gas in the CO_2 group compared with the air group; these were measured with a variety of techniques, including visual analog scales, Likert scales, and radiologic scales.
‡This study reports pain 10 minutes after the procedure, with 81% pain free in the air group and 94% pain free in the CO_2 group.

less postprocedural pain for at least 6 hours in the CO_2 insufflation group compared with the air group. The data at the 24-hour time point were conflicting, with some studies that showed a persistent benefit in the CO_2 group and others that showed no difference among the groups by this time point. In addition, in the few studies that examined flatus or bowel distention, there was less flatus and less distention in the CO_2 group compared with the air group.

The literature is also remarkably consistent from the standpoint of safety of CO_2 insufflation. No significant respiratory events were reported in any of the studies reviewed, both for the RCTs and the non-RCTs. Moreover, several studies focused on the safety of CO_2 insufflation by assessing either arterial, end-tidal, or transcutaneous pCO2; no pathologic rise in pCO_2 levels, CO_2 retention, or ventilatory compromise was observed. A caveat to this finding, however, is that the majority of studies excluded patients with severe pulmonary comorbidities, and some early studies reported results for unsedated patients. In addition, it is possible that the consistency across these findings could also be explained, because a single group of investigators (Bretthauer et al[3,4,8,10,12,14]) initiated or participated in 6 of the 9 RCTs included in our analysis. Although additional confirmation from other centers would be helpful, the fact that the results are consistent across trial designs and endoscopic modalities speaks to their validity.

TABLE 3. Safety data from nonrandomized studies of CO_2 for insufflation in GI endoscopy

Study	Y	Procedure	Safety information
Hirai et al[15]	2007	DBE	No adverse respiratory complications reported
Saito et al[16]	2007	Submucosal dissection during colonoscopy	No adverse respiratory complications reported
Phaosawasdi et al[2]	1986	Colonoscopy followed by barium enema	No adverse respiratory complications reported
Rogers[23]	1985	Colonoscopy	No adverse respiratory complications reported
Hussein et al[6]	1984	Colonoscopy	No adverse respiratory complications reported
Rogers[5]	1974	Colonoscopy	No adverse respiratory complications reported; minimal increase in pCO2 without change in pH

Despite the consistent results from publications over the past 4 decades showing a benefit of CO_2 over air insufflation for a number of outcomes and endoscopic procedures, it appears that the use of CO_2 for insufflation has not been widely adopted in practice in the United States. In a cross-sectional study, Phaosawasdi et al[2] noted that only 15 of 146 hospitals in Illinois used CO_2 for colonoscopy. We hypothesize that there are several potential explanations for this. First, specialized equipment and a source of CO_2 are needed for insufflation with this gas. In the past, this was a major obstacle, but there are currently 2 U.S. Food and Drug Administration–approved devices that are commercially available and compatible with current endoscopic technology (CO_2-EFFICIENT [E-Z-EM Inc, Lake Success, NY] and Olympus Endoscopy CO_2 Regulator (Olympus ECR) [KeyMed Ltd, Essex, U.K.]). It may be that the cost of these devices exceeds the perceived benefit of using CO_2, or it may be that gastroenterologists are not aware of these devices, but these conjectures remain to be studied.

Second, it is possible that the currently known benefits of CO_2 insufflation (decreased postprocedural pain, flatus, and bowel distention) are not felt to be "important" enough to warrant the use of new equipment, especially given that most of the differences between the groups appear to merge at 24 hours. The true impact of these outcomes on patients, however, is not known. It is possible that, if CO_2 use leads to shorter procedure times, more effective procedures (eg, in the case of DBE), lower doses of sedation medications, and faster recovery times, then the overall costs of endoscopic procedures could be decreased, with an increase in procedural efficiency.

The indirect costs of endoscopy, including next-day absenteeism, may be substantial and potentially underappreciated by endoscopists. This point is illustrated by studies that examined the total time required for screening colonoscopy and recovery from a patient perspective. Jonas et al[30] reported that 17% of patients require more than 24 hours to recover from screening colonoscopy. Similarly, Ko et al[31] reported that 20% of subjects need at least 2 or more days before they are able to return to their normal activities, including work. In both circumstances, the investigators thought that decreased productivity from missed work should factor into the overall cost:benefit ratio of endoscopic procedures. These observations, in the context of the suboptimal screening colonoscopy uptake rate (in the 30%-40% range)[32,33] and large numbers of procedures already performed,[1,34] imply that any improvement in patient tolerance is important. Whether individual benefits that might result from CO_2 insufflation could translate to larger benefits on a population scale in the form of increased colorectal cancer screening rates or decreased absenteeism is unclear.

Third, there may also be a concern about the safety of CO_2 insufflation, particularly in patients with pulmonary disease. In patients without underlying pulmonary disease, however, the current literature is clear: CO_2 insufflation for endoscopic procedures is safe. Because it is possible that patients with respiratory disorders, sleep apnea, or morbid obesity, or with known CO_2 retention may be at risk for ventilatory compromise with CO_2 insufflation, it would be prudent to continue to use room-air insufflation in these potentially at-risk populations until the question is further studied. An additional benefit of using CO_2 for insufflation is that this gas reduces the risk of colonic gas explosion during colonoscopies with electrocautery compared with air insufflation.[35]

In conclusion, this systematic review of the use of CO_2 insufflation for GI endoscopic procedures shows that RCT-level evidence for a number of difference endoscopic techniques supports the safety and efficacy of the use of CO_2 compared with insufflation of room air. Additional work is needed, however, to address the extent to which CO_2 insufflation has or has not been adopted, the factors explaining the lack of adoption in light of the published evidence, and the effect of CO_2 insufflation in higher-risk populations.

REFERENCES

1. Seeff LC, Richards TB, Shapiro JA, et al. How many endoscopies are performed for colorectal cancer screening? Results from CDC's survey of endoscopic capacity. Gastroenterology 2004;127:1670-7.
2. Phaosawasdi K, Cooley W, Wheeler J, et al. Carbon dioxide–insufflated colonoscopy: an ignored superior technique. Gastrointest Endosc 1986;32:330-3.

3. Bretthauer M, Thiis-Evensen E, Huppertz-Hauss G, et al. NORCCAP (Norwegian colorectal cancer prevention): a randomised trial to assess the safety and efficacy of carbon dioxide versus air insufflation in colonoscopy. Gut 2002;50:604-7.
4. Bretthauer M, Seip B, Aasen S, et al. Carbon dioxide insufflation for more comfortable endoscopic retrograde cholangiopancreatography: a randomized, controlled, double-blind trial. Endoscopy 2007;39: 58-64.
5. Rogers BH. The safety of carbon dioxide insufflation during colonoscopic electrosurgical polypectomy. Gastrointest Endosc 1974;20: 115-7.
6. Hussein AM, Bartram CI, Williams CB. Carbon dioxide insufflation for more comfortable colonoscopy. Gastrointest Endosc 1984;30:68-70.
7. Stevenson GW, Wilson JA, Wilkinson J, et al. Pain following colonoscopy: elimination with carbon dioxide. Gastrointest Endosc 1992;38: 564-7.
8. Bretthauer M, Hoff G, Thiis-Evensen E, et al. Carbon dioxide insufflation reduces discomfort due to flexible sigmoidoscopy in colorectal cancer screening. Scand J Gastroenterol 2002;37:1103-7.
9. Sumanac K, Zealley I, Fox BM, et al. Minimizing postcolonoscopy abdominal pain by using CO(2) insufflation: a prospective, randomized, double blind, controlled trial evaluating a new commercially available CO(2) delivery system. Gastrointest Endosc 2002;56:190-4.
10. Bretthauer M, Hoff GS, Thiis-Evensen E, et al. Air and carbon dioxide volumes insufflated during colonoscopy. Gastrointest Endosc 2003;58:203-6.
11. Church J, Delaney C. Randomized, controlled trial of carbon dioxide insufflation during colonoscopy. Dis Colon Rectum 2003;46:322-6.
12. Bretthauer M, Lynge AB, Thiis-Evensen E, et al. Carbon dioxide insufflation in colonoscopy: safe and effective in sedated patients. Endoscopy 2005;37:706-9.
13. Nakajima K, Lee SW, Sonoda T, et al. Intraoperative carbon dioxide colonoscopy: a safe insufflation alternative for locating colonic lesions during laparoscopic surgery. Surg Endosc 2005;19:321-5.
14. Domagk D, Bretthauer M, Lenz P, et al. Carbon dioxide insufflation improves intubation depth in double-balloon enteroscopy: a randomized, controlled, double-blind trial. Endoscopy 2007;39:1064-7.
15. Hirai F, Matsui T, Yao K, et al. Efficacy of carbon dioxide insufflation in endoscopic balloon dilation therapy by using double balloon endoscopy. Gastrointest Endosc 2007;66:S26-9.
16. Saito Y, Uraoka T, Matsuda T, et al. 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;65:537-42.
17. Brandt LJ, Boley SJ, Sammartano R. Carbon dioxide and room air insufflation of the colon. Effects on colonic blood flow and intraluminal pressure in the dog. Gastrointest Endosc 1986;32:324-9.
18. Yasumasa K, Nakajima K, Endo S, et al. Carbon dioxide insufflation attenuates parietal blood flow obstruction in distended colon: potential advantages of carbon dioxide insufflated colonoscopy. Surg Endosc 2006;20:587-94.
19. Moher D, Schulz KF, Altman D. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. JAMA 2001;285:1987-91.
20. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;283:2008-12.
21. Cook DJ, Sackett DL, Spitzer WO. Methodologic guidelines for systematic reviews of randomized control trials in health care from the Potsdam Consultation on Meta-Analysis. J Clin Epidemiol 1995;48:167-71.
22. Rogers BH. Carbon dioxide for colonoscopy. Gastroenterology 1980;78:1659-60.
23. Rogers BH. CO_2 during colonoscopy for safety and comfort. Gastrointest Endosc 1985;31:108-9.
24. Williams CB. Who's for CO_2? Gastrointest Endosc 1986;32:365-7.
25. Jackson FW. CO_2 is easy. Am J Gastroenterol 2001;96:3035-6.
26. Bretthauer M, Hoff G. The use of CO_2 in colonoscopy. Gastrointest Endosc 2003;57:436-7; author reply 437–8.
27. Nakajima K, Yasumasa K, Endo S, et al. A versatile dual-channel carbon dioxide (CO_2) insufflator for various CO_2 applications. The prototype. Surg Endosc 2006;20:334-8.
28. Nelson DB, Freeman ML, Silvis SE, et al. A randomized, controlled trial of transcutaneous carbon dioxide monitoring during ERCP. Gastrointest Endosc 2000;51:288-95.
29. Yucel C, Lev-Toaff AS, Moussa N, et al. CT colonography for incomplete or contraindicated optical colonoscopy in older patients. AJR Am J Roentgenol 2008;190:145-50.
30. Jonas DE, Russell LB, Sandler RS, et al. Patient time requirements for screening colonoscopy. Am J Gastroenterol 2007;102:2401-10.
31. Ko CW, Riffle S, Shapiro JA, et al. Incidence of minor complications and time lost from normal activities after screening or surveillance colonoscopy. Gastrointest Endosc 2007;65:648-56.
32. Lieberman DA, Holub J, Eisen G, et al. Utilization of colonoscopy in the United States: results from a national consortium. Gastrointest Endosc 2005;62:875-83.
33. Maciosek MV, Solberg LI, Coffield AB, et al. Colorectal cancer screening: health impact and cost effectiveness. Am J Prev Med 2006;31:80-9.
34. Hur C, Gazelle GS, Zalis ME, et al. An analysis of the potential impact of computed tomographic colonography (virtual colonoscopy) on colonoscopy demand. Gastroenterology 2004;127:1312-21.
35. Ladas SD, Karamanolis G, Ben-Soussan E. Colonic gas explosion during therapeutic colonoscopy with electrocautery. World J Gastroenterol 2007;13:5295-8.

Received April 24, 2008. Accepted May 28, 2008.

Current affiliations: Center for Esophageal Diseases and Swallowing (E.S.D., N.J.S.), Center for Gastrointestinal Biology and Disease (E.S.D., N.J.S.), Division of Gastroenterology and Hepatology (E.S.D., J.S.H., I.S.G., N.J.S.), Department of Medicine, University of North Carolina School of Medicine, Chapel Hill, North Carolina, USA.

Reprint requests: Evan S. Dellon MD, Medicine—Gastroenterology/ Hepatology, CB 7080, Bioinformatics Bldg, 130 Mason Farm Rd, University of North Carolina—Chapel Hill, Chapel Hill, NC 27599-7080.