

# Challenging Propofol Sedation In Gastrointestinal Endoscopy: High Risk Patients And High Risk Procedures

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## Abstract

Sedation is increasingly becoming a must for most endoscopic procedures. Non-anesthesiologist administration of propofol is the standard of practice in many European countries. Nevertheless, despite anesthesiology societies concerns about sedation guided by endoscopist, practitioners find some limits to propofol administration, related to high risk patients or high risk and complex procedures, which can be long lasting and technically challenging.

The main patient related risk factors for sedation are elderly patients, obesity, ASA $\geq$ 3 patients, individuals with craniofacial abnormalities or with pharyngolaryngeal tumors, patients with an acute gastrointestinal bleeding, under pain medications, sedatives, antidepressants, or who consume significant amounts of alcohol or drugs. Procedure related risk factors have more to do with the duration and complexity of the procedure than with other factors, in which considering a general anesthesia allows the endoscopist to concentrate on a difficult task.

Published papers addressing the most challenging sedation groups in endoscopy are exploring and even trespassing previously assumed frontiers, and new scenarios are opening to the endoscopist, increasing his/her autonomy, reducing costs and giving patients levels of comfort previously unknown.

In this review we analyse each risk group determining the ones in which a sedation protocol could be widely applied, and other in which the published evidence does not guarantee a safe endoscopist guided propofol sedation.

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## Introduction

Non-anesthesiologist administration of propofol (NAAP) is an expanding sedation regimen throughout Europe. Many patients have been successfully sedated with this drug, and the increasing population demands for comfort as well as the need to reduce costs in medical procedures determined its expanded use among medical practitioners not directly related with anesthetics departments or intensive care units.<sup>(1)</sup>

Still, anesthesiology societies have concerns regarding propofol use by non-anesthesiologists, but they are mostly based on expert opinion rather than in well designed studies.<sup>(2,3)</sup> Indeed, collaborative efforts between different endoscopy and anesthesiology societies have recently produced guidelines for the wide use of NAAP in endoscopy,<sup>(4)</sup> and a vast European and US NAAP experience has been published in different settings.<sup>(1,5-11)</sup> As time goes by, propofol use by gastroenterologists is spreading and showing its safety. Nevertheless, when a therapy or medical procedure spreads it also finds its burdens,

and sedation ones are the same as those found in anesthesiology and sedation in regular patients, in which elderly, comorbidities, cardiovascular or lung diseases can limit our possibilities. Certainly, the guidelines suggest endoscopist to be careful and even to refer some patients to an anesthesiologist before undergoing NAAP when some risk factors are found, including ASA category  $\geq 3$ , a Mallampati's class of 3, or other conditions at risk for airway obstruction, patients who chronically receive significant amounts of pain medications or in cases of predictable long-lasting procedures.<sup>(4)</sup>

High risk sedation has therefore two main groups of risk factors: patient dependent and procedure dependent. Regarding patient dependent risk factors, elderly patients,<sup>(8,9,12)</sup> obesity,<sup>(13)</sup> ASA  $\geq 3$  patients, individuals with craniofacial abnormalities or with pharyngolaryngeal tumors,<sup>(4)</sup> patients with an acute gastrointestinal bleeding<sup>(14)</sup> who are under pain medications, sedatives, antidepressants, or who consume significant amounts of alcohol or drugs are more difficult to sedate, and sometimes require the participation of an anesthesiologist. Procedure dependent factors are related to the duration of the procedure, painful maneuvers associated to endoscopy (e.g. percutaneous gastrostomy), the need of a motionless patient for complex techniques and the type of endoscopy required, upper or lower, because upper endoscopy causes more discomfort to patients and comprise a higher risk of airway complications.

It is essential for a gastroenterologist who usually, maybe daily, performs NAAP, to do so under a strict sedation protocol and always knowing when to require the assistance of an anesthesiologist. In a valuable effort, a multi-society joint in the US has established a curriculum for sedation in gastrointestinal endoscopy,<sup>(15)</sup> in which authors recommend to require this assistance in the following settings:

- Prolonged or therapeutic endoscopic procedures requiring deep sedation or general anesthesia.
- Anticipated intolerance, paradoxical reaction or allergy to standard sedation regimens.
- Increased risk of complications because of severe comorbidity (ASA class 4 and higher)

- Increased risk of airway obstruction
  - History of stridor
  - History of severe sleep apnea
- Dysmorphic facial features
  - Trisomy 21
  - Pierre-Robin syndrome
- Oral abnormalities
  - <3 cm oral opening in adults
  - Protruding incisors
  - Macroglossia
  - High arched palette
  - Tonsillar hypertrophy
  - Mallampati score of 4
- Neck abnormalities
  - Decreased hyoid-mental distance ( 3 cm in adults)
  - Short thick neck
  - Limited neck extension
  - Cervical spine disease (eg, advanced rheumatoid arthritis) or trauma
  - Severe tracheal deviation
- Jaw abnormalities
  - Retrognathia
  - Micrognathia
  - Trismus
  - Severe malocclusion

In general, we strongly agree with these limitations to NAAP. Nevertheless, recent reports provide new evidence to support the practice of NAAP in some previously considered high risk scenarios. In this review we are going to establish these situations in which the gastroenterologist could safely sedate a patient otherwise considered of high risk.

The first recommendation for a non-anesthesiologist who is planning to develop a NAAP protocol, is to undergo a structured training for this purpose, to receive an extensive instruction in basic life support and even in advanced cardiac life support (ACLS), if an ACLS caregiver is not immediately available in the endoscopy unit. Self training has been strongly discouraged in this item.<sup>(4)</sup> Thus, every gastroenterology or endoscopy training program should have a specific scheduled training in NAAP.

## Patient Related Risk Factors

### 1. ASA $\geq$ 3

Although some guidelines recommend the assistance of an anesthesiologist with these patients, the general recommendation in the main guidelines is to adjust propofol doses and maintain an adequate monitoring, because they are at a higher risk of sedation-related side effects.<sup>(4,16)</sup> In a paper focused on high risk octogenarian which underwent therapeutic endoscopy, 34/74 patients in the propofol group were ASA-III and 12/76 ASA-IV.<sup>(8)</sup> The authors observed a higher decrease in blood pressure and a higher oxygen desaturation rate with propofol, when comparing NAAP with a standard sedation with Midazolam. Nevertheless, NAAP was safe, with no major adverse events a no procedure interrupted due to sedation related events in ASA-III-IV patients. Of note, neither propofol doses (60-870 mg) nor mean examination times (47 $\pm$ 16 minutes) were lower than what is expected for average risk patients. In another recent paper from our group, 138/456 ASAIII-IV patients were included in a study focused on EUS. Per protocol, high risk patients received between a quarter and half the dose of propofol comparing to average risk patients. As an obvious consequence to this dosage, we found that the total propofol dose was lower in high risk patients (164.8 $\pm$ 84.3), finding no differences in procedure duration, recovery time, patients' and endoscopist's satisfaction with the procedure, and adverse events.<sup>(10)</sup> No major adverse events have been observed in our series.

Consequently, we think there is enough evidence to support cautious propofol sedation in patients with high anesthetic risk, under a strict sedation protocol (ASA-III/IV).

### 2. NAAP in the Elderly

Many studies have tested NAAP in high risk elderly patients, finding no differences with other sedation regimes regarding safety.<sup>(8,9,12)</sup> The first paper addressing this issue,<sup>(9)</sup> in which the authors included 1435 patients who were 70-85 years of age and 351 with more than 85 years, considered very old, is remarkable. In this study, the investigators found that doses could be reduced in these patients as much as a 35-40% of that administered to younger adults. They found a slightly increased rate of oxygen desaturation in old patients, but without clinical consequences, concluding that propofol is safe in this group of patients.

Interestingly, investigators agree in lowering initial propofol doses in the elderly, with repeated doses of 20 mg, normally following the 20/20 rule, which consists in a careful titration in steps of 10-20 mg against the clinical response, making pauses lasting at least 20 seconds between each bolus.<sup>(9,12)</sup> This schedule allows an effective and cautious sedation in old patients, leading to a safety comparable to young patients in the studies which specifically addressed this population.

### 3. Obese Patients

Obesity has been recognised as a potential risk factor for sedation in endoscopy,<sup>(17,18,19)</sup> and obese patients have a high prevalence of sleep obstructive apnea, which can make individuals more prone to hypoxemia when sedated. Indeed, propofol accentuates airway collapse, potentially increasing the risk of cardiopulmonary adverse events.<sup>(20)</sup> Data on the association of obesity and sedation-related outcomes in patients undergoing endoscopy are limited. A recent paper addressed the safety of propofol administered by anesthesiologist for endoscopy in obese patients. Although the author concluded that propofol sedation in this situation is safe, the frequency of every airway maneuvers to treat hypoxemia was significantly higher in obese patients, even with an anesthesiologist on charge.<sup>(13)</sup> In our experience, sedation in the very obese patient (BMI>35-40kg/m<sup>2</sup>) is challenging, because of propofol dosage, accumulation of the drug in the adipose tissue and frequent airway occlusion; for this reason we usually require an anesthesiologist for those patients.

## 4. Acute Gastrointestinal Bleeding

Propofol can cause a significant hypotension, and has been proscribed in situations as gastrointestinal bleeding, considered as a high risk situation.<sup>(21,22)</sup> No sedation at all or sedation with the assistance of an anesthesiologist has been advocated in these patients by many authors. A paper describes the safety of NAAP for patients with upper gastrointestinal bleeding, in 120 patients with average and high anesthetic risk.<sup>(14)</sup> Excluding unconscious patients or the ones who presented a severe cardiovascular depression, the authors found no significant differences in neither mean decrease in systolic blood pressure nor bradycardia, despite the mean time required to complete the endoscopic procedure and mean dosage of propofol were both significantly higher in the group with gastrointestinal bleeding. There were no differences in the frequency of hypoxemia between both groups, and the authors concluded that propofol sedation in patients with acute gastrointestinal bleeding is safe. Interestingly, the authors titrated propofol dosage by age, giving 0.8 mg/kg for patients <70 years of age and 0.6 mg/kg for patients aged ≥70 years or older, with subsequent boluses of 10 mg with the target of a moderate sedation.

Although we think gastrointestinal bleeding is a high risk condition, propofol might be safe in patients with no signs of hypovolemic shock and always with a careful administration scheme and monitoring.

## 5. Concomitant Pharmacologic Therapies

The use of some drugs, alcoholic drinks and medications like sedatives or antidepressants usually enhances propofol metabolism by the liver, requiring increasing doses of the drug, which can be difficult to titrate because patients can quickly shift from a mild sedation to a deep one and even apnea.<sup>(16)</sup> When we have this type of patient, we tend to apply in otherwise healthy individuals the usual induction doses. If the patient is adequately induced, we proceed with the procedure as regularly, if not we administer half the initial dose of propofol after about 90 seconds. If endoscopy is impossible after this second propofol infusion, we finish the procedure and ask for the participation of an anesthesiologist in a subsequent endoscopy.

In general, with this scheme, sedation is possible in most of the patients. We find more difficulties with heavy alcohol consumers, in which an anesthesiologist is frequently required. Of note, we have an anesthesiologist specially dedicated to endoscopy who hardly ever induces sedation but general anesthesia with orotracheal intubation, also in these patients, arguing a difficult control of the sedation level even when performed by anesthesiologists.

## Procedure-Related Risk Factors

Some guidelines recommend evaluating the nature of endoscopic intervention, indication, duration, invasiveness and complexity before deciding between NAAP and general anesthesia.<sup>(16)</sup> The more complex procedures in endoscopy comprise those with interventional or advanced endoscopy, i.e. ERCP, EUS and some other. Many studies have shown that NAAP is safe and better than previous methods of sedation in those procedures. NAAP has been successfully tested in ERCP, EUS, double balloon enteroscopy (DBE) and other.<sup>(6-8,10,12,17-19)</sup> Nevertheless, in our opinion, some long lasting or potentially painful procedures are not suitable for NAAP, which can be applied if needed, but are performed with much more comfort for the endoscopist under general anesthesia. We think there is a subtle difference between what can be safely performed and what should be done in order to be more comfortable and aggressive when planning the goals of an intervention. In our practice, ERCP, a procedure which can be long-lasting and very complex is always performed under general anesthesia. The same happens with DBE, which takes a mean time of two hours and can be painful. We do sedate with propofol patients undergoing EUS with or without FNA. However, if we have to perform a pseudocyst drainage, a cholangiography guided by EUS, or other complex long-lasting procedures we opt for a general anesthesia. Indeed, in our experience, a regular EUS with or without FNA takes less than one hour,<sup>(10)</sup> a period of time in which the endoscopist can safely complete the procedure and sedate the patient. As a general rule, if something is foreseen to last more than an hour, or if it can be significantly painful, we do not despise the help of our anesthesiologist.

## Conclusions

NAAP has spread in most of western countries,

with an especial impact in Europe. Trained nurses and clinicians have learnt to apply propofol and are doing it safely, with an increasing comfort for patients. With the growing experience in many centers, propofol use is expanding to patients with a theoretical higher risk, and endoscopists are in some cases toying with the burdens of safety. For this reason we have tried to address for practitioners what to do in some borderline situations in which evidence is far from pristine. In some aspects, as in patients with high anesthetic risk or in old patients there are data enough to begin a NAAP sedation protocol. In these groups, an accurate titration of the infused doses, with induction doses of about 0.5 mg/kg or less and reinfusions of half this first dose, is safe and valuable for an effective sedation. More concern arise in other situations, like in patients with an acute upper gastrointestinal bleeding, or in the very obese patients, in which caution is advised by some authors and, in our opinion, it is wise to require an anesthesiologist or to perform the procedure

without sedation, if this is possible. Regarding procedure related risk, we consider a general rule to require an anesthesiologist for endoscopies with a high complexity or potentially long lasting. General anesthesia is always applied to patients undergoing ERCP in our unit, and, although NAAP is feasible and, indeed, we have sedated ERCP patients before, we really think it is much more comfortable for both the patient and the endoscopist to undergo general anesthesia. Anyway, improvements in sedation by non endoscopist, increasing needs to reduce healthcare costs and the demand of more comfort related to endoscopy by the population will for sure change the way we do things in the coming years.

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