



## Digestive Endoscopy

# Italian Society of Digestive Endoscopy (SIED) position paper on the non-anaesthesiologist administration of propofol for gastrointestinal endoscopy



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## ABSTRACT

Propofol sedation by non-anesthesiologists in GI endoscopy, despite generally considered a safe procedure, is still a matter of debate. Benefits of propofol sedation include rapid onset of action, greater patient comfort and fast recovery with prompt discharge from the endoscopy unit.

The use of propofol for sedation in GI endoscopy, preceded by dedicated training courses, has been approved by several anaesthesiologist and gastroenterologist societies but an Italian position paper taking into account the Italian law is lacking.

In the present document, the Italian Society of Digestive Endoscopy (SIED) Sedation Group, on behalf of the SIED, presents a series of updated position statements concerning propofol sedation in GI endoscopy. The paper summarizes the advantages of propofol, how it should be administered and how patients should be monitored. Moreover, details concerning proper training of non-anaesthesiologist personnel involved in its use are provided. Protocols concerning propofol use must be shared with the hospital's anaesthesiology staff and approved by the hospital's Executive Director.

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## 1. Introduction

Propofol is an ultra-short acting sedative increasingly used worldwide for gastrointestinal endoscopy (GI) [1]. According to the most recent guideline published by the European Society of Gastrointestinal Endoscopy [2], compared with traditional sedation propofol-based sedation provides higher post-procedure patient satisfaction for most endoscopic procedures, decreases time to sedation, and decreases recovery time. Moreover, propofol-based sedation presents similar rates of adverse effects and may also increase the quality of the endoscopic examination [2]. Several scientific societies have approved the non-anaesthesiologist administration of propofol (NAAP) in GI endoscopy [2–5], provided that it is administered by adequately trained personnel [6].

However, it must be recognized that appropriate patient selection, use of an established protocol for drug administration, and careful monitoring of patient throughout the procedure are of paramount importance.

A position paper about the use of propofol for GI endoscopy in Italy has not yet been published. In the present document, the Italian Society of Digestive Endoscopy (SIED) Sedation Group, on behalf of the SIED and in accordance with Italian law, presents a series of updated position statements on the use of propofol.

## 2. Methodology

In the present paper, the SIED supports the previous recommendation of the joint American Gastroenterology Societies and of the European Societies of Gastroenterology and Endoscopy. A four-member committee, on behalf of the SIED, prepared the first draft of the document which was revised by an independent magistrate, and then reviewed and approved by the SIED legal and governing boards. The development process for this document included

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online discussion among members of the committee between 2015 and 2016.

A literature search was conducted for English-language articles from 1997 to 2016. Databases included Medline (via PubMed) and Cochrane with search for terms that included propofol, GI endoscopy, and non-anaesthesiologist. Full-text articles were carefully reviewed and reported in the position paper if concerning non-anaesthesiologist administration of propofol (NAAP) or if considered pertinent. Since this is a position paper, evidence was not graded.

### 3. Position Statements

#### Statement 1. Has propofol advantages over standard agents used for conscious sedation, i.e. benzodiazepines and opiates?

Propofol is a short-acting intravenous agent that has a favourable pharmacokinetic profile in comparison to benzodiazepines and opioids with regard to rapid onset of action, short recovery profile, anti-emetic properties, equivalent amnesic effects and better patient's comfort; moreover, its short context-sensitive half-life makes it very easy to titrate.

Several studies have suggested that propofol offers significant advantages over benzodiazepines and opioids for reaching and maintaining an adequate level of sedation during GI endoscopy with better recovery and shorter discharge periods [2]. Moreover, it has long been recognised that propofol-based sedation may also increase the quality of the endoscopic examination [7]. A recent meta-analysis of twenty-two RCTs showed that propofol is highly effective and safe for all GI endoscopy procedures [8]. Accordingly, the most recent European Guidelines confirm the high efficacy of propofol usage for sedation in GI endoscopy [2].

#### Statement 2. Is propofol safe for use as a sedation agent for endoscopy when used by appropriately trained endoscopists and endoscopy nurses?

NAAP is safe when performed by properly trained personnel. According to a worldwide safety survey on NAAP, extremely low rates of serious complications were reported in 646,080 cases [1].

A meta-analysis found no increased risk of cardiopulmonary complications with propofol as compared with traditional sedative agents; moreover, cases requiring intubation or deceased were not reported [9]. However, appropriate patient selection is crucial, because a high complications rate has been reported in patients with a high American Society of Anaesthesiologists (ASA) class who underwent propofol sedation during interventional GI endoscopy procedures [10].

In a multicenter German survey of 53 ambulatory gastroenterology practices, data on 24,441 patients who received NAAP were prospectively evaluated [11]. Before starting the study, all endoscopists received a training course of advanced cardiac life support and airway management with mask ventilation, followed by a final written examination. Major adverse events occurred in four patients (0.016%), all resolved with mask ventilations. All patients with major adverse effects showed no signs of persistent impairment.

A recent retrospective observational cohort study, conducted on 1,388,235 patients, was aimed to determine whether anaesthesiologist-directed sedation (ADS) provides a safety advantage when compared with endoscopist-directed sedation (EDS) [12]. The observed serious adverse events for patients receiving ADS was similar for colonoscopy (OR, 0.93; 95% CI 0.82–1.06) but higher for gastroscopy (OR, 1.33; 95% CI 1.18–1.50) in comparison to EDS. Additionally, with further stratification by ASA class, the use of ADS was associated with a higher risk for SAEs in ASA I/II and ASA

**Table 1**

Typical program of a training course for non-anesthesiologist administration of propofol.

|                                                                                                                                                             |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Theoretical part                                                                                                                                            |
| • Pharmacology, pharmacokinetics, and interactions of sedatives, analgesics, and respective antidotes                                                       |
| • Principles of sedation and monitoring patients including analysis of ECG monitoring                                                                       |
| • Different sedation concepts                                                                                                                               |
| • Pre-, intra- and post-endoscopy patient care concerning sedation, monitoring, recovery, discharge criteria, management of complications and documentation |
| • Legal aspects (e.g. delegation, informed consent)                                                                                                         |
| Practical part                                                                                                                                              |
| • Basic airway management (e.g. freeing of airways, jaw thrust, bag-valve mask ventilation)                                                                 |
| • Use of different tubes for airway ventilation (e.g. Mayo and Guedel tube, laryngeal tube)                                                                 |
| • Treatment of acute respiratory problems                                                                                                                   |
| • BLS and ACLS, including the use of defibrillators                                                                                                         |

ACLS, advanced cardiac life support; BLS, basic life support.

III subjects undergoing gastroscopy and showed no difference for either group undergoing colonoscopy [12].

Finally, a recent non-inferiority RCT in low risk patients by Ferreira et al. [13] could not show any difference in safety of NAAP versus ADS.

#### Statement 3. Can also appropriately trained endoscopy nurses administer propofol for endoscopy?

Nurse-administered propofol sedation (NAPS) for GI endoscopy has been evaluated in several clinical trials [14–16]. Specific knowledge and skills are necessary for NAPS to ensure patient comfort and safety. NAPS providers must have the required training to deal with significant respiratory depression in order to maintain airways patency (e.g. using a Mayo or Guedel cannule, laryngeal tubes and/or ventilation mask) while waiting for anaesthesiologist's support.

A study conducted in more than 27,000 NAAP procedures showed that even an endoscopic team constituted by one endoscopist and one nurse can safely administer propofol for GI endoscopy [17]. However, a trend toward less frequent circulatory complications with a person dedicated to NAAP was observed in a more recent study [18]. Overall, it is generally recommended that nurses administering propofol must be dedicated to monitoring of the patient and not involved in the endoscopic procedure [2–5].

#### Statement 4. Is training of endoscopy staff required before administration of propofol in clinical practice?

Training courses for sedation in GI endoscopy, embedding a theoretical and a practical part, have been recommended by the American society of Gastrointestinal Endoscopy (ASGE) [19], the American Gastroenterological Association (AGA), the American College of Gastroenterology, the European Society of Gastrointestinal Endoscopy (ESGE) and the Canadian Association of Gastroenterology [2–6]. A final test aimed to document successful training is desirable. Tutors should teach techniques of basic life support (BLS) to all participants. Moreover, personnel trained in advanced cardiac life support (ACLS) should always be present in the endoscopic area [2].

Training and re-training programs have been recommended in European Guidelines [6] (Table 1). According to European Guidelines, in Italy training of endoscopists and nurses can be provided by an anaesthesiologist in cooperation with another person with previous experience of >300 NAAP cases. During training procedures, NAAP must be carried out with an anaesthesiologist

present in the endoscopic area [6].

#### Statement 5. Is administration of propofol by non-anesthesiologists cost-effective?

Sedation with propofol administered by non-anesthesiologists may be more cost-effective than sedation with opiates and benzodiazepines in ASA I/II patients because anaesthesiologist assistance is costly and is not advantageous [7,20–22]. In a study carried out in France on cost-effectiveness of colorectal cancer screening, anaesthesiologist involvement added 285% to the cost of a colonoscopy (€ 757 vs. € 192 for a colonoscopy with or without anaesthesiologist support, respectively) [23]. The worldwide safety survey on NAAP demonstrated that the administration of propofol by anaesthesiologists during routine endoscopic procedures for healthy, low-risk patients (ASA < III) is not cost-effective [1].

Available evidence suggests that cost-effectiveness of routinely involving anaesthesiologists in providing sedation for endoscopic procedures is questionable. German Guidelines [24] state that ADS is cost-effective only for patients with a high-risk profile, such as patients with ASA grade III or higher, or cases with pathological or anatomical features associated with a high risk of airway obstruction during sedation. To date, no randomised study proving the superiority of anaesthesiologist's assistance for propofol sedation and contradicting this recommendation has been published. Furthermore, an Italian study investigating Monitored Anaesthesia Care during propofol administration demonstrated a respiratory complication rate comparable to ADS (1.4%) [25].

#### Statement 6. Should patients receiving propofol for endoscopy be monitored?

Heart rate, arterial oxygen saturation and blood pressure should be routinely monitored before, during (every 3–5 min) and after administration of sedation/analgesia, regardless of the drug administered [26,27]. Since NAAP is not a general anaesthesia procedure and the target is moderate sedation, routine continue ECG monitoring is required only in selected patients with specific cardiovascular risk. Nonetheless, a defibrillator must be immediately available in the endoscopic area.

As far as monitoring of respiratory function is concerned, pulse oximetry can detect hypoxemia but not hypercarbia, an early warning sign of hypoventilation [2,28]. In order to prevent hypoxemia, supplemental oxygen is widely used during sedation in GI endoscopy despite some risk of delayed recognition of hypoventilation [29]. Capnography allows monitoring of CO<sub>2</sub> levels, their increase denoting hypoventilation. However, only side-stream capnography can be used in an unintubated patient: since it entrains ambient air into the analysis chamber, only respiratory rate but not hypercarbia can reliably be monitored and apnoea can reliably be detected. Currently, there is no clear-cut demonstration that clinical outcomes or care quality can be improved with the use of capnography in adults undergoing targeted moderate sedation for GI endoscopy [28].

Overall, direct observation of the patient and direct assessment of the patient's state of consciousness, ventilation and oxygenation cannot be substituted with the most sophisticated monitoring equipment. For this reason, recent guidelines from Europe and USA [2,4,5] state that a trained person should be dedicated to patient monitoring, which should represent his/her sole task. According to German Guidelines [24], “for simple endoscopic examination and in low-risk patients, sedation with propofol should be induced by a properly qualified physician and can then be monitored by an experienced person with appropriate training. This person must not have any other tasks while monitoring the sedation. Propofol may be administered by a properly trained and experienced person who has this as his or her sole task (recommendation grade A, strong consensus)”. International guidelines by Scientific Soci-

**Table 2**

Modified observer's assessment of alertness/sedation scale (MOAA/S).

| Responsiveness                                              | Score |
|-------------------------------------------------------------|-------|
| Agitated                                                    | 6     |
| Responds readily to name spoken in normal tone (“Alert”)    | 5     |
| Lethargic response to name spoken in normal tone            | 4     |
| Responds only after name is called loudly and/or repeatedly | 3     |
| Responds only after mild prodding or shaking                | 2     |
| Does not respond to mild prodding or shaking                | 1     |
| Does not respond to deep stimulus                           | 0     |

eties recommended the standardization of evaluation of alertness level throughout the procedure by use of a scoring systems such as the Modified Observer's Assessment of Alertness/Sedation Scale (MOAA/S SCALE) [30] (Table 2).

Following the end of sedation, the patient must be monitored during the recovery phase by a person who is aware of the potential adverse events related to the drug(s) administered. Heart rate, arterial oxygen saturation and blood pressure must be monitored; aspirators, oxygen delivery systems, airway equipment of different sizes, pharmacologic antagonists, resuscitative medications and equipments for intravenous equipment must be present in the recovery room. Complications may occur up to 30 min after the administration of standard sedation with benzodiazepine and opioids, representing approximately 10% of adverse events. Special attention should be paid after the administration of antagonists (flumazenil and naloxone) with monitoring prolonged up to 2 h [31,32]. Serious post-procedures adverse events are less frequent with propofol than with standard sedation [33]. However, no more than 5 patients can be monitored by one person, and personnel in the recovery room must be adjusted on the basis of actual activity and vice-versa. After NAAP/NAPS, the patient can be discharged only when psychomotor functions are those preceding sedation; he must be accompanied by a responsible person and must abstain from driving, operating heavy machinery, or engaging in legally binding decisions for at least 12 h. Patient must receive written instructions for any possible complications [2]. European Guidelines [2] suggest usefulness of the post-anaesthetic discharge scoring system (e.g. PADSS) (Table 3), as suggested by a recent study [34], despite the level of evidence is admittedly low [2].

#### Statement 7. Which protocol must be followed for dosing propofol?

Currently, there are no formal dosing protocols for NAAP/NAPS during GI endoscopy [2–5]. A level of moderate sedation is the NAAP/NAPS target. There are at least two different methods for propofol administration, either alone or in combination with one or more additional agents (balanced propofol sedation, BPS).

Moreover, propofol may be used with different modes and protocols:

- In incremental bolus loads,
- By continuous infusion,
- By targeted controlled infusion (TCI),
- By patient controlled sedation (PCS).

#### 7.1 Propofol as sole agent

Propofol alone is usually administered as a 10- to 50-mg bolus followed by additional boluses of 10–20 mg after at least 20–30 s. The total dosage 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, higher doses are typically required to achieve adequate sedation, and deeper sedation level may be required to keep the patient comfortable [35].

**Table 3**  
Post-anaesthetic discharge scoring system (PADSS) for patient discharge.

| Categories                                                                                                                | Points |
|---------------------------------------------------------------------------------------------------------------------------|--------|
| <b>Vital signs</b>                                                                                                        |        |
| • BP and HR $\pm 20\%$ of pre-endoscopy value                                                                             | 2      |
| • BP and HR $\pm 20\%$ to $40\%$ of pre-endoscopy value                                                                   | 1      |
| • BP and HR $\pm 40\%$ of pre-endoscopy value                                                                             | 0      |
| <b>Activity</b>                                                                                                           |        |
| • Steady gait, no dizziness or meets pre-endoscopy level                                                                  | 2      |
| • Requires assistance                                                                                                     | 1      |
| • Unable to ambulate                                                                                                      | 0      |
| <b>Nausea and vomiting</b>                                                                                                |        |
| • No or minimal/treated with oral medication                                                                              | 2      |
| • Moderate/treated with parenteral medication                                                                             | 1      |
| • Severe/continues despite treatment                                                                                      | 0      |
| <b>Pain</b>                                                                                                               |        |
| • Minimal or no pain (numerical analogue scale = 0–3)                                                                     | 2      |
| • Moderate (numerical analogue scale = 4–6)                                                                               | 1      |
| • Severe (numerical analogue scale = 7–10)                                                                                | 0      |
| <b>Bleeding</b>                                                                                                           |        |
| None or Minimal (not requiring intervention)                                                                              | 2      |
| Moderate (1 episode of hematemesis or rectal bleeding)                                                                    | 1      |
| Severe ( $\geq 2$ episodes of hematemesis or rectal bleeding)                                                             | 0      |
| <b>Total score</b><br>(Patients' scoring $\geq 9$ for two consecutive measurements are considered fit for discharge home) | ..     |

BP, blood pressure; HR, heart rate.

## 7.2 Balanced propofol sedation (BPS)

BPS combines propofol with small induction doses of fentanyl (1 mcg/kg) and/or midazolam. The co-administration of propofol with one or more additional agents reduces the total dose of propofol required, improves sedation and analgesia, and adds elements of reversibility. Indeed, if it is necessary to reduce the level of sedation reversal agents to opioid and benzodiazepine can be administered.

## 7.3 BPS: bolus loads and continuous infusion

After fentanyl and/or midazolam, propofol is administered in small titrated doses of 5–15 mg until moderate sedation is achieved. Otherwise, in a BPS regimen propofol can be administered by a continuous intravenous infusion of 0.3 mg/kg/min. With BPS, a smaller dose of propofol is required to obtain adequate sedation, resulting a lower risk of adverse events. Of note, BPS is associated with significantly shorter recovery times and discharge than propofol alone titrated to deep sedation throughout the procedure [36].

## 7.4 Targeted controlled infusion (TCI)

Among the different methods currently available for propofol administration, TCI is undoubtedly one of the most sophisticated. It consists of an automatic system of drug administration based on algorithms which take into account age, weight, desired plasma concentration: the optimal infusion rate is determined in order to avoid the serum peak concentrations associated with serious side effects. In propofol TCI, following a small induction dose of fentanyl (1 mcg/kg) for pain control, propofol is administered until a target concentration of 1.2–1.6  $\mu\text{g/ml}$  is reached, titrated on the basis of patient's characteristics. Propofol TCI represents an excellent and safe procedure during sedation for GI endoscopy [37].

## 7.5 Patient controlled sedation (PCS)

For PCS, the patient self-administers the medication; therefore, he/she must be conscious enough to press the hand-held button. A lock-out time is usually programmed in order to prevent the delivery of additional doses until the previous dose has taken full effect. Some trials have demonstrated that PCS is a feasible option for propofol administration during GI endoscopy because of its ease of use, lower dosages of propofol used and quick recovery [38].

Summing up, there is no clear-cut advantage of a technique over the others. The Authors prefer BPS with the TCI technique, but recommend adoption of propofol administration protocols shared with the anaesthesiology staff and approved by the Institutional Review Board. NAAP and NAPS both require adoption of protocols including details for patient selection, education and training of nursing and medical staff, modalities of drug administration, and parameters to be monitored throughout the procedure, independently of the technique of propofol administration chosen. Furthermore, an informed consent form reporting the main characteristics of propofol, the type and setting of administrations (NAAP and/or NAPS), possible complications, and modalities of discharge must be signed by the patient before the procedure.

## Statement 8. Is routine involvement of anesthesiologists required for administering propofol to low-risk patients undergoing GI endoscopy?

The risk of sedation-related complications parallels increases in ASA score [39,40]. The risk for a cardio-respiratory event is comparable for ASA I and ASA II patients and many ASA III cases undergoing non-propofol sedation, while the risk of complications steadily increases from ASA III to ASA IV and V. Similar problems have been encountered with propofol sedation. The risk of respiratory complications appears to be somewhat greater during gastroscopy than during colonoscopy [1].

There is unanimous agreement among published position statements and practice guidelines that ASA I and II patients are appropriate candidates for sedation by a qualified non-anaesthesiologist sedation team.

Anaesthesiologist's support is required for ASA IV and ASA V cases and for patients who do not consent to NAAP.

For ASA III patients, careful evaluation of the patient is required also with regard to the procedure scheduled [2–5,39].

Anaesthesiologist's support should always be considered for:

- Patients with anatomic obstacles for ventilatory support (e.g. obesity, thick necks);
- Uncooperative patients;
- Long-lasting or high-risk interventional procedures.

## 4. Closing remarks

NAAP and NAPS are uncommonly used in Italy [42] but are widely adopted in many countries, such as USA, Germany and Spain [2–5,41]. Their safety and efficacy have been recognised by many guidelines and position papers [2–5,24,39].

In 2010, the European Society of Gastrointestinal Endoscopy, the European Society of Gastroenterology and Endoscopy Nurses and Associates, and the European Society of Anaesthesiology released an official guideline regarding non-anaesthesiologist administration of propofol for GI endoscopy [43]. Owing to strong internal opposition, the European Society of Anaesthesiology retired endorsement in the April 2012 issue of European Society of Anaesthesiologists (ESA) [44], a position agreed by the Italian Society of Anaesthesiologist (SIAARTI).

Recently, Italian Professional Ethics Code (Article 13) [45] stated that a physician can prescribe any drug, provided he has adequate knowledge of the drug and tolerability and efficacy of the drug

**Table 4**  
Non-anaesthesiologist administration of propofol (NAAP)—recommendations.

1. NAAP is safe when administered by trained personnel in carefully selected patients.
2. Structured educational courses for NAAP are mandatory. Periodical retraining programs (at 2–3 year intervals) are strongly recommended.
3. Training in endotracheal intubation is not required for NAAP. Personnel providing NAAP must be trained to deal with significant respiratory depression in order to maintain airways patency (e.g. usage of a Mayo cannule); anaesthesiologist support must be promptly available.
4. Regular monitoring by trained personnel is warranted. The level of alertness must be checked every 5 min using the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) Scale. Pulse oxymetry and arterial pressure, and ECG monitoring whenever deemed necessary, with acoustic alarms are required. Monitoring of the patient by a dedicated person is safer.
5. Supplemental oxygen administration with nasal cannula is recommended in patients considered at risk.
6. Protocols concerning patient selection, education and training of nurse and medical staff, modalities of drug administration, and parameters to be monitored must be shared with the anaesthesiologist staff and approved by the Institutional Review Board.
7. The patient cannot be discharged before complete recovery of the initial performance status.
8. In ASA I and ASA II patients, NAAP is cost-effective in comparison to anaesthesiologist-assisted sedation and should be preferred.
9. Anaesthesiologist's support is required for ASA IV and ASA V cases and for patients who do not consent to NAAP.
10. Anaesthesiologist's support should always be considered for:
  - a) patients with anatomic obstacles for ventilatory support (e.g. obesity, thick necks);
  - b) ASA III cases;
  - c) uncooperative patients;
  - d) long-lasting or high-risk interventional procedures.

has been documented so that the risks are proportionate to the expected benefits. Moreover, according to the evaluation of AIFA (Italian Drug Agency) [46] propofol usage is limited to hospital settings, but prescription and administration by a specialist is not warranted, also according to some drug packages. SIED will propose to reconsider these restrictions to AIFA, in order to license the administration of propofol and patient monitoring by trained personnel not involved in the endoscopic procedure. Our recommendations are summarised in Table 4.

**Conflict of interest**  
None declared.

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