

## Sedation and anesthesia in GI endoscopy

*This is one of a series of statements discussing the use of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy (ASGE) prepared this text. In preparing this guideline, a search of the medical literature was performed by using MEDLINE and PubMed databases through May 2008 that related to the topic of "sedation and anesthesia for gastrointestinal endoscopy" by using the key word(s) "sedation," "anesthesia," "propofol," "gastrointestinal endoscopy," "endoscopy," "endoscopic procedures," and "procedures." The search was supplemented by accessing the "related articles" feature of PubMed, with articles identified on MEDLINE and PubMed as the references. Pertinent studies published in English were reviewed. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When little or no data exist from well-designed prospective trials, emphasis is given to results from large series and reports from recognized experts. Guidelines for appropriate use of endoscopy are based on a critical review of the available data and expert consensus at the time the guidelines are drafted. Further controlled clinical studies may be needed to clarify aspects of this guideline. This guideline may be revised as necessary to account for changes in technology, new data, or other aspects of clinical practice. The recommendations were based on reviewed studies and were graded on the strength of the supporting evidence (Table 1).*

*This guideline is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. This guideline is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical decisions in any particular case involve a complex analysis of the patient's condition and available courses of action. Therefore, clinical considerations may lead an endoscopist to take a course of action that varies from these guidelines.*

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### BACKGROUND

Sedation may be defined as a drug-induced depression in the level of consciousness. The purpose of sedation and analgesia is to relieve patient anxiety and discomfort, improve the outcome of the examination, and diminish the patient's memory of the event. Practice guidelines have been put forth by the American Society of Anesthesiologists (ASA) Committee for Sedation and Analgesia, Non-Anesthesiologists, and approved by the ASGE.<sup>1,2</sup>

Four stages of sedation have been described, ranging from minimal to moderate, deep, and general anesthesia (Table 2). In general, most endoscopic procedures are performed with the patient under moderate sedation, a practice that was formerly referred to as "conscious sedation."

At the level of moderate sedation, the patient, while maintaining ventilatory and cardiovascular function, is able to make purposeful responses to verbal or tactile stimulation. In contrast, a patient undergoing deep sedation cannot be easily aroused but may still respond purposefully to repeated or painful stimulation. Airway support may be required for deep sedation. At the level of general anesthesia, the patient is unarousable to painful stimuli, and cardiovascular function may be impaired.

The level of sedation should be titrated to achieve a safe, comfortable, and technically successful endoscopic procedure. Knowledge of the pharmacologic profiles of sedative agents is necessary to maximize the likelihood that the desired level of sedation is targeted accurately.

Individuals differ in their response to sedation, so patients may require different levels of sedation for the same procedure and patients may attain varying levels of sedation during a single procedure. Therefore, practitioners should possess the skills necessary to resuscitate or rescue a patient whose level of sedation is deeper than initially intended. This statement will evaluate the strength of evidence in the medical literature to provide guidelines for the use of sedation and anesthesia during GI endoscopic procedures and is an update of 3 previous ASGE documents.<sup>2-4</sup>

### PREPROCEDURE PREPARATION AND ASSESSMENT

Patients should be informed of and agree to the administration of sedation/analgesia/anesthesia, including

**TABLE 1. Grades of recommendation**

Grade of recommendation	Clarity of benefit	Methodologic strength/supporting evidence	Implications
1A	Clear	Randomized trials without important limitations	Strong recommendation; can be applied to most clinical settings
1B	Clear	Randomized trials with important limitations (inconsistent results, nonfatal methodologic flaws)	Strong recommendation; likely to apply to most practice settings
1C+	Clear	Overwhelming evidence from observational studies	Strong recommendation; can apply to most practice settings in most situations
1C	Clear	Observational studies	Intermediate-strength recommendation; may change when stronger evidence is available
2A	Unclear	Randomized trials without important limitations	Intermediate-strength recommendation; best action may differ depending on circumstances or patients' or societal values
2B	Unclear	Randomized trials with important limitations (inconsistent results, nonfatal methodologic flaws)	Weak recommendation; alternative approaches may be better under some circumstances
2C	Unclear	Observational studies	Very weak recommendation; alternative approaches likely to be better under some circumstances
3	Unclear	Expert opinion only	Weak recommendation; likely to change as data become available

Adapted from Guyatt G, Sinclair J, Cook D, et al. Moving from evidence to action: grading recommendations—a qualitative approach. In: Guyatt G, Rennie D, eds. *Users' guides to the medical literature*. Chicago: AMA Press; 2002. pp. 599-608.

**TABLE 2. Levels of sedation and anesthesia**

	Minimal sedation (anxiolysis)	Moderate sedation (conscious sedation)	Deep sedation	General anesthesia
Responsiveness	Normal response to verbal stimulation	Purposeful response to verbal or tactile stimulation	Purposeful response after repeated or painful stimulation	Unarousable even with painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

Modified from Gross JB, Bailey PL, Connis RT, et al. Practice guidelines for sedation and analgesia by nonanesthesiologists. *Anesthesiology* 2002;96:1004-17.

discussion of its benefits, risks, and limitations and possible alternatives.

The anticipated level of sedation should be congruent with the patient's expectation of the sedation level whenever possible. There are no absolute guidelines as to timing of cessation of oral intake before administration of sedation because of the absence of supporting data with regard to a direct relationship between duration of fasting and risk of pulmonary aspiration. The ASA guidelines recommend that patients should not consume fluids or solid foods for a sufficient period of time so as to permit ade-

quate gastric emptying.<sup>1</sup> The ASA guidelines state that patients should fast a minimum of 2 hours after consuming clear liquids and 6 hours after consuming light meals before the administration of sedation. The American College of Emergency Physicians<sup>5</sup> states, "recent food intake is not contraindicated for administering procedural sedation and analgesia, but should be considered in choosing the timing and target of sedation."

In situations where gastric emptying is impaired or in emergency situations, the potential for pulmonary aspiration of gastric contents must be considered in determining

(1) the target level of sedation, (2) whether the procedure should be delayed, or (3) whether the airway should be protected by endotracheal intubation. All patients undergoing endoscopic procedures require preprocedural evaluation to assess the risk of sedation and to manage problems related to preexisting medical conditions.

A history and physical examination, with particular emphasis on sedation-oriented issues, should be performed at the time of endoscopy. The following historic details should be sought: (1) abnormalities of major organ systems; (2) snoring, stridor, or sleep apnea; (3) drug allergies, current medications, and potential for drug interactions; (4) prior adverse reaction(s) to sedatives or anesthetics; (5) time of and type of last oral intake; and (6) tobacco, alcohol, or substance use.<sup>1</sup> The physical examination should include the following: measurement of vital signs, determination of baseline level of consciousness, and examination of the heart and lungs and airway anatomy.<sup>1</sup> Table 3 shows the ASA classification used to risk stratify patients for sedation.

In addition, all women of childbearing age should be queried about the possibility of pregnancy. Pregnancy testing may be considered in women of childbearing age unless they have had a total hysterectomy, bilateral tubal ligation, or absent menses for 1 year (menopause). The preprocedure assessment should be documented and a "time out" should be performed before patients are sedated. This includes verification of patient identification and confirmation of correct procedure by the procedural team.

## UNSEDATED ENDOSCOPY

Selected patients may be able to undergo endoscopic procedures without sedation. Small-diameter endoscopes (less than 6 mm) can improve the tolerability of upper endoscopy when sedation is not used.<sup>6,7</sup> In general, topical anesthesia is used during unsedated endoscopy. Successful colonoscopy may be performed in selected patients who receive no sedation or sedation only if needed.<sup>8,9</sup> Older patients, men, patients who are not anxious, or patients without a history of abdominal pain may have better tolerance of upper endoscopy or colonoscopy with little or no sedation. For procedures performed without medications, the types of and levels of monitoring should be individualized. However, preparation should be the same as described for sedation in the event that sedation is administered.

## TOPICAL ANESTHESIA

Topical pharyngeal sprays with lidocaine, tetracaine, and benzocaine are often used for anesthetic purposes during upper endoscopy, particularly when unsedated endoscopy is performed. A meta-analysis of pharyngeal anesthesia use in conjunction with intravenous or intra-

**TABLE 3. ASA classification**

Class	Description
I	The patient is normal and healthy.
II	The patient has mild systemic disease that does not limit activities (eg, controlled hypertension or controlled diabetes without systemic sequelae).
III	The patient has moderate or severe systemic disease that does not limit the activities (eg, stable angina or diabetes with systemic sequelae).
IV	The patient has severe systemic disease that is a constant threat to life (eg, severe congestive heart failure, end-stage renal failure).
V	The patient is morbid and is at a substantial risk of death within 24 hours (with or without a procedure).
E	Emergency status: in addition to indicating the underlying ASA status (1-5), any patient undergoing an emergency procedure is indicated by suffix "E."

muscular sedation was associated with improved ease of endoscopy or improved patient tolerance as judged by the endoscopist during upper endoscopy.<sup>10</sup> Topical anesthetic agents have been associated with serious adverse effects, including aspiration, anaphylactoid reactions, and methemoglobinemia.

## SEDATION AND ANALGESIA AGENTS USED FOR ENDOSCOPY

The level of sedation required to perform a successful procedure may range from minimal sedation to general anesthesia. Patient age, health status, concurrent medications, preprocedural anxiety, and pain tolerance influence the level of sedation required to achieve the desired result.

The procedural variables include the degree of invasiveness, the level of procedure-related discomfort, the need for the patient to lie relatively motionless (eg, EUS-FNA) and the duration of examination. Typically, diagnostic and uncomplicated therapeutic upper endoscopy and colonoscopy are successfully performed with moderate sedation. Deeper levels of sedation may be considered for longer and more complex procedures, including, but not limited to, ERCP and EUS. Additionally, deep sedation or general anesthesia should be considered for patients who have been difficult to manage with moderate sedation and are anticipated to be poorly responsive to sedatives. This includes patients who have had long-term use of narcotics, benzodiazepines, alcohol, or neuropsychiatric medications.

The choice of sedative is largely operator dependent and is based on maximizing patient comfort while minimizing risks. The choice of sedatives generally consists of benzodiazepines used either alone or in combination

with an opiate. The most commonly used benzodiazepines are midazolam and diazepam. The efficacy of sedation with these 2 benzodiazepines is comparable.<sup>11</sup> However, most endoscopists favor midazolam for its fast onset of action, short duration of action, and high amnesic properties.<sup>3</sup> Opioids, such as meperidine and fentanyl administered intravenously, provide both analgesia and sedation. Fentanyl has a more rapid onset of action and clearance and has a lower incidence of nausea compared with meperidine. Combinations of benzodiazepine and opioid agents are frequently used for synergism. These pharmacologic profiles of the benzodiazepines and opioids are discussed in a previously published ASGE document.<sup>3</sup> Specific antagonists of opiates (naloxone) and benzodiazepines (flumazenil) are available and should be present and readily available in every endoscopy unit.

Adjuncts to the benzodiazepine/narcotic combination include diphenhydramine, promethazine, and droperidol. These medications potentiate the action of the benzodiazepine/narcotic regimen; thus, a deeper level of sedation may result. Droperidol is a neuroleptic agent in the same class as haloperidol with sedative effects. Randomized trials have demonstrated the efficacy of droperidol in patients undergoing therapeutic endoscopy, particularly those who are difficult to sedate.<sup>12-15</sup>

The Food and Drug Administration (FDA) black box warning for droperidol states that the drug should be used only when first-line sedative agents fail to provide adequate sedation.<sup>16</sup> The use of droperidol is contraindicated in patients with prolongation of the QTc interval (defined as >440 milliseconds in men and >450 milliseconds in women), and its use should be avoided in patients who are at an increased risk for the development of a prolonged QT interval. These risks include a history of congestive heart failure, bradycardia, diuretic use, cardiac hypertrophy, hypokalemia, hypomagnesemia, and use of other drugs that prolong the QT interval. Other risk factors may include age more than 65 years, alcohol abuse, and use of agents such as benzodiazepines, volatile anesthetics, and intravenous opiates.<sup>17</sup> Droperidol should be initiated at a low dose and adjusted upward, with caution, as needed to achieve the desired effect.<sup>17</sup>

Guidelines for the use of droperidol have been published in a consensus statement issued by the ASGE (Table 4).<sup>2</sup>

Sedation during pregnancy and lactation raises specific issues that are discussed in a previous ASGE document.<sup>18</sup> Guidelines for sedation and anesthesia in the pediatric population have also been addressed in a previous ASGE document.<sup>19</sup>

## Propofol

Propofol (2,6-diisopropyl phenol) is classified as an ultrashort-acting hypnotic agent that provides sedative, amnesic, and hypnotic effects with no analgesic properties. Propofol rapidly crosses the blood-brain barrier and

**TABLE 4. Guidelines for the use of droperidol for endoscopic procedures**

- Use only in select patients with:
  - Inability to achieve an acceptable response or intolerance to standard sedatives
  - Anticipated long procedure
- Obtain 12-lead ECG before procedure. Droperidol is contraindicated if the QTc is prolonged (>440 milliseconds in males, >450 milliseconds in females).
- Patients should remain on a cardiac monitor during the procedure and for 2-3 hours afterward.
- Use with caution in patients at high risk for development of prolonged QT syndrome such as congestive heart failure, bradycardia, cardiac hypertrophy, hypokalemia/magnesemia, or other drugs known to prolong the QTc interval.
- Dosage: In adults, the initial dose should not exceed 2.5 mg. Additional doses should be in 1.25 mg aliquots to achieve the desired patient sedation.

causes a depression in consciousness that is likely related to potentiation of the  $\gamma$ -aminobutyric acid A receptor in the brain.<sup>20</sup> The drug is highly lipophilic. Two preparations exist. One is prepared as an oil/water emulsion consisting of 1% propofol, 10% soybean oil, 2.25% glycerol, and 1.2% egg lecithin. Therefore, propofol is contraindicated in patients with propofol allergy or hypersensitivity to eggs or soybean.<sup>21</sup> Another preparation has bisulfites; therefore, allergies/reactions to bisulfites also have to be taken into account. It is a pregnancy category B drug and should be used with caution during lactation. Propofol is 98% plasma-protein bound, and it is metabolized primarily in the liver by conjugation to glucuronide and sulfate to produce water-soluble compounds that are excreted by the kidney. Typically, the time from injection to the onset of sedation is 30 to 60 seconds. Its duration of effect is 4 to 8 minutes. The pharmacokinetic properties do not significantly change in patients with renal failure or moderately severe chronic liver disease. Dose reduction is required in patients with cardiac dysfunction and in the elderly as a result of decreased clearance of the drug.<sup>22</sup>

Propofol potentiates the central nervous system effects of narcotic analgesics and sedatives such as benzodiazepines, barbiturates, and droperidol; therefore, the dose requirements of these agents may be reduced. Pain on injection is frequent, occurring in up to 30% of patients receiving an intravenous bolus of propofol.<sup>23</sup> The cardiovascular effects of propofol include decreases in cardiac output, systemic vascular resistance, and arterial pressure.<sup>24</sup> Negative cardiac inotropy and respiratory depression can be seen with the use of propofol. These effects reverse rapidly with dose reduction or interruption of drug infusion<sup>25</sup> and rarely require temporary ventilatory

support. There is no reversal agent for propofol.<sup>26,27</sup> Personnel specifically trained in the administration of propofol with expertise in emergency airway management must be present during use of this agent, and the patient's physiologic parameters must be continuously monitored (Table 5). Details of preprocedure assessment, intra-procedural monitoring and documentation, and postprocedure recovery of patients undergoing sedation with propofol are discussed in a previously published ASGE training guideline.<sup>4</sup> Recently, a water-soluble prodrug of propofol (fospropofol sodium) has been developed,<sup>28</sup> although it is not yet FDA approved. The prodrug is activated to propofol after removal of the water-soluble moiety by endothelial alkaline phosphatase. Preliminary studies suggest that it is relatively safe and effective for sedation during colonoscopy.<sup>29</sup>

Additional anesthetic agents that have been used for endoscopic procedures include ketamine, dexmedetomidine, and inhalational agents.

### Who is qualified to give propofol?

The use of propofol for endoscopic sedation has increased markedly during the past 10 years. Twenty-five percent of respondents to one U.S. survey indicated that propofol is used for sedation during routine endoscopic procedures.<sup>30</sup> However, only 7.7% of these respondents administer propofol without an anesthesiologist or a nurse anesthetist.

The use of propofol varies considerably from one region of the country to another, depending on a variety of factors such as reimbursement by insurance carriers for anesthesia services, institutional and state policies, and variations in practice patterns.<sup>30</sup> Propofol administered by endoscopists or endoscopy nurses is more prevalent in other countries.<sup>31</sup>

Sixty-eight percent of U.S. endoscopists using conventional sedation indicate that they would like to administer propofol but are reluctant to do so because of a widespread perception of increased complication risks.<sup>30</sup> Additionally, some endoscopists are either unwilling or unable to administer propofol themselves because of local institutional policy, state regulatory restrictions, or concern for the medicolegal implications of off-label use of propofol.<sup>32</sup>

These concerns are at least partly due to the current FDA-approved product label, which states that propofol should be administered only by individuals trained in the administration of general anesthesia.<sup>33</sup>

Nonanesthesiologist-administered propofol for GI procedures is termed gastroenterologist-directed propofol (GD-P). FDA-approved product labels can be used as evidence in court in a case related to the off-label use of GD-P in cases involving adverse outcomes.<sup>16</sup> However, U.S. courts and jurisdictions differ on whether the label alone establishes the standard of care in individual cases. At this time, data and expert editorial opinions have accrued supporting the use of GD-P, including endorsement by gastro-

**TABLE 5. Recommendations for propofol use during endoscopy**

- A sedation team with appropriate education and training. At least 1 person who is qualified in advanced life support skills (ie, airway management, defibrillation and the use of resuscitative medications).
- Trained personnel dedicated to the uninterrupted monitoring of the patient's clinical and physiologic parameters throughout the procedure
- Physiologic monitoring must include pulse oximetry, electrocardiography, and intermittent blood pressure measurement. Monitoring oxygenation by pulse oximetry is not a substitute for monitoring ventilatory function. Capnography should be considered because it may decrease the risks during deep sedation. Continuous monitoring will allow recognition of patients who have progressed to a deeper level of sedation.
- Personnel should have the ability to rescue a patient who becomes unresponsive or unable to protect his or her airway or who loses spontaneous respiratory or cardiovascular function.
- Age-appropriate equipment for airway management and resuscitation must be immediately available.
- A physician should be present throughout propofol sedation and remain immediately available until the patient meets discharge criteria.

enterology specialty societal guidelines. U.S. courts and jurisdictions may or may not consider this this mass of opinions and guidelines supporting GD-P to be medicolegally reasonable or a respectable minority practice.

The narrow therapeutic window of propofol that distinguishes it from conventional sedative hypnotics used for endoscopy increases the risk for cardiopulmonary complications if it is not administered appropriately. Hence, specific training in the administration of propofol and patient monitoring during use of this agent are required. The appropriate personnel and equipment for propofol administration are listed in Table 5.

The ASA Task Force recommends that patients receiving propofol should receive care consistent with deep sedation and that those personnel should be capable of rescuing the patient from general anesthesia.<sup>11</sup> However, there is abundant evidence that propofol can be administered safely by nonanesthesiologists.

Because there are data to support the safety of GD-P and the ability to safely use propofol at levels adequate to achieve moderate sedation when GD-P is performed, the restricted use of propofol to anesthesiologists has been questioned.<sup>16</sup> The ASGE, the American Gastroenterological Association, and the American College of Gastroenterology support the used of GD-P. In a joint statement, the 3 societies endorse physician-supervised nurse administration of propofol when adequate training for its use has been achieved.<sup>34</sup>

## GD-P

GD-P includes propofol administered directly by gastroenterologists, administered by registered nurses under the direction of gastroenterologists (NAPS), and patient-controlled systems (PCS).

NAPS involves administration of propofol and patient monitoring by a trained registered nurse who has no other responsibilities to patient care.<sup>16</sup> NAPS dosing protocols vary.<sup>5,35,36</sup> Initial bolus doses of propofol of 10 to 60 mg are typically administered; additional bolus doses are administered after a minimum interval of 20 to 30 seconds between doses.<sup>16</sup> The amount of dosing and depth of sedation are titrated as appropriate for the procedural goals. It is important to note that propofol does not possess analgesic properties so that, if it is administered as the sole agent, deep sedation may be required to keep the patient comfortable.<sup>16</sup>

Propofol may be used as the sole sedation agent or in combination with other sedative-hypnotics (multidrug propofol sedation). When using a multidrug protocol with propofol, the clinician may be able to exploit the therapeutic actions of the individual agents while reducing the possibility of sedation dose-related complications. As mentioned above, when propofol is used alone for sedation, higher doses are typically required to achieve adequate sedation, which results in a level of deep sedation. Thus, dose-related propofol effects including hypotension, respiratory depression, or bradycardia are more likely to occur.<sup>37</sup> These adverse effects can be minimized through the use of combination propofol because analgesia and amnesia can be achieved with the other agents and resultant lower doses of propofol. Subsequently, moderate sedation is more likely to be achieved.<sup>38,39</sup> Precise titration of propofol is possible when lower bolus doses of propofol are used. In addition, the ability to reverse the concomitantly administered opioid and benzodiazepine medications can be maintained with naloxone and flumazenil, respectively.<sup>16,25,40</sup>

Although combination propofol may theoretically decrease the rapid recovery benefit seen with propofol alone, this has not been borne out in clinical practice.<sup>39</sup> In a randomized controlled trial of propofol alone titrated to deep sedation compared with 3 different regimens of balanced propofol sedation titrated to moderate sedation in subjects undergoing elective colonoscopy, the balanced regimens were associated with a significantly shorter recovery times than was propofol alone.

Target-controlled sedation involves a pharmacokinetically based model with an infusion system that may or may not be computer controlled. The system then adjusts the medication to the desired plasma concentration or physiologic parameters. An open loop system adjusts to a target drug concentration. A closed loop system uses feedback from a real-time measure of drug effect and desired level of sedation. This may involve either

**TABLE 6. Advantages and disadvantages of propofol for sedation**

### Advantages

- Rapid onset
- Favorable pharmacodynamics
- Mild antiemetic properties
- Potentially more effective
- Rapid termination of effect
- Expedited recovery

### Disadvantages

- Potency
  - Potential to induce general anesthesia
  - Potential to cause hemodynamic and respiratory depression
  - No pharmacologic antagonist

patient or physician-controlled administration of the medications.

PCS with propofol has been reported in several randomized trials. Kulling et al<sup>41</sup> randomized 150 patients to 3 sedation arms: PCS with propofol/alfentanil (group I), continuous propofol/alfentanil infusion (group II), and nurse-administered midazolam/meperidine (group III). Group I exhibited a high degree of patient satisfaction and more complete recovery at 45 minutes compared with conventional sedation and analgesia. In a similar study, Ng et al<sup>42</sup> randomized 88 patients undergoing colonoscopy to PCS with propofol alone or midazolam alone. Patients receiving propofol PCS exhibited significantly shorter mean recovery times (43 minutes vs 61 minutes) and improved comfort. PCS for ERCP, however, has not been successful. In a pilot study of a software system designed to deliver a “ceiling” for the plasma propofol concentration, only 80% of patients received safe and fully effective sedation.<sup>43</sup>

## Propofol efficacy/safety for endoscopic sedation

Studies have demonstrated an advantage of sedation with propofol for endoscopy over sedation with an opioid/benzodiazepine combination for several important outcomes, although there are some disadvantages to its use<sup>16</sup> (Table 6). Data do support that propofol administration is superior to other agents with regard to recovery time and physician satisfaction.<sup>16,44</sup> Additionally, at discharge, propofol-sedated patients have better scores on psychomotor testing, reflective of greater learning, memory, and mental speed.<sup>38</sup> Similarly propofol use provides similar<sup>45,46</sup> or higher levels of patient satisfaction.<sup>47-51</sup> However, a benefit in this regard over traditional

benzodiazepine/narcotic combinations has not been uniformly demonstrated.<sup>40</sup> Studies have shown a high level of safety for propofol monotherapy and combination therapy that compares favorably with conventional sedative agents. However, none of the trials are adequately powered to demonstrate superior safety of propofol compared with traditional sedative regimens. A meta-analysis of 12 randomized controlled trials totaling 1162 patients compared the relative safety of GD-P and benzodiazepine/opioid sedation.<sup>52</sup> The risk of sedation complications with study end points of hypoxemia and hypotension were similar for all procedures except colonoscopy, where the risk was lower with propofol. When the 2002 ASA Practice Guidelines for Sedation and Analgesia by Non-Anesthesiologists was published, it was unclear whether propofol administered moderate or deep sedation was associated with a more adverse outcomes than when similar levels of sedation with other agents was achieved.<sup>1</sup> Since that publication, more than 500,000 subjects have received propofol for endoscopic sedation.<sup>38,47,49-56</sup> From these data, the use of propofol in appropriate patients with trained personnel is associated with an excellent safety profile. Transient hypoxia occurs in 3% to 7% of cases and transient hypotension in 4% to 7%. Time to recovery ranged between 14 and 18 minutes.

In a retrospective review of NAPS in several centers and involving greater than 36,000 endoscopies, the rate of clinical adverse events, defined as apnea or airway compromise that required assisted ventilation (bag-mask), ranged from 0.1% to 0.2%.<sup>37</sup> No patients required endotracheal intubation, and none had permanent injury or death. There have been other published series showing similar results.<sup>16,35,54,57</sup>

In a recent abstract by Deenadayalu et al,<sup>56,57</sup> a worldwide multicenter safety review of more than 521,000 patients was conducted. Mask ventilation rates were 0.4:1000 patients for upper endoscopy and 0.1:1000 patients for colonoscopy. Endotracheal intubations, neurologic injuries, and death occurred in 4, 1, and 3 patients, respectively. The 3 deaths occurred in patients with significant comorbid illnesses such as widely metastatic malignancy and polysubstance abuse.

### Propofol use for complex GI procedures

Propofol may have clinically significant advantages compared with conventional sedative-hypnotic agents when used for prolonged or complex therapeutic procedures where deep sedation is the targeted level of sedation. Two randomized controlled trials with 80 and 198 patients, respectively, compared propofol alone with midazolam alone for ERCP.<sup>55,56</sup> Improved patient cooperation and a significantly shorter onset of effective sedation and reductions in procedure and recovery room times were seen in the propofol group. No difference in patient assessment of sedation quality was seen. Two patients in the propofol group had prolonged apnea that necessi-

tated discontinuation of the procedure and temporary ventilatory support. Important limitations of these studies include the lack of concomitant opiate administration in the nonpropofol sedation regimen and absence of endoscopist blinding. Vargo et al<sup>46</sup> conducted a randomized controlled trial comparing GD-P with meperidine/midazolam for elective ERCP and EUS in 75 patients. In this study, a gastroenterologist dedicated to administration and monitoring administered propofol while using capnography to detect apnea or hypercapnea. Patients randomized to propofol exhibited a faster induction time and a shorter mean recovery time (19 vs 71 minutes), could perform independent transfer after the procedure, and were able to achieve a return to baseline food intake and activity level more quickly. A recent study demonstrated the safety of propofol when administered to high-risk elderly patients undergoing ERCP. One hundred fifty high-risk (ASA class  $\geq$ III) octogenarians were randomized to receive propofol or combined midazolam and meperidine.<sup>58</sup> The propofol group was more cooperative, but the procedure tolerability was similar. The mean recovery time was shorter with fewer hypoxic episodes in the propofol group. In these studies, untoward effects such as hypotension and hypoxemia occurred equally. Therefore, for complex procedures propofol appears to be at least comparable in efficacy and safety to conventional sedation.

### INTRAPROCEDURAL MONITORING

Monitoring may detect changes in pulse, blood pressure, ventilatory status, cardiac electrical activity, and clinical and neurologic status before clinically significant events occur. For both moderate and deep sedation, the level of consciousness must be periodically assessed in addition to documentation of heart rate, blood pressure, respiratory rate, and oxygen saturation. These physiologic parameters should be assessed and recorded at a frequency that depends on the type and amount of medication administered, the length of the procedure, and the general condition of the patient. At a minimum, this should be (1) before the procedure is begun, (2) after administration of sedative-analgesic agents, (3) at regular intervals during the procedure, (4) during initial recovery, and (5) just before discharge. If recording is performed automatically, device alarms should be set to alert the care team to critical changes in patient status.<sup>1</sup> Equipment and medications for emergent resuscitation should be immediately available when sedation and analgesia are being administered.

An individual other than the physician performing the endoscopy who understands the stages of sedation, has the ability to monitor and interpret the patient's physiologic parameters, and possesses the skills to initiate appropriate intervention in the event of an adverse sedation event should monitor the patient throughout the

procedure.<sup>16</sup> This person must be certified in basic or advanced cardiac life support. If moderate sedation is achieved, this person assigned may also perform tasks of short duration that may be interrupted. If deep sedation is undertaken, this individual should have no procedure-related responsibilities other than observation and monitoring of the patient.<sup>16</sup> When deep sedation is administered, at least one other person in the room should have advanced cardiac life support certification, be able to provide a secure airway, and be able to provide bag ventilation.<sup>1,5,16</sup>

### Monitoring techniques

The ASA guidelines recommend continuous electrocardiogram (ECG) monitoring of patients with significant cardiovascular disease or arrhythmia during moderate sedation.<sup>1</sup> Other patients who may benefit from ECG monitoring include those with a history of significant pulmonary disease, elderly patients, and those in whom prolonged procedures are anticipated. The necessity of ECG monitoring in healthy patients is unclear. In addition, all patients receiving intravenous sedation should be monitored with noninvasive blood pressure devices. Oximetry effectively detects oxygen desaturation and hypoxemia in patients undergoing sedation and analgesia.<sup>59</sup> Measurement of oxygen saturation is relatively insensitive to the earliest signs of hypoventilation because significant changes in arterial partial pressure of oxygen may occur with little alteration in oxygen saturation. This is particularly true for those individuals receiving supplemental oxygen. Therefore, monitoring of ventilatory function must also include patient observation or auscultation throughout the procedure. Risk factors for hypoxemia include a baseline oxygen saturation of less than 95%, an emergency indication for the endoscopic procedure, a procedure of long duration, difficulty with esophageal intubation, and the presence of comorbid illness.<sup>60</sup> Despite the lack of data linking pulse oximetry to a reduction in complications, both the ASA and ASGE recommend that pulse oximetry be used during all endoscopic procedures.<sup>1,3</sup>

The routine administration of supplemental oxygen has been shown to reduce the magnitude of oxygen desaturation during endoscopic procedures. The ASA Task Force recommends that supplemental oxygen should be considered for moderate sedation and should be administered during deep sedation unless specifically contraindicated for a particular patient or procedure. Furthermore, if hypoxemia is anticipated or develops during sedation/analgesia, supplemental oxygen should be administered.<sup>1</sup> However, one study suggested that routine oxygen supplementation results in a higher rate of cardiopulmonary unplanned events related to conscious sedation.<sup>61</sup>

Capnography is a noninvasive approach to measure respiratory activity that is based on the principle that carbon dioxide absorbs light in the infrared region of the electromagnetic spectrum. Quantification of the absorption leads to the generation of a curve that represents a real-time dis-

play of the patient's respiratory activity. It more readily detects hypoventilation compared with pulse oximetry or visual observation and thereby provides an opportunity for early recognition of depressed respiratory activity. Capnography can be achieved through the use of end-tidal carbon dioxide monitoring. Given that hypoxemia resulting from depressed respiratory activity is a principal risk factor for adverse respiratory events during sedation, integrating capnography into patient monitoring protocols may improve safety.<sup>62</sup> Currently, there is insufficient evidence to support its use during routine upper and lower endoscopic sedation.<sup>47,63,64</sup> Data are available, however, to support its use during ERCP and EUS. A recent randomized controlled trial using the combination of an opioid and benzodiazepine for elective ERCP and EUS found significantly less hypoxemia in the subjects who received sedation with capnography compared with standard monitoring.<sup>65</sup> The ASA recommends carbon dioxide monitoring, stating capnography "should be considered for all patients receiving deep sedation and for patients whose ventilation cannot be observed directly during moderate sedation."<sup>1</sup>

Bispectral (BIS) index monitoring is an electroencephalographic (EEG)-based method of assessing a patient's level of consciousness by using a complex algorithm to generate a weighted index.<sup>66</sup> In 2 studies<sup>67,68</sup> BIS monitoring values exhibited a significant lag time compared with the clinical assessment of the level of sedation. Additionally, titration with BIS was not associated with any improvement in clinical outcomes, such as recovery times, or any reduction in propofol dose. In addition, the new BIS algorithm was not found to be useful for sedation with benzodiazepine/opioid sedation. Other EEG-based systems used to guide propofol administration during ERCP resulted in improved patient tolerance, shorter recovery time, and fewer hemodynamic side effects.<sup>69,70</sup> The use of EEG monitoring may have a role in the future for delivery of sedation during selected endoscopic procedures.

Computer-assisted personalized sedation (CAPS) uses multiple physiologic feedback parameters, including electrocardiography, capnography, and automated response monitoring, which periodically assess patient response to otic and vibratory stimuli. CAPS has been used in 24 patients undergoing ambulatory upper endoscopy and colonoscopy.<sup>71</sup> Oxygen desaturation occurred in only 6% of subjects to whom minimal to moderate sedation was delivered. No device-related adverse events occurred.

A small case series demonstrates the feasibility of CAPS and may provide endoscopists an alternative safe and effective means to deliver propofol without the assistance of an anesthesiologist. Recently, the results of a multicenter randomized controlled trial that compared CAPS with the combination of an opioid and benzodiazepine in 1000 patients undergoing ambulatory upper endoscopy and colonoscopy was presented. CAPS was superior to standard sedation in terms of a significantly shorter duration and less severity of hypoxemia and recovery parameters.



Patient satisfaction was high in both groups. CAPS is not yet FDA approved.

After completion of endoscopic procedures, patients are to be observed for adverse effects from either instrumentation or sedation. Standardized discharge criteria should be used to assess recovery from sedation. Postprocedure monitoring has been discussed in a previously published ASGE guideline.<sup>3</sup>

## ANESTHESIOLOGIST ASSISTANCE FOR ENDOSCOPIC PROCEDURES

Sedation-related risk factors, the depth of sedation, and the urgency and type of endoscopic procedure play important roles in determining whether the assistance of an anesthesiologist is needed. Patient risk factors include significant medical conditions such as extremes of age; severe pulmonary, cardiac, renal, or hepatic disease; pregnancy; the abuse of drugs or alcohol; uncooperative patients; a potentially difficult airway for positive-pressure ventilation; and individuals with anatomy that is associated with more difficult intubation. The ASA Task Force states that airway management may be difficult in patients with the following situations: (1) previous problems with anesthesia or sedation, (2) a history of stridor, snoring, or sleep apnea, (3) dysmorphic facial features, such as Pierre-Robin syndrome or trisomy 21, (4) oral abnormalities, such as a small opening (<3 cm in an adult), edentulous, protruding incisors, loose or capped teeth, high arched palate, macroglossia, tonsillar hypertrophy, or a nonvisible uvula, (5) neck abnormalities, such as obesity involving the neck and facial structures, short neck, limited neck extension, decreased hyoid-mental distance (<3 cm in an adult), neck mass, cervical spine disease or trauma, tracheal deviation, or advanced rheumatoid arthritis, and (6) jaw abnormalities such as micrognathia, retrognathia, trismus, or significant malocclusion.<sup>11</sup>

The ASA Task Force guidelines states that the presence of one or more sedation-related risk factors coupled with the potential for deep sedation will increase the likelihood of adverse sedation-related events. If the practitioner confronted with these situations is not trained in managing these complex patients, consultation with an anesthesiologist to provide sedation should be considered (Table 7).<sup>11</sup>

## ECONOMICS OF GI ENDOSCOPY

Gastroenterologists in the United States have routinely sedated patients as a part of the endoscopic service. In recent years, a greater number of endoscopists use anesthesiologists or nurse anesthetists to provide sedation. Numerous factors are driving this transition, including increasing use of propofol, efforts to offset falling reimbursements, and effective marketing by anesthesiologists.<sup>72</sup> The routine assistance of an anesthesiologist for

**TABLE 7. Guideline for anesthesiology assistance during GI endoscopy**

Anesthesiologist assistance may be considered in the following situations:

- Prolonged or therapeutic endoscopic procedures requiring deep sedation
- Anticipated intolerance to standard sedatives
- Increased risk for complication because of severe comorbidity (ASA greater than class III)
- Increased risk for airway obstruction because of anatomic variant

average-risk patients undergoing standard upper and lower endoscopic procedures is cost prohibitive. In fact, some health carriers may not reimburse for anesthesia assistance during routine endoscopy.

## RECOMMENDATIONS

Refer to Table 1 for recommendation grades.

1. Adequate and safe sedation can be achieved in most patients undergoing routine esophagogastroduodenoscopy and colonoscopy by using an intravenous benzodiazepine and opioid combination (1B).
2. In patients who are not adequately sedated with an intravenous benzodiazepine and opioid combination, the addition of other intravenous agents such as droperidol, promethazine, or diphenhydramine (Benadryl) may allow adequate and safe sedation to be achieved (1B).
3. Sedation providers must have a thorough understanding of medications used for endoscopic sedation and the skills necessary for the diagnosis and treatment of cardiopulmonary complications (3).
4. Noninvasive blood measurement and pulse oximetry are supplemental to—and do not replace—clinical observation of the patient during endoscopic sedation. Newer methods of monitoring are available but data to assess their impact on clinical outcomes is lacking, and their routine use for sedation must be individualized (2B).
5. During moderate sedation, the person assigned responsibility for patient assessment may also perform tasks that are interruptible and of short duration. When deep sedation is planned, this individual should be dedicated to observation and monitoring and have no other procedure-related responsibilities (3).
6. Extended monitoring techniques may provide sensitive measures of patient's ventilatory function (capnography) and level of sedation (BIS index monitoring); however, there is insufficient evidence in the literature to support the routine use of extended monitoring devices during moderate sedation. The ASA states that

- automated monitoring for apnea (capnography) should be considered for patients receiving deep sedation and for all patients in whom ventilatory function cannot be observed adequately (1B).
7. Propofol has the advantages of more rapid onset of action and shorter recovery time compared with traditional sedative regimens. However, clinically important benefits in average-risk patients undergoing upper endoscopy and colonoscopy have not been consistently demonstrated with regard to patient satisfaction and safety. Therefore, the routine use of propofol in average-risk patients cannot be endorsed (1B).
  8. Propofol can be safely and effectively given by non-anesthesiology physicians and nurses provided they have undergone appropriate training and credentialing in administration and rescue from potential pulmonary and cardiovascular complications (1C).
  9. A patient targeted for one level of sedation may become more deeply sedated than planned. Therefore, an individual administering sedation/analgesia should be trained to and possess the skills necessary to rescue a patient who has reached a level of sedation deeper than that intended. Thus, a physician targeting moderate sedation must be able to rescue a patient who is deeply sedated. Similarly, an ability to rescue a patient from general anesthesia is necessary when providing deep sedation (3).
  10. The assistance of an anesthesia specialist should be considered for ASA physical status III, IV, and V patients. Other possible indications for involvement of an anesthesia professional during sedation include emergency endoscopic procedures, complex endoscopic procedures, and patients with a history of (1) adverse reaction to sedation, (2) inadequate response to moderate sedation, (3) anticipated intolerance of standard sedatives (eg, alcohol or substance abuse), and (4) those at increased risk for sedation-related complications, such as patients with severe comorbidities or with anatomic variants predictive of increased risk for airway obstruction or difficult intubation (eg, morbid obesity or sleep apnea) (3).
  11. An anesthesia specialist is not cost-effective for average-risk patients undergoing routine upper and lower endoscopic procedures (3).

*Abbreviations:* ASA, American Society of Anesthesiologists; ASGE, American Society for Gastrointestinal Endoscopy; BIS, bispectral index; CAPS, computer-assisted personalized sedation; ECG, electrocardiogram; EEG, electroencephalogram; FDA, Food and Drug Administration; GD-P, gastroenterologist-directed propofol; NAPS, propofol administered by registered nurses under the direction of gastroenterologists; PCS, patient-controlled sedation.

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