



## The use of carbon dioxide in gastrointestinal endoscopy

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This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy (ASGE).

*The American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee provides reviews of existing, new, or emerging endoscopic technologies that have an impact on the practice of gastrointestinal endoscopy. Evidence-based methodology is used by performing a MEDLINE literature search to identify pertinent clinical studies on the topic as well as a MAUDE (U.S. Food and Drug Administration Center for Devices and Radiological Health) database search to identify the reported adverse events of a given technology. Both are supplemented by accessing the “related articles” feature of PubMed and by scrutinizing pertinent references cited by the identified studies. Controlled clinical trials are emphasized, but in many cases, data from randomized, controlled trials are lacking. In such cases, large case series, preliminary clinical studies, and expert opinions are used. Technical data are gathered from traditional and Web-based publications, proprietary publications, and informal communications with pertinent vendors. Technology Status Evaluation Reports are drafted by 1 or 2 members of the ASGE Technology Committee, reviewed and edited by the Committee as a whole, and approved by the Governing Board of the ASGE. When financial guidance is indicated, the most recent coding data and list prices at the time of publication are provided. For this review, the MEDLINE database was searched through December 2014 for relevant articles by using the key words “carbon dioxide” and “gastrointestinal endoscopy,” combined with other relevant terms such as “esophagogastroduodenoscopy,” “ERCP,” “balloon enteroscopy,” “colonoscopy,” and “complications or adverse events,” among others. Technology Status Evaluation Reports are scientific reviews provided solely for educational and informational purposes. Technology Status Evaluation Reports are not rules and should not be construed as establishing a legal standard of care or as encouraging, advocating,*

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### BACKGROUND

Adequate distension of the GI lumen is required for safe advancement of endoscopes and for careful visualization of the mucosa. Room air, which is widely used for GI luminal distension, possesses the advantages of universal availability and low cost. However, room air is poorly absorbed by the GI tract and is largely evacuated through belching or passage of flatus. To minimize postprocedural abdominal distention, endoscopists commonly suction out as much air as possible after completion of the procedure and immediately before removal of the endoscope. Despite this practice, older studies indicated that 50% of patients reported pain after completion of colonoscopy, with 12% of patients describing the pain as severe, even at 24 hours after the procedure.<sup>1</sup> Despite improvements in endoscope technology and techniques leading to shorter procedure times with lower amounts of air insufflated, some patients still experience postprocedure pain related to distension. Carbon dioxide (CO<sub>2</sub>) is rapidly absorbed by the GI mucosa, driving increased interest in its use as an insufflation agent for endoscopic procedures. The ASGE has previously published a Technology Status Evaluation Report on methods of luminal distention, including CO<sub>2</sub>, for colonoscopy alone.<sup>2</sup> This document discusses CO<sub>2</sub> as an insufflation agent for all endoscopic procedures within the GI tract.

### TECHNOLOGY UNDER REVIEW

CO<sub>2</sub> is absorbed from the GI tract approximately 160 times faster than nitrogen, the major gaseous ingredient of ambient air,<sup>3</sup> and is therefore considered by many to be a superior alternative to room air for insufflation during GI endoscopy.<sup>4,5</sup> It is passively absorbed through the mucosal lining into the bloodstream and eventually exhaled through the lungs. The rapid absorption of CO<sub>2</sub>

and the potential associated benefits were initially demonstrated in rat colon model studies, which indicated that CO<sub>2</sub> insufflation was associated with a significantly shorter duration of recovery from luminal distension and elevated intraluminal pressures, compared with room air.<sup>6,7</sup> A human study, evaluating colonoscopy performed with CO<sub>2</sub> insufflation for the localization of colonic lesions during laparoscopic surgery, demonstrated complete colonic decompression over a mean period of 21 minutes.<sup>8</sup>

Randomized studies comparing CO<sub>2</sub> and air insufflation during colonoscopy have indicated no significant differences in the volume of gas insufflated during the procedure.<sup>9,10</sup> Procedure time, dosage of sedation medications, and intraprocedural discomfort experienced by patients were similar between CO<sub>2</sub> and air insufflation groups. However, CO<sub>2</sub> insufflation was associated with less postprocedural pain and distension, indicating that the benefits of CO<sub>2</sub> insufflation predominantly manifest after completion of the endoscopic procedure. The lower pain scores and smaller increases in abdominal girth reported after procedures with CO<sub>2</sub> insufflation compared with air insufflation suggest that the benefits of CO<sub>2</sub> are related to its rapid absorption from the GI tract. This theory is further supported by a randomized controlled study in which 100 patients undergoing colonoscopy were divided into 3 groups: air insufflation only during both colonoscope insertion and withdrawal, air during insertion and CO<sub>2</sub> during withdrawal, and CO<sub>2</sub> only during both colonoscope insertion and withdrawal.<sup>11</sup> Patients in both the CO<sub>2</sub> only and air plus CO<sub>2</sub> combination groups experienced significantly less postprocedural pain than those in the air only group an hour after the procedure (both  $P \leq .001$ ). These results also suggest that residual gaseous distension after completion of endoscopic procedures causes postprocedural pain and that CO<sub>2</sub>, which dissipates significantly faster than air, is associated with less postprocedural pain.

Animal studies suggest that an additional potential mechanism for the reduction in pain postprocedure may be the vasodilator effect of CO<sub>2</sub> and its consequent impact on blood flow within a distended colon.<sup>4,7</sup> The mean blood flow within the inferior mesenteric artery of dogs during use of CO<sub>2</sub> as an insufflation agent increased by 109% to 155% above baseline during periods of transiently elevated intraluminal pressure compared with mean blood flows at or below baseline noted with air insufflation.<sup>4</sup> In another study, parietal blood flow in rats decreased after either CO<sub>2</sub> or air insufflation but returned to baseline within 5 minutes in the CO<sub>2</sub> group compared with a persistent decrease for 30 minutes in the air insufflation group.<sup>7</sup> The authors have speculated that the prolonged bowel distension and associated decrease in parietal blood flow seen with air insufflation may contribute to abdominal pain.

## CO<sub>2</sub> delivery

Currently, CO<sub>2</sub> delivery during endoscopy is performed by using CO<sub>2</sub> regulators. The primary purpose of the CO<sub>2</sub> regulator is to govern gas flow to rates that are safe for use in endoscopy. A CO<sub>2</sub> source, either a wall-based CO<sub>2</sub> outlet (in endoscopy suites that are equipped with a medical gas pipeline) or a portable CO<sub>2</sub> cylinder is connected by tubing to the CO<sub>2</sub> regulator (Fig. 1). Disposable tubing then delivers CO<sub>2</sub> from the regulator to a dedicated water bottle attached to the endoscopy light source.

CO<sub>2</sub> regulators are commercially available from 3 manufacturers in the United States, including Medivators Inc (Minneapolis, Minn), Bracco Diagnostics Inc (Monroe Township, NJ), and Olympus America Inc (Center Valley, Pa) (Table 1). All of these CO<sub>2</sub> regulators are compact, lightweight units that are easily integrated into standard endoscopy workstations. All are capable of connecting to either a wall-based CO<sub>2</sub> source or a portable CO<sub>2</sub> cylinder. The CO<sub>2</sub> regulators have various flow rate settings and visual or auditory alerts to indicate a low gas reserve and/or inflow pressure. Although all 3 units are compatible with all major endoscopy systems available in the United States, only 2 of the major endoscope manufacturers (Fujifilm Endoscopy, Fujinon Inc, Wayne, NJ) and Pentax (Pentax of America Inc, Montvale, NJ) have endorsed compatibility of the CO<sub>2</sub> regulators with their systems. One CO<sub>2</sub> regulator has an integrated warmer, which allows delivery of CO<sub>2</sub> at body temperature (98.6°F).

## Clinical experience

A systematic review of 9 randomized controlled studies (6 colonoscopy studies and 1 study each for sigmoidoscopy, ERCP, and double-balloon endoscopy [DBE]) evaluating CO<sub>2</sub> as an insufflation agent for GI endoscopy demonstrated improved outcomes after use of CO<sub>2</sub> for endoscopic procedures.<sup>12</sup> All studies found that CO<sub>2</sub> was superior to room air, with CO<sub>2</sub> insufflated patients experiencing less postprocedural pain and bowel distention. The review concluded that CO<sub>2</sub> insufflation appeared to be safe. Of note, patients with underlying pulmonary disease were excluded from most studies.

To date, there are 36 published randomized controlled studies, 30 performed in a double-blind fashion, that have compared CO<sub>2</sub> with ambient air or water as insufflation agents during GI endoscopy.<sup>1,9,10,13-45</sup> Most of the studies evaluated insufflation during colonoscopy (23 studies) and ERCP (6 studies). Three studies were designed to compare air with CO<sub>2</sub> as insufflation agents during balloon-assisted enteroscopy, 2 during endoscopic submucosal dissection (ESD), 1 during combined colonoscopy and EGD, and 1 during flexible sigmoidoscopy. CO<sub>2</sub> was

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