Sedation for gastrointestinal endoscopy
Clinical practice guidelines of the Spanish Society of Digestive Endoscopy

F. Igea, J. A. Casellas, F. González-Huix, C. Gómez-Oliva, J. S. Baudet, G. Cacho, M. A. Simón, E. De la Morena, A. Lucendo, F. Vida

Coordinator: Leopoldo López-Rosés
On behalf of the Spanish Society of Digestive Endoscopy (SEED)

Introduction

Sedation for gastrointestinal endoscopic procedures has become indispensable, hence sedation is now a mandatory requirement to be offered to all patients before an endoscopic exam following the discussion of its benefits, risks, drawbacks, and alternative options. Patient sedation pursues a dual purpose – on the one hand the achievement of a good perceived quality by suppressing pain; on the other hand an avoidance of untimely movements that may compromise efficacy and safety. In the past twenty years a huge amount of papers were published showing that properly trained non-anesthesiologist doctors and nurses may effectively, safely, and efficiently take responsibility for the administration of sedatives and painkillers, as well as patient monitoring during endoscopy. Also, major scientific societies involved in gastrointestinal endoscopy have published guidelines with recommendations in this respect. The Sociedad Española de Endoscopia Digestiva (SEED) is no exception and published in 2006 their sedation guidelines, which included all major indications, contraindications, drug classes, and other related topics [1]. Presently, the SEED Board of Directors has decided to update these guidelines by publishing a new version with revised major aspects and the addition of recent findings.

Guidelines development approach

Cooperation was requested from a number of endoscopists experienced and interested in sedation at various hospitals throughout Spain. Following the development of a table of contents, each one of them drafted a chapter based on an updated literature revision, including evidence-based recommendations in accordance with the SIGN classification at the end [2]. Each initial draft was reviewed by all authors, and corrections deemed relevant were incorporated in order to provide a definitive edition. The notion behind the development of these guidelines was to obtain a concise, clear text with scientific rigor and readily applicable to clinical practice.

Sedation goals. Sedation levels

The goals of sedation and analgesia include decreasing anxiety, relieving discomfort and pain, and reducing the memory of endoscopic procedures [3, 4]. Sedation levels should be adjusted to each individual’s needs and each procedure to ensure safety, comfort, and technical success. Sedation levels entail a continuum of states ranging from minimal sedation or anxiolysis to general anesthesia (Table 1):

- **Minimal sedation or anxiolysis**: A drug-induced state during which patients respond normally to verbal commands. While cognition and coordination may have functional alterations, ventilation and cardiovascular functioning are usually preserved.
- **Moderate or superficial sedation**: A drug-induced depression of conscience during which patients respond correctly to verbal commands and mild tactile stimulation. No intervention is necessary to maintain airway permeability, and spontaneous ventilation is adequate. Cardiovascular functioning is usually preserved.
- **Deep sedation**: A drug-induced depression of conscience during which patients cannot be easily awakened but respond to repeated or painful stimuli. The ability to maintain ventilation independently may be impaired. Patients may need help to keep their airway permeable, and spontaneous ventilation may be inadequate. Cardiovascular function is usually preserved.
- **General anesthesia**: This involves a drug-induced loss of conscience in which patients do not respond to stimuli. The ability to maintain ventilation independently is often impaired. Patients usually require help to keep their airway permeable, and positive-pressure ventilation may be needed when spontaneous breathing or neuromuscular function is depressed. Cardiovascular function may become impaired [4].

Dosis titration and pharmacological variability: A well-known, key principle in sedative administration is that drugs must be administered in escalated doses – effects being assessed at each step – until the desired action is achieved. While certain patient characteristics may help predict the required dose for adequate sedation (e.g., age, comorbidity, body mass, race, response to prior sedation or concurrent use of oral narcotics or benzodiazepines), the precise dose that will be needed for any given patient is impossible to forecast with accuracy. This is due to the fact that response to sedatives in individual patients is variable. For instance, blood drug levels may show up to five-fold differences in age-matched patients receiving identical doses. Also, even if blood drug levels are similar, the perceived experiences of patients may differ a lot [3].

<table>
<thead>
<tr>
<th>Sedation level</th>
<th>Minimal sedation (anxiolysis)</th>
<th>Moderate sedation</th>
<th>Deep sedation</th>
<th>General anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responsiveness</td>
<td>Normal</td>
<td>Verbal or tactile stimuli</td>
<td>Repeated painful stimuli</td>
<td>Unresponsive to painful stimuli</td>
</tr>
<tr>
<td>Airway</td>
<td>Normal</td>
<td>No intervention required</td>
<td>Intervention may be required</td>
<td>Intervention usually required</td>
</tr>
<tr>
<td>Spontaneous ventilation</td>
<td>Normal</td>
<td>Adequate</td>
<td>May be inadequate</td>
<td>Usually inadequate</td>
</tr>
<tr>
<td>Cardiovascular function</td>
<td>Normal</td>
<td>Normal</td>
<td>Usually maintained</td>
<td>May be impaired</td>
</tr>
</tbody>
</table>
Table 2  Indications for sedation/analgesia.

<table>
<thead>
<tr>
<th>Type of procedure</th>
<th>Sedation level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rigid and flexible sigmoidoscopy; rectal endosonography</td>
<td>Sedation not considered routinely required (moderate or superficial sedation optional for anxious patients when pain is anticipated and during therapeutic procedures)</td>
</tr>
<tr>
<td>Diagnostic, non-complex gastroscopy and colonoscopy</td>
<td>Moderate sedation required</td>
</tr>
<tr>
<td>Complex or prolonged procedures such as ERCP or EUS</td>
<td>Deep sedation required</td>
</tr>
</tbody>
</table>

Modified from Overview of Endoscopic Sedation, SCNA Position Statement

For a given exploration type required sedation levels may vary from one patient to the next. In addition, one patient may require different sedation levels within a given procedure. For instance, a patient undergoing colonoscopy may experience more pain and require more sedation at certain points during an examination. In prolonged or complex procedures, or under other circumstances, deep sedation or even anesthesia may be required. However, basic, routine endoscopic gastrointestinal procedures may be performed with moderate sedation [5] (Table 2).

Different studies have shown that in basic endoscopic procedures superficial sedation is adequate, whereas deep sedation achieves better outcomes for longer, more complex exams [6–10]. Finally, the staff responsible for sedation must always be ready and able to rescue patients progressing to sedation levels deeper than intended.

Recommendations

- Sedation level and drug type depend on procedure characteristics, individual patient-related factors, patient preferences, and need for patient cooperation (evidence level 4, recommendation grade D).
- For non-complex diagnostic or therapeutic gastroscopy and colonoscopy superficial sedation suffices (evidence level 1+, recommendation grade A).
- For complex or prolonged procedures (ERCP, EUS, etc.) deep sedation is to be preferred (evidence level 1+, recommendation grade A).
- Patient monitoring in the recovery room and discharge time scheduling.

Skills required to perform sedation during gastrointestinal endoscopy.

General rules for sedation.

Sedation training for endoscopists

All scientific societies agree that specific training is required for practitioners involved in sedation, as well as official certification for basic life support. Endoscopy units where sedation is applied must have at least one person certified in advanced cardiopulmonary resuscitation techniques. Theoretical and practical sedation skills for endoscopy should be included in the specialty curriculum.

Multiple clinical practice guidelines are available that include sedation recommendations for digestive endoscopy, but it was not until the last decade that several European and US societies eventually established specific rules regarding sedation training [11,12].

The Sociedad Española de Endoscopia Digestiva has been offering training courses on deep sedation for endoscopists for four years now. These courses allowed a widespread use of sedation, mainly using propofol, in endoscopy units.

General rules for sedation to be met by all endoscopy unit staff members:

1. Understanding the minimal sedation equipment that needs to be available in an endoscopy unit.
2. Having a unit-specific sedation protocol according to recommendations in clinical practice guidelines.
3. Understanding the characteristics of drugs to be used for sedation.
4. Recognizing the various sedation levels and possessing skills to rescue patients anytime from a deeper-than-intended level.
5. Having the necessary skills for airway management and certification on basic life support, to be renewed every three years.

Sedation training for endoscopists must include both theoretical and practical education [13,14]. Theoretical contents must include the following:

1. Required documentation: sedation-specific informed consent; medical record; sedation record; databases.
4. Knowledge of drugs used for sedation: pharmacological and pharmacodynamic characteristics, administration regimens, dosage, synergies, interactions, and side effects. Drug preparation and administration mode (boluses, infusion pumps).
5. Understanding of sedation levels and related assessment scales.
7. Sedation during pregnancy and lactation.
10. Legal aspects of sedation. Practical training: Practical skills should be acquired in certified units and must include the following:

1. Pre-sedation history taking and risk assessment.
2. Indication and administration of all drugs necessary for each procedure at the appropriate dosage to achieve the desired sedation level.
3. Patient and vital sign monitoring during sedation.
4. Implementing appropriate corrective maneuvers for desaturation or any other events that may arise.
5. Patient monitoring in the recovery room and discharge time scheduling using the various assessment scales available.

In Spain both basic and advanced life support certificates should be officially recognized by one of the scientific societies and health care institutions included in the Consejo Español de Reanimación Cardio-Pulmonar (CERCP) – intensive medicine (SEMICYUC), cardiology (SEC), anesthesia (SEDAR) and emergency medicine (SEMES).
Recommendations:
- All endoscopy team members involved in sedation must be certified in both theoretical and practical sedation techniques (evidence level 4, recommendation grade D).

Traditional sedation (benzodiazepines and opiates).

Drugs. Dosage. Antagonists ▼

This has been the commonest form of sedation for gastrointestinal endoscopy when performed by non-anesthetist doctors. Drugs may be administered alone or in combination, and as intravenous boluses (see boxes). Usually, the goal of traditional sedation is the achievement of superficial sedation. Its use is particularly suited for basic diagnostic techniques, primarily gastroscopy and colonoscopy [15].

In elderly patients or individuals with renal, liver or respiratory failure caution and reduced doses are advised [16].

Benzodiazepines: Both midazolam and diazepam may be considered. Midazolam has a rapid onset and a short duration of action, and provides useful though variable amnestic effects. Because of this it is now the benzodiazepine of choice [16, 17]. It has minimal cardiovascular effects.

Opiates: Meperidine and fentanyl are most commonly used. Caution is advisable when given to patients receiving other central nervous system depressants, and administration should be avoided in individuals on monoamine oxidase inhibitors.

Meperidine: Meperidine has a wide margin of safety; however, nausea is more common when compared to fentanyl, and metabolites accumulate particularly in patients with renal disease. Both sedative and analgesic effects are less predictable than with other opiates.

Fentanyl: Analgesic potency is much higher than meperidine’s, and its pharmacodynamic profile is better because of a shorter half-life. It may induce respiratory depression, which persists longer than analgesia. It fits the duration of endoscopic procedures as 20–25 min after dosing most patients show stabilized vital signs and may be discharged. In addition to respiratory depression high doses may result in bradycardia and hypotension, which should be borne in mind. While meperidine was the most commonly used opiate among endoscopists in the past, it is now being gradually replaced by fentanyl [18, 19].

Antagonists: They counteract the effects of benzodiazepines and opiates in patients with oversedation not reversed following appropriate ventilation and stimulation. Its routine use to speed up recovery after endoscopy is not recommended [16]. Their half-life is shorter than that of antagonized compounds, hence re sedation is possible.

Flumazenil. A benzodiazepine antagonist. It should not be administered to patients with seizures on benzodiazepines or high intracranial pressure.

Midazolam
- Initial dose: 1–2 mg
- Additional doses: 0.5–1 mg every 2 min
- Onset of action: 1–2 min
- Peak effect: 3–4 min
- Duration of effect: 15–80 min

Fentanyl
- Initial dose: 50–100 mcg
- Additional doses: 25 mcg every 2–5 min until desired effect1
- Onset of action: 1–2 min
- Peak effect: 3–5 min
- Duration of effect: 30–60 min

Flumazenil
- Initial dose: 0.2 mg in 30 sec
- Additional doses: up to four 0.2-mg doses may be given at 60-sec intervals (max. dose 1 mg)
- Onset of action: 1–2 min
- Peak effect: 3 min
- Duration of effect: variable, 10–120 min

1 Caution with repeated doses because of risk for plasma redistribution

Naloxone. Opioid antagonist. When used together with benzodiazepines and opiates, and the patient develops respiratory depression, naloxone should be administered first because of its greater effect on respiratory depression.

Recommendations
- When benzodiazepines are used midazolam is recommended (evidence level 2+, recommendation grade B).
- Moderate sedation using currently available drugs for routine endoscopic procedures (colonoscopies and gastroscopies) is highly satisfactory for patients and physicians alike given their low risk for adverse events (evidence level: 1–, recommendation grade: A).
- If a patient has respiratory depression during sedation with benzodiazepines and/or opiates and does not respond to stimulation or oxygen ventilation, the administration of antagonists for said drugs is recommended (evidence level 2–, recommendation grade D).
- Time to recovery following routine endoscopy is shorter when fentanyl rather than meperidine is used (evidence level 1, recommendation grade B)

Sedation with propofol. Dosage and mode of administration ▼

Propofol (2–6-diisopropylphenol) is a drug structurally unrelated to other sedatives and with pharmacokinetic characteristics that, in many respects, make it an ideal drug for gastrointestinal endoscopy. Its main features include a rapid onset of action (30–40 seconds) and short half-life (4–5 minutes). This fast action is based on its formulation’s high liposolubility. Also, its antiemetic properties and absence of many undesirable effects that are common with other drugs allow a really fast, pleasing awakening and provide patients with outstanding perceived comfort. Its safety profile when used by endoscopists or trained nurses has been consistently demonstrated in clinical trials, showing a rate of complications
equal to or lower than traditional sedation [20, 21]. In contrast, its main drawback is a very narrow therapeutic window that renders precise dose titration mandatory. Furthermore, its pharmacokinetics is influenced by multiple factors – drugs, tobacco, alcohol, age, obesity, and other circumstances may influence patient response to propofol. From the above, individualized dosing is key, with titration according to observed clinical response. In addition, as this drug may bring about significant hemodynamic changes, its use is advised under close supervision by trained healthcare personnel and using adequate surveillance with at least arterial O₂ saturation, heart rate, respiratory rate, and blood pressure monitoring [15].

Administration modes depend on the examination’s duration and complexity, and on the unit’s staff. Overall, it is recommended that sedation be induced with repeated boluses every 20–30 seconds for short, non-complex explorations (mainly diagnostic gastroscopy). The initial bolus depends on patient characteristics, weight, and age – in a young, healthy ASA I patient sedation may be induced with a 40–60-mg bolus, whereas lower initial doses (10–20mg) are recommended for elderly, weak subjects; successive doses of 10–20mg will then be administered until the patients spontaneously closes his or her eyes with absent response to verbal stimuli. With this induction additional doses are usually not needed for a short diagnostic exam. For longer explorations (colonoscopy, therapeutic gastroscopy) a staff member should be present to administer booster doses or perhaps propofol using an infusion pump. Infusion rate varies from 2 to 8mg/kg/hr depending on individual response and examination-related discomfort. A formula to estimate infusion rate based on response to initial induction has been recently reported [22]. Using a syringe pump deep sedation is induced at a constant rate of 200mL/hour (150–100mL/hour for weak or elderly patients) for 1% propofol (10mg/mL). Once deep sedation is reached the pump is stopped and a calculation is made where the infused volume in mL is multiplied by four. The resulting amount will be used as infusion rate in mL/hour.

Combined use with midazolam: Under some circumstances so-called balanced sedation becomes useful. A prior administration of midazolam (1–2mg two minutes in advance) reduces propofol requirements and propofol-related adverse hemodynamic effects [23, 24]. This is particularly useful for weakened patients, most particularly with heart disease and impaired ejection fraction. It may also be appropriate for younger patients or drug addicts with foreseeable higher propofol requirements.

Contraindications: Propofol is contraindicated in patients allergic to propofol and in patients with a low ejection fraction or at risk for bronchoaspiration. The presence of soy and egg components in the emulsion initially advised against its use in patients with allergy to these foods. However, there is now evidence that propofol may be safely used in subjects with egg allergy provided they never developed anaphylaxis [25]. It is nevertheless prudent to assess such cases on an individual basis and consider the use of alternative medications. Special care should be used with ASA IV patients, where the presence of an anesthetist or other options should be considered.

Recommendations

- Propofol is an ideal drug to provide sedation for endoscopic examinations (evidence level 1+, recommendation grade A).
- The use of propofol by endoscopists or trained nurses is as safe as traditional sedatives when monitoring is adequate (evidence level 1++, recommendation grade A).
- The use of propofol by endoscopy staff in ASA III patients is feasible and safe in experienced endoscopy units (evidence level 3, recommendation grade D).
- Propofol dosing must be tailored according to patient response and baseline status (evidence level 1++, recommendation grade A).
- Midazolam administration before propofol allows to reduce dosage and adverse effects, particularly hypotension in cardiac patients or in hypovolemia, but recovery is delayed (evidence level 1+, recommendation grade B).

Human and material resources necessary for effective, safe sedation. Monitoring. When is an anesthesiologist essential?

Human resources:
Sedation guidelines and propofol label indicate that deep sedation should be administered by qualified personnel other than those carrying out the examination [18, 26]. However, no scientific evidence has shown any benefits versus sedation with propofol administered by the same staff aiding in the procedure [27, 28]. Exploration characteristics and patient risks must be considered when making such a decision (Fig. 1). Non-invasive, non-complex diagnostic exams in ASA I-III patients with no risk factors may be effectively and safely performed in the absence of dedicated sedation staff, with no increase in the number of people inside the room. In complex therapeutic procedures and/or examinations in advanced ASA (>III) individuals or subjects at risk regarding sedation (short neck, sleep apnea, severe decompensated chronic conditions, etc.) (Table 3) sedation-related adverse events are more common, hence the presence of an additional qualified practitioner responsible for sedation is highly advisable. Help from an anesthesiologist, intensivist or qualified nurse is recommended in such cases [29].

Required qualifications: The staff performing sedation and the members of the endoscopy unit where propofol is used must have knowledge, experience and training regarding this drug, as previously discussed. The whole staff must be qualified for basic life support, and at least one member should be certified in advanced life support; otherwise, an anesthesiologist or intensivist should be available within five minutes.

Roles of staff responsible for sedation:
These include the design and management of the whole sedative administration process. Depending on the type of exploration to be performed and on patient characteristics, the following should be assessed: 1) sedation level necessary, 2) induction and maintenance doses, 3) administration mode, 4) maintenance and patient monitoring using the relevant scales (Table 4) [17, 30], 5) control of activity or breathing movements (with the aid of capnography, bispectral index or narcotrend when available) [31].

Preparing propofol for IV administration requires special care as this is a lipophilic drug with a high risk for bacterial or fungal contamination [32]. Strict handling includes: opening a vial for each patient immediately before administration, disposing of vial remnants and infusion pumps, and changing adapters, conduits and syringes for each case.

Material resources:
The Unit should have all sorts of sedation-related materials available, including: 1) Sedatives and their antagonists. 2) IV systems and infusion pumps. 3) Oximetry.
Deep sedation with propofol for basic endoscopic procedures and patients with ASA I-II risk may be carried out effectively and safely in the absence of dedicated sedation staff and with no increase in the number of people inside the room (evidence level 2+, recommendation grade C).

For complex therapeutic procedures having an additional, qualified person responsible for sedation is advisable (evidence level 4, recommendation grade D).

For procedures performed in patients with advanced ASA scores (> III) or with risk factors for sedation (short neck, sleep apnea, chronic decompensated serious diseases, etc.) the presence of an anesthesiologist or intensivist is to be recommended (evidence level 4, recommendation grade D).

In endoscopy units where deep sedation is used an anesthesiologist or intensivist should be available within 5 minutes (evidence level 2+, recommendation grade C).

Given propofol’s high risk of contamination the aseptic technique must be maximized during handling, particularly avoiding multidose containers and reusable infusion materials (evidence level 1++, recommendation grade A).

Endoscopy units should be fitted with all items necessary for safe, effective sedative dosing, as well as monitoring and cardiopulmonary resuscitation equipment (evidence level 2++, recommendation grade B).

A recovery room with nurses, gurneys, oxygen, aspiration, monitors, and cardiopulmonary support devices is advisable (evidence level 4, recommendation grade D).

ECG, and blood pressure monitors. A capnograph and bispectral index/narcotrend are desirable, particularly for higher-risk examinations [31]. 4) Resuscitation equipment. 5) Defibrillator. 6) Basic and advanced respiratory care systems. 7) Drugs for cardiopulmonary resuscitation. Good venous access, patient preoxygenation for 5 minutes before sedative dosing, a readily available independent aspirator, and a well-checked crash cart are all key components.

Appropriate gurneys and transportation means are also essential that provide space for resuscitation maneuvers, protection against falls, and ergonomics for both patients and staff.

The widespread use of sedation in endoscopy units makes mandatory an architectural design adapted to the use of deep sedation techniques.

The increasing use of propofol, which provides deep sedation with a rapid recovery, requires resuscitation systems available until the patient fully regains consciousness and the health status present before the procedure. To achieve maximal efficiency in the Unit a recovery ward with 1.5–2.0 boxes per operating endoscopy room is considered a must [33]. The recovery ward should be staffed with nurses and fitted with cardiopulmonary support systems, monitors, gurneys, accessory rails, oxygen outlets, and aspiration inlets.

Recommendations:

- Deep sedation with propofol for basic endoscopic procedures and patients with ASA I-II risk may be carried out effectively and safely in the absence of dedicated sedation staff and with no increase in the number of people inside the room (evidence level 2+, recommendation grade C).

- For complex therapeutic procedures having an additional, qualified person responsible for sedation is advisable (evidence level 4, recommendation grade D).

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- A recovery room with nurses, gurneys, oxygen, aspiration, monitors, and cardiopulmonary support devices is advisable (evidence level 4, recommendation grade D).
Supplementary oxygen administration by s\textsubscript{at}O\textsubscript{2} < 90\% is the most common complication, possibly more common than usually thought as it is not recorded on many occasions. Incidence is highly variable (4\% – 50\%). The risk is greater during oral endoscopy since a deeper level of sedation is needed, the airway is compressed, and laryngospasm occasionally develops. The combined administration of benzodiazepines and opiates increases the risk for respiratory depression [36]. In recent studies with oxygenated, monitored patients the incidence of desaturation events during endoscopies performed under propofol was lower than 10\% [37], and the need for endotracheal intubation remained marginal.

Does oxygen administration prevent hypoxemia? All guidelines issued by national scientific societies advise that supplementary oxygen be used during endoscopic procedures. However, oxygen administration may delay apnea recognition and increase hypercapnia, hence a pulse oximeter is also recommended to provide visual monitoring for breathing movements, as well as capnography when feasible [35].

If desaturation develops sedatives must be discontinued and the patient must be stimulated using increased oxygen flow, jaw thrust to secure the airway, secretion aspirations, and a Guedel tube when required. If benzodiazepines and/or opiates were used their action may be reverted with flumazenil and/or naloxone. When desaturation is severe and persistent, ventilation should be provided using an oxygen mask (Ambu), but this is only necessary in 0.1\% of cases. Should these measures fail, respiratory resuscitation maneuvers must be initiated using a laryngeal mask or orotracheal intubation; need for the latter is exceptional [38].

Hypotension: Defined by a maximal blood pressure <90 mmHg, it develops more commonly in cases where sedatives and pain killers are associated or when propofol is used; it usually has no clinical implications. Management usually includes electrolyte IV infusion.

Arrhythmia: Arrhythmia develops in 4\% – 72\% of sedations; most are sinus tachycardia events possibly related to procedure-associated stimuli, but other clinically relevant arrhythmias may occur (extrasystoles, bradycardia, ectopic rhythms, etc.). Their development depends on patient age, presence of concurrent, particularly heart diseases, endoscopy type, and anxiety. Electrocardiographic changes appear in 4\% – 42\% of cases, most commonly ST segment alterations that remain unchanged by oxygen administration and are believed to be unrelated to ischemia. Should bradycardia occur (<50 bpm) atropine must be provided (0.5 mg IV, to a maximum of 2 – 3 mg).

Aspiration: This occurs in few cases (0.10\%) and usually defies recognition. However, the risk for bronchopulmonary aspiration is much higher in patients with active upper gastrointestinal bleeding or gastric retention; in such cases orotracheal intubation is recommended before the endoscopic procedure.

Phlebitis: The frequency of phlebitis is low but higher when diazepam is used in small-caliber veins. Some propofol preparations irritate venous walls, and extravasation results in pain and swelling; lidocaine may be added to the infusion to prevent this; cold application is advisable should extravasation develop.

A marginal yet possible, potentially severe complication is the transmission of bacterial, fungal or viral infections (including hepatitis C virus) because of multidose containers and propofol contamination.

Can we identify patients with higher cardiopulmonary risk? Multiple risk factors have been associated with a greater frequency of cardiopulmonary complications. Some are patient-related, including a history of ischemic heart disease or arrhythmia, lung disease, hospitalization, baseline O\textsubscript{2} saturation < 95\%, age older than 70 years, and ASA III and IV [35,36,39 – 41]. Other factors are associated to procedure type and are more common in emergency procedures or oral endoscopy [38,42]; finally, they may also be related to drug dosage, and oxygen administration status [35].

A thorough assessment prior to sedation may identify these factors and allow actions to prevent complications. The best way to prevent them is by adequate training and having expert staff – both doctors and nurses – to manage sedation [38].

**Recommendations:**

- Supplementary oxygen administration during endoscopic procedures reduces the incidence of hypoxemia but may delay apnea recognition and increase hypercapnia; hence, besides using a pulse oximeter, visual monitoring of breathing movements is advisable, and a capnograph is recommended [3] (evidence level 1+, recommendation grade B).

- In situations with an increased risk for bronchoaspiration, as is the case with active upper GI bleeding or gastric retention, orotracheal intubation is required before the endoscopic procedure (evidence level 2+, recommendation grade B).

**Pre-, intra-, and post-sedation monitoring. Records**

- Having a sedation form available is advisable to record clinical data and vital signs before, during and after sedation. Similarly, all incidents occurring during sedation, as well as actions taken to solve them, should be recorded. This record form should be attached to the patient’s medical record. The following sequence is advisable:

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**Table 4 Rating scales that may be used to assess sedation level during endoscopy.**

<table>
<thead>
<tr>
<th>RAMSAY SCORE</th>
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<tbody>
<tr>
<td>IA: Anxious, agitated, restless</td>
<td></td>
</tr>
<tr>
<td>IIC: Cooperative, oriented, calm</td>
<td></td>
</tr>
<tr>
<td>III: Sedated but responds to verbal commands</td>
<td></td>
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<tr>
<td>IV: Sleep but rapidly responds to light tactile stimuli</td>
<td></td>
</tr>
<tr>
<td>V: Sleep but slowly responds to stimuli</td>
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<tr>
<td>VI: Sleep, unresponsive to stimuli</td>
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</table>

**Observer Assessment of Alertness and Sedation (OAAS)**

| Level 6 – Agitated                          |
| Level 5 – Readily responds to name spoken (alertness) |
| Level 4 – Lethargic response to name spoken |
| Level 3 – Responds only when name called loudly or repeatedly |
| Level 2 – Responds only to prodding or shaking   |
| Level 1 – Does not respond to prodding or shaking |
| Level 0 – Does not respond to noxious stimuli |

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**Guidelines**

**Newsletter... Endoscopy 2014; 46: 720–731**
1. Pre-sedation monitoring

Anamnesis: The patient’s individual risks should be assessed. The aim is identifying all factors that may increase sedation-associated risks. Except for specific cases neither referral for a pre-anesthetic check-up nor additional studies such as chest x-rays or electrocardiography are necessary. Good history taking immediately before a procedure is currently considered a proper replacement for conventional pre-sedation visits, which to date have not been proven essential [43].

Medical history: Confirm the patient has been fasting for 6–8 hour for solids and 2–4 hours for liquids, and is accompanied by a responsible adult. Record the medical history likely to complicate sedation: severe cardiopulmonary or neurological disease; sleep apnea; prior adverse events with sedation/anesthesia or a history of difficult intubation; alcohol or other drug abuse; allergies to medications and, specifically, to egg and soy; potential risk for bronchoaspiration (intestinal occlusion, active gastrointestinal bleeding, gastric stasis, etc.).

Physical exploration: Vital signs (blood pressure, heart rate, oxygen saturation) and prior level of consciousness; assess the presence of obesity and of anatomic changes in the neck and oropharynx that might ultimately hinder intubation (Mallampati classification) [44].

According to medical record and examination findings the patient’s risk regarding sedation is evaluated using the ASA classification [14].

Peripheral vein cannulation and supplementary oxygen administration: Supplementary oxygen administration is recommended prior to the procedure (nasal cannula or mouth opener with oxygen tubing) as it reduces the incidence of arterial desaturation.

2. Monitoring during sedation

The patient must remain monitored throughout the procedure. Using a pulse oximeter is mandatory in all instances. For deep sedation as well as for patients with severe heart disease surveillance with blood pressure (every 3–5 minutes), electrocardiogram, and ventilatory function recorders is compulsory [38, 45–50]. Ventilation may be assessed by observing breathing movements or, if available, with a capnograph. However, the use of a capnograph has not proven indispensable. Monitorization data must be included in the medical record form.

Level of consciousness: An assessment will be made of the response to verbal or tactile stimuli. Several scales or instruments are available to help us establish the level of consciousness, including the bispectral index/narcotrend [17, 30]. This assessment must be performed every 3–5 minutes by the person responsible for sedation in order to maintain the desired sedation level and rescue the patient from a deeper level if needed.

3. Monitoring after procedure completion

Post-sedation surveillance: All patients having undergone sedation must be adequately monitored until they recover their baseline status, out of danger, and ready to be discharged from the endoscopy unit. Once the endoscopic procedure is completed, and the defensive reflexes recovered, patients may be transferred to a recovery room with the above-mentioned staff and equipment.

As already discussed, the use of scores is recommended to assess discharge time. In practice, Aldrete’s scale is the most commonly used score – 9 or 10 – to decide this [51] (Table 5). The fact that this scale assesses physical parameters rather than psychomotor activity should be taken into account. It is for this reason that discharged patients should be in the company of a responsible adult. It is recommended that sedation be avoided for outpatients with no companions.

It is also relevant to bear in mind that, as the hal-life of sedatives is longer than that of their agonists, when the latter are administered patients will need to stay longer in the recovery room to prevent potential resedation events. Providing precise written instructions for the 24 hours following sedation is highly advisable, including a phone number to contact the endoscopy unit should any adverse events or concerns arise after discharge.

Recommendations:

- Sedation requires monitoring before, during and after the endoscopic procedure until the patient is no longer at risk (evidence level 4, recommendation grade D).
- All actions and incidents occurring during sedation must be recorded and attached to the patient’s medical records (evidence level 4, recommendation grade D).
- With exceptions, a pre-anesthetic visit and check-up including chest x-rays and ECG is not necessary for gastrointestinal endoscopic procedures (evidence level 4, recommendation grade D).
- To undergo sedation patients must fast 6–8 hour for solids and 2–4 hours for liquids (evidence level 4, recommendation grade D).
- It is recommended that Aldrete’s or other similar scales be used to establish discharge time for patients, who should leave the endoscopy unit accompanied by a responsible adult (evidence level 4, recommendation grade D).
- Stay time in the recovery room will be longer for patients having received sedative antagonists (evidence level 4, recommendation grade D).

Table 5 Modified Aldrete Scale.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity</td>
<td></td>
</tr>
<tr>
<td>Moves 4 limbs voluntarily</td>
<td>2</td>
</tr>
<tr>
<td>Moves 2 limbs voluntarily</td>
<td>1</td>
</tr>
<tr>
<td>Unable to move limbs</td>
<td>0</td>
</tr>
<tr>
<td>Breathing</td>
<td></td>
</tr>
<tr>
<td>Able to breathe deeply</td>
<td>2</td>
</tr>
<tr>
<td>Dyspnea or limited breathing</td>
<td>1</td>
</tr>
<tr>
<td>Apnea</td>
<td>0</td>
</tr>
<tr>
<td>Circulation</td>
<td></td>
</tr>
<tr>
<td>Blood pressure&lt;20 %</td>
<td>2</td>
</tr>
<tr>
<td>Blood pressure 20–49 %</td>
<td>1</td>
</tr>
<tr>
<td>Blood pressure&gt;50 %</td>
<td>0</td>
</tr>
<tr>
<td>Awareness</td>
<td></td>
</tr>
<tr>
<td>Wide awake</td>
<td>2</td>
</tr>
<tr>
<td>Responds to calling</td>
<td>1</td>
</tr>
<tr>
<td>Does not respond</td>
<td>0</td>
</tr>
<tr>
<td>Arterial O2 saturation</td>
<td></td>
</tr>
<tr>
<td>Saturation&gt;95 % in room air</td>
<td>2</td>
</tr>
<tr>
<td>Needs oxygen to maintain</td>
<td>1</td>
</tr>
<tr>
<td>Saturation&lt;90 % with oxygen</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 5 Modified Aldrete Scale.
Table 6  FDA (Food and Drug Administration) pregnancy categories.

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Drugs used during endoscopy and sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Adequate and well-controlled human studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy</td>
<td>None</td>
</tr>
<tr>
<td>B</td>
<td>Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women OR Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester.</td>
<td>Meperidine, Propofol, Naloxone, Glucagon, Lidocaine, Mepivacaine</td>
</tr>
<tr>
<td>C</td>
<td>Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.</td>
<td>Midazolam, Fentanyl, Morphine, Flumazenil, Simethicone</td>
</tr>
<tr>
<td>D</td>
<td>There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.</td>
<td>Diazepam</td>
</tr>
<tr>
<td>X</td>
<td>Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.</td>
<td>None</td>
</tr>
</tbody>
</table>

Sedation in special situations: Pregnancy, lactation, pediatric age

Sedation during pregnancy: The safety of endoscopic procedures under sedation during pregnancy has not been thoroughly studied. The fetus is particularly responsive to hypoxia and hypotension in the mother [52]; it is because of this that elective non-obstetric procedures, including GI endoscopy, are recommended only for a clear indication, and should be delayed to the second trimester when possible [52, 53] in order to reduce the potential risks associated with perioperative stress, the procedure itself, and the effects of all drugs administered. However, numerous studies have confirmed the relative harmlessness of a single clínica exposure to anesthesia and surgery during the first trimester [54–57].

Today’s sedative and anesthetic agents have no proven teratogenicity (Table 6). Meperidine and propofol (class B) or fentanyl and midazolam (class C) may be used safely during pregnancy. Pregnancy-related physiological changes increase responsiveness to thiopental and volatile anesthetics, whose induction doses should be reduced. In contrast, no reduction is required for propofol induction dosing [58].

Sedation and lactation: The responsiveness of breastfeeding women to sedatives is similar to that of other adults [53]. Usual sedatives may be safely administered to women during lactation with no particular risk to the infant provided a number of recommendations are followed [59] – Among opiates fentanyl is preferable to meperidine; fentanyl levels in breastmilk are low enough to lack pharmacologic effects [60, 61] whereas meperidine does concentrate in breastmilk and may thus reduce infant alertness and interfere with feeding [59, 62]. As regards midazolam, breastfeeding should be delayed at least 4 hours following its dosing; breastmilk should be expressed and disposed of before feeding the child. Propofol concentration in breastmilk is only 0.015% of plasma levels, hence lactation needs not be withheld after this drug [60].

Sedation in children: In contrast to adults children require sedation for most invasive procedures as anxiety must be usually controlled, movements restrained, and pain and discomfort avoided. Sedation requirements outside operating rooms, by multiple specialists, and for a variety of diagnostic procedures are increasing in the pediatric setting [63]. Limited anesthetic resources, increased efficiency in patient management, and both patient and physici-an convenience drive a steady increase in pediatric sedation by non-anesthetist clinicians [64,65], with no differences being reported in the frequency of adverse events among the various specialists in charge of sedation [66].

In pediatric endoscopy and in selected cases, sedation is an alternative as effective as general anesthesia. Oral premedication with midazolam (0.5 mgr/kg) [69,70] or ketamine (5 mgr/Kg) [71] could facilitate the separation of parents and cannulation of venous access, further reducing the required doses of sedatives. Single or combined sedatives have been used for endoscopy-related sedation in children. A combination of sedatives does not increase the potential for adverse events as compared to sedation with only one drug, but does increase the intricacy of the sedation process [69–71]. As in adults, propofol doses are reduced when combined with midazolam and/or fentanyl [69, 70]. The combination of midazolam and ketamine provides better sedation for endoscopy versus midazolam or midazolam/fentanyl, as well as a faster recovery [71]. The use of midazolam alone has been reported as likely ineffective [67].

Propofol has been shown to shorten induction time and recovery from sedation versus midazolam [72] or midazolam/meperidine [73].

A recent systematic review suggests that propofol-based sedation is the most effective regimen for digestive endoscopy in the pediatric setting [67] – Propofol ensured an excellent level of successful procedures, better time management, and maximum patient comfort, particularly when midazolam was previously administered. In most studies propofol was administered by non-anesthetist clinicians (including endoscopists) with no increase in adverse events; the authors conclude that propofol may be safely administered by trained physicians. Repeated deep sedation with propofol in infants/toddlers has proven to be safe [74,75], although human research on this subject is scarce and potential risks should be weighed [76]. Beyond infancy, in the absence of organ-specific dysfunction or disease sedative effects and clearance is proportional to adults.

Recommendations:

- Indications should be unequivocal during pregnancy, and procedures should be postponed when possible until the second trimester (evidence level 4, recommendation grade D).
- Benzodiazepines, opiates, and propofol may be used during pregnancy. Propo-
If midazolam is used during breast-feeding breastmilk must be expressed and discarded, and feeding must be delayed to at least 4 hours after sedation; among opioids fentanyl is to be preferred to meperidine. Breastfeeding needs not be delayed after sedation with propofol (evidence level 3, recommendation grade D).

In the pediatric setting sedation may be an option as effective as general anesthesia. Oral premedication with midazolam may result in easier separation from parents, easier venous access cannulation, and lower sedative dose requirements (evidence level 1+, recommendation grade A).

In children sedation with propofol is effective and safe, and works better when midazolam is used for premedication (evidence level 1+, recommendation grade A).

Efficiency. Sedation costs

The use of sedation during gastrointestinal endoscopy reduces the discomfort and anxiety usually experienced by patients through the procedure, increases cooperation, and facilitates the examination. This translates into higher tolerance and satisfaction levels with the care received (perceived quality), and greater readiness to undergo repeated procedures when needed. The use of sedation has been shown to even improve the scientific-technical quality of explorations both for gastroscopy, where a better view of the esophago-gastro-duodenal tract is achieved [77], and colonoscopy, where sedation improves major quality indices, including the percentage of complete exams and adenoma resection rates [78]. However, these undeniable benefits of sedation may be burdened with increased exploration costs and reduced efficiency in the endoscopy unit. Sedation increases cost by rising pharmacy (drugs and IV fluids) and both fungible (venous access catheters, drip systems, oxygen administration devices, etc.) and non-fungible (monitoring equipment) material expenses. However, even more relevant than cost increases is the impact sedation may have on procedure length. Endoscopic procedures under sedation require additional time for previous venous access cannulation and sedation induction. On the other hand, patients must be monitored during recovery until their discharge from the endoscopy unit. This longer time is the factor that most significantly may impact efficiency. Furthermore, the use of sedation requires appropriately trained personnel to monitor patients during sedation and recovery, including an anesthesiologist for some cases, which further boosts costs. Therefore, before an endoscopy sedation program is implemented the characteristics of the involved unit and its patient population should be properly analyzed in order to decide which of the above sedation strategies fits better our needs and means. Assessing the cost-effectiveness of endoscopy sedation is challenging. On the one hand, the main goal of sedation during endoscopy, the achievement of higher tolerance and satisfaction levels, is a perceived quality parameter that cannot be easily quantified in economic terms. On the other hand, sedation cost-effectiveness is influenced by multiple factors that vary within and among countries. Thus, a hard-pressed unit will need fast patient turnover to keep upspace. In such a case a sedation strategy allowing shorter induction times and most particularly shorter recovery times would be of choice. In contrast, when care burdens are low such times are not so much a determinant of efficiency. Similarly, another core issue in determining the impact of sedation on efficiency is the amount of recovery beds per examination room. When few recovery beds are available sedation should allow faster recovery times to keep patient turnover high. Otherwise, when two or more recovery beds are available per endoscopy room delayed patient recovery will have no major impact on the unit’s efficiency. Also important is an assessment of the endoscopy unit’s patient population characteristics. If most are younger individuals or persons with minor conditions any of the above sedation strategies may be used without influencing efficiency. In contrast, if the patient population includes mostly elderly or multidiseased individuals (ASA > III), the use of anesthetics such as propofol will often require the help of an anesthetist in the unit, which will increase overall costs and decrease efficiency.

If a benzodiazepine is to be used, midazolam is the drug of choice for endoscopy-related sedation because of its short onset of effect and shorter half-life as compared to other drugs in this class [79]; midazolam provides rapid sedation induction and earlier patient recovery after the procedure. Regarding opiates, fentanyl significantly shortens induction and patient recovery versus meperidine [80,81]. This shortening of times results in increased efficiency at the endoscopy unit. Induction and recovery times for both basic and advanced endoscopy are shorter with propofol than with benzodiazepines and opioids [82,83]. Sedation with propofol administered by a non-anesthetist clinician may improve efficiency when compared to sedation with opiates and benzodiazepines [82,83]. Also, the administration of propofol by an anesthetist during a routine endoscopic procedure for a healthy, low-risk patient (ASA<III) is not cost-effective [38]. As discussed above, different sedation strategies exist. Some are based on the use of benzodiazepines either alone or associated with opioids, and others on the use of propofol either alone or in combination with opiates and/or benzodiazepines. Selecting one must be based primarily based on staff experience and training, and available technical resources. However, we must also assess the impact the selected approach may have on our endoscopy unit’s efficiency. We should reach an appropriate balance between the benefits obtained with sedation and increased costs as well as potential efficiency reductions.

Recommendations:

- When benzodiazepines are used, midazolam is the drug of choice for endoscopy-related sedation as it provides fast sedation induction and earlier patient discharge after the procedure (evidence level 2++, recommendation grade B).

- The use of fentanyl rather than meperidine significantly reduces patient indution and recovery times. This reduction results in increased efficiency at the endoscopy unit (evidence level 2++, recommendation grade B).

- Sedation induction time is shorter with propofol than with benzodiazepines and opiates (evidence level 1+, recommendation grade A).

- Recovery time after sedation is shorter when propofol is used alone (evidence level 1+, recommendation grade A).

- Sedation with propofol administered by non-anesthetist clinicians may improve endoscopy unit efficiency as compared to sedation with opiates and
benzodiazepines (evidence level 1+, recommendation grade A 1+).

- Routine propofol administration by an anaesthesiologist to healthy, low-risk patients (ASA < III) in the endoscopy setting is not cost-effective (evidence level 1+, recommendation grade A).

**Informed consent**

To provide sedation in the digestive endoscopy setting patients must provide their informed consent (IC) in accordance with the Basic Law of Patient Autonomy [84] and the Medical Code of Deontology [85]. For patients younger than 16 or if factual incapacity to receive information and/or give consent for the procedure is present the IC must be obtained from the patient’s legal representatives. In life-threatening emergencies in the absence of legal representatives the circumstances leading to the waiving of informed consent must be accurately detailed in the medical record. The information given and the IC obtained by the physician prescribing the endoscopy do not exempt the endoscopist/sedator from his or her obligation to inform and obtain an IC. This obligation cannot be delegated to nurses or auxiliary staff. The verbal and written information provided on sedation must be accurate and understandable by the patient. It must include a discussion on the benefits and risks of sedation (including those related to vehicle driving and other dangerous activities after the procedure), potential complications, both typical and more severe, and available alternatives (including an optional endoscopy with no sedation). The fact that sedation will be administered by qualified personnel under the responsibility of an endoscopist, anaesthesiologist or intensivist should also be made explicit. The informed consent represents a medical, legal and ethical aspect not amenable to scientific research, hence no “scientific evidence” exists to establish recommendations thereupon. Its regulation depends on national laws, in this case the Spanish Basic Law of Patient Autonomy [84], and on the jurisprudence thereof. It is “scientifically” considered an expert opinion with the lowest grade of recommendation, but recommendations are both legally and ethically mandatory. Medico-legal implications of sedation administered by non-anesthesiots: In Spain, any Graduate of Medicine and Surgery is entitled to perform any medical act for which he or she has acquired appropriate training and skills, including sedation without a specialist’s degree in Anesthesiology and Resuscitation. However, these clinicians must be aware of their own limitations and seek the help of expert colleagues whenever it is advisable. Under the Spanish legal system [86–91] that of “physician” is the only “medical profession” acknowledged. There is no “medical specialist” profession. “Specialties” are variations within a single medical profession. The profession of “physician” is acquired by obtaining the academic degree of Graduate of Medicine and Surgery, which entitles to practice the medical profession in its totality [87], in any or all of its branches but without claiming a specialist’s degree in any of them. A specialist physician degree does not establish the specialty’s sphere of competence [88], and no limits exist between medical specialties [89, 90]. No law expressly restricts to specialist physicians the performance of any specific activities of procedures [91]. Academic degrees (graduate) and official degrees (specialist) do not grant: a) necessary competence in an automatic, indefinite way; b) immunity against negligence or misjudgement; c) the right to exclusively exploit any specific procedure; d) the monopoly to practice in a specific field. Physicians are entitled to unlimited professional practice, unless they act in ethically unsound ways [92]. The Criminal Code [93] defines the crime of unauthorized practice as “the performance of activities specific of a profession by a person not licensed to do so”, hence no graduate of medicine and surgery may be charged with this crime. Unauthorized practice is nonexistent between medical specialties [91].

**Recommendations:**

- A specific informed consent must be obtained whereby the patient receives information on the characteristics of sedation, the staff responsible for it, its risks, and the available alternatives (evidence level 4; recommendation grade D)
- The patient may withdraw his or her consent at any time by informing of his or her decision in writing (evidence level 4; recommendation grade D)
- To perform sedation for endoscopy appropriate competence must be acquired and maintained through initial and continuing training programs (evidence level 4; recommendation grade D)

- The endoscopist must be aware of the limits of his or her own competence, and seek the help of a competent colleague (anaesthetist or otherwise) whenever a sedation process goes beyond his or her expertise (evidence level 4; recommendation grade D).

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Corresponding author
Leopoldo López Rosés
Servicio de Aparato Digestivo
Hospital Universitario Lucus Augusti. Lugo. Avda. Dr. Ulices Romero s.n. 27003 – Lugo
Spain
Phone: +34982296671
Fax: 982296671
leoleoperezroses@gmail.com