Safety of deep sedation in the endoscopy suite

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**Purpose of review**
As the complexity of endoscopic procedures increases, the use of propofol and the desire for deep sedation are becoming more common in the endoscopy suite. This review explores sedation depth, agents used for sedation, recommended monitoring, and adverse event risks that occur during sedation for endoscopy.

**Recent findings**
The sedation provider for endoscopy varies by practice location and with regulatory requirements. As increasingly deep levels of sedation are used in this setting, the need for all providers to have training in the ability to rescue patients from sedation-related side effects is paramount. Propofol has an important role for prolonged and uncomfortable endoscopic interventions and has a strong safety record in the endoscopy suite. Vital signs monitoring is recommended during all endoscopy sedation, and there is emerging interest in advanced monitoring (e.g., capnography, processed electroencephalogram, respiratory monitoring) in this setting. The reported rate of adverse events during endoscopy sedation varies widely; however, advanced age and increasing American Society of Anesthesiologists physical status score are consistently associated with increased risk. Whether anesthesiologist-administered sedation is safer than non-anesthesiologist-administered sedation remains controversial.

**Summary**
This review provides some guidance to providers who administer sedation in the endoscopy suite and is intended to improve the safety of patients. The recommendations are based on best available evidence and expert opinion.

**Keywords**
deep sedation, endoscopy, patient safety, propofol, sedation

**INTRODUCTION**
Anesthesia providers are increasingly involved in providing sedation in the endoscopy suite. This has occurred to meet the clinical needs of expanded screening programs and rapidly developing therapeutic endoscopic procedures. Endoscopic procedures range from simple diagnostic or screening esophagogastroduodenoscopy (EGD) and colonoscopy to the treatment of acute pathology or definitive management of neoplastic disease. With the expansion of endoscopy services, there has been a shift toward administration of deeper levels of sedation – mostly propofol-based – that improve patient tolerance for prolonged or uncomfortable procedures. In addition, patients presenting for endoscopy are increasingly older and have a greater number of comorbidities. The purpose of this review is to explore the safety of deep sedation in the endoscopy suite. Topics to be covered include the depth of sedation, drug choice, and patient and provider factors that optimize patient safety and improve outcomes.

**SEDATION DEPTH**
Sedation exists on a spectrum from mild anxiolysis to deep unconsciousness. Clinical scales such as the Ramsay et al.[1] sedation score or the Modified Observer’s Assessment of Alertness/Sedation [2,3] can be used to target ‘conscious sedation’ (MOAA/S level 3–5 = verbally responsive) (Table 1) [4]. The traditional agents used to achieve conscious (or moderate) sedation are a benzodiazepine in
combination with a short-acting opioid. However, as the complexity of endoscopic procedures has increased, so has the desire for deeper levels of sedation which may at times overlap with general anesthesia (MOAA/S level 0–2 = responds only to physical stimulus or unresponsive). These deep levels of sedation are most commonly achieved with the administration of propofol.

SEDATION PROVIDERS

Several organizations throughout the world have issued recommendations meant to guide the provision of well tolerated sedation in the endoscopy suite. In the United States, the American Society of Anesthesiologists (ASA) has a practice advisory addressing nonanesthesiologist-administered deep sedation [5]. The recommendations include a dedicated sedation provider distinct from the proceduralist, formal training in monitoring, sedation and rescue techniques, and knowledge of other ASA guidelines relevant to deep sedation. The National Institute of Health has released a broad-range guideline on safety for gastrointestinal endoscopy that in part addresses sedation practice [6]. Expectations for the sedation provider include documented training in sedation for endoscopy and knowledge of associated adverse events, recognition of deeper than intended sedation, and skills for cardiorespiratory rescue. Comparable guidelines exist in Australia and New Zealand, and Japan and Europe [7–9]. None of these guidelines explicitly identify who the preferred sedation provider should be (i.e., nurse, proceduralist, anesthesiologist), but the preference for an anesthesia professional when deep sedation is targeted is expressed.

A survey of anesthesiologist and nurse-anesthetist representatives across Europe (responses from: Spain, Italy, The Netherlands, Germany, Austria, Poland, France, Switzerland, Belgium, Bulgaria, Czech Republic, England, Luxembourg, Norway, Portugal, and Sweden) has shown highly variable practices in the provision of sedation in the endoscopy suite [10]. There was no uniformity in sedation provider, targeted depth of sedation, or sedative agents. Furthermore, awareness of and adherence to sedation guidelines were incomplete. The authors highlight that a shortage of anesthesiologists may be a particular challenge to providing well tolerated sedation for endoscopy [10].

A nurse-administered sedation model is attractive from a cost and practitioner availability perspective. Several studies, including a meta-analysis, have recently reported well tolerated propofol sedation by nurses; [11,12,13] however, proceduralist and patient satisfaction scores were lower compared with when propofol was administered by an anesthesiologist. Where nurse administered sedation is planned, rigor must be used in patient selection. In addition, strict protocols should be in place to determine when anesthesiology ‘rescue’ is needed.

In Australia, sedation for endoscopy is more commonly administered by anesthesiologists and less commonly administered by nurses overseen by gastroenterologists trained in the rescue of...
Predicting which patients will be difficult to sedate for endoscopy is difficult. The stratifying clinical outcomes prior to endoscopy (SCOPE) score was developed to help answer this question [15]. This score used patient characteristics from a database of past procedures where sedation was described as difficult or patients required high sedative doses (80th percentile or higher) to identify patient risk factors for challenging sedation. The score was then prospectively validated in patients undergoing endoscopy sedation. The authors suggest the SCOPE score can be used to identify patients likely to be difficult to sedate for endoscopy and allow triage to sedation by anesthesia providers. Deep propofol-based sedation was not studied and patients sedated by anesthesiologists were specifically excluded.

An alternative approach was taken in a single-center study of patients, who were booked for simple endoscopy under conscious sedation. The use of a three-level preprocedure triage tool (a web-based form, a telephone interview with trained personnel, and an educational pack sent to patients to screen for which patients may need anesthesiologist-administered sedation) was used to define which group of patients could have sedation provided by a proceduralist and which required an anesthesiologist. The final determination of suitability was by interview with a nurse and/or the gastroenterologist on the day of the procedure. The triage tool was found to produce less than a 1% failure rate for correctly identifying patients as not requiring anesthesiologist-administered sedation [16*]. Such an approach may be an efficient way to direct resourcing for endoscopy sedation.

**ADVANCED MONITORING DURING ENDOSCOPY SEDATION**

Anesthesia professional bodies have recommendations for the use of routine patient monitors during anesthesia care. These include pulse oximetry, noninvasive blood pressure (BP) measurement, and continuous ECG. When intravenous sedation is given, capnography is also advised. From a survey of Australian anesthesiologists’, it appears that these recommendations are incompletely applied [14*]. Pulse oximetry was used by all respondents and BP was measured by most respondents (88–99% for elective and emergency EGD, colonoscopy, and ERCP). However, electrocardiography and capnography were used less commonly (39–90% across elective and emergency EGD, colonoscopy, and ERCP cases).

The use of capnography during sedation for endoscopy is an area of interest due to its ability to detect hypoventilation before the consequent hypoxia is evident on pulse oximetry. Capnography's use during moderate-to-deep sedation has been endorsed by the ASA since 2011. However, these recommendations are somewhat controversial. The use of capnography has been investigated in patients undergoing colonoscopy with moderate gastroenterologist-directed sedation; in this study, the costs of care were increased without evidence of improved patient safety [17*]. However, this study was conducted in a healthy patient cohort, predominantly ASA physical status 1 and 2 patients. A more in-depth health economic model for the use of capnography for endoscopy sedation concluded that the costs of care were reduced when capnography was added to standard care [18**]. The authors report a number needed to treat of 7 for the prevention of an adverse event and 591 to prevent an adverse outcome. Cost modeling favored the use of capnography for both moderate and deep sedation, with greater savings for deep sedation.

Use of integrated advanced monitoring (acoustic respiratory monitoring and processed electroencephalogram – SEDLine brain function monitor) Masimo
These findings are consistent with other studies. The respiratory monitor alarmed for desaturation (SpO₂ < 92%) or respiratory depression (rate < 8 bpm) and unintentionally deep sedation (Patient State Index < 50) also resulted in an alarm. The number of patients who suffered respiratory depression and desaturation events was substantially reduced with the intensive monitoring, presumably by alerting the sedation provider and allowing timely intervention. Further investigation of such systems and extension to patients undergoing deep sedation would be welcome.

With deeper sedation, there is interest in objective assessment of sedation level by processed electroencephalogram monitors. Bispectral index (BIS) values of 60–80 are consistent with moderate sedation [20]. The use of depth of anesthesia monitors in procedural sedation is growing with the development of computerized or protocolized regimens for adjusting propofol-based sedation. In one study, despite prolonged procedure times (89 ± 59 min), satisfactory sedation levels were maintained with a standardized BIS-guided propofol infusion regimen [20]. Limitations to the routine use of BIS monitoring for sedation include lack of robust definitions of the range to be targeted, the lag time between clinical response and the index number, and lack of health economic data on their cost-effectiveness.

MEDICATIONS USED FOR SEDATION FOR ENDOSCOPY
A recent US study evaluated the use of propofol for deep sedation for ERCP by certified registered nurse anesthetists under the supervision of anesthesiologists. ERCP is a high-risk procedure due to the required prone positioning and prolonged duration in often unwell patients. This study included 47% of patients scored ASA 3 or greater and concluded that propofol had an acceptable safety profile even in complex situations [21]. In this study, airway maneuvers to resolve hypoxia were common (28%), but progression to intubation was infrequent and significant hypotension was rare. These findings are consistent with other studies [4,12,20,22*,23] that have established the acceptability and safety of propofol for deep sedation in advanced endoscopy. Deep propofol sedation has also been safely provider-administered or patient-controlled, even for advanced endoscopy procedures such as ERCP [24*]. In one study, patient-controlled propofol–alfentanil sedation resulted in rates of cardiorespiratory adverse events similar to anesthesiologist administered propofol sedation. However, the utility of this technique was limited by patient comprehension and intervention by the sedation provider was needed in 19% of patients [24*].

Due to the respiratory depressant effects of propofol and the specialized training required to administer it, alternative regimens to provide deep sedation for advanced endoscopy have been investigated. In a small, single-center study, the use of dexmedetomidine and ketamine was compared with propofol sedation [25**]. In this study, the dexmedetomidine–ketamine combination showed a promising safety profile with no significant cardiorespiratory complications occurring. However, recovery time was longer in the group that received this combination compared with propofol.

ADVERSE EVENTS DURING SEDATION FOR ENDOSCOPY
In a large German study (n = 24,441) of gastroenterologist administered propofol sedation in ASA physical status 1–3 patients, the rate of cardiorespiratory complications was very low (major events 0.016%, minor events 0.46%) [26]. Increasing age and propofol dose were associated with minor adverse events. Overall, these results were reassuring that propofol-based sedation for endoscopy was well tolerated. Comparison of the safety of sedation administered by anesthesiologists and gastroenterologists has been addressed using a very large US national database study (n = 1.38 million procedures) [27**]. Higher ASA physical status grade and older age were significant predictors of complications. Interestingly, in this study, the odds of adverse events were higher for anesthesiologist compared with endoscopist-directed sedation for EGD (1.33; 95% confidence interval 1.18–1.50). For colonoscopy, adverse events were similar between groups. There was also no information reported on the actual sedation medications administered by the providers or the method by which patients were selected for either anesthesiologist-administered or proceduralist-administered sedation. This information makes it difficult to interpret the findings. Nevertheless, the results are interesting and emphasize the need for further research on this subject.

A recent closed claims analysis of complications of sedation for colonoscopy with and without the presence of an anesthesia provider showed increased risk associated with the involvement of an anesthesia provider [28*]. When an anesthesia provider was present, there was a 13% increased risk of any complication despite adjustment for patient sex, age,
and comorbidity. However, the data were derived from an administrative database, and there was no information reported on why anesthesia services were needed in the patients who had an anesthesia provider involved in their care.

A small prospective study of adverse events during endoscopy performed in a hospital setting revealed a median of one event per procedure, ranging from minor to sentinel events [29*]. Examples of adverse events observed in this study included sedation without oxygen administration, omission of pulse oximetry monitoring, and patient misidentification resulting in performance of the incorrect procedure. The prospective collection of adverse event data is important, as most events will not result in poor patient outcomes and, therefore, will not be detected in studies that rely on administrative databases.

An audit of elective and emergency endoscopy sedation administered by anesthesiologists revealed propofol was used in 98.5% of cases, commonly in combination with midazolam and an opioid [30*]. This deep sedation has been shown to be the predominant strategy amongst anesthesiologists in Australia [14*]. This study also found a high (23%) unplanned event rate, consisting of airway obstruction, hypoxia, unplanned intubation, hypotension, bradycardia, abandoned procedure, prolonged recovery stay, unplanned admission, resuscitation, or 30-day mortality. The predictors of inaprocedure events were: old age, ASA physical status grade 3–4, low BMI, colonoscopy, and planned intubation. The predictors of death by 30 days were: ASA physical status 4–5 and emergency cases. The overall 30-day mortality was 1.2% (0.2% elective, 6% emergency) [30*]. These findings are important when deciding upon a sedation plan and consenting patients for sedation for gastrointestinal endoscopy.

**PATIENT FACTORS RELATED TO SAFETY DURING ENDOSCOPY SEDATION**

Endoscopic, rather than surgical treatment is generally preferred in elderly and frail patients, but their inaprocedure care is challenging. In a study of patients undergoing endoscopic submucosal dissection for gastric cancer under propofol sedation, those aged over the age of 80 required a lower dose of propofol and had more episodes of desaturation than younger patients [22*]. In patients undergoing colonoscopy, the extremely elderly (>90 years) suffered more cardiorespiratory events than patients in the elderly (75–79 year old control) group (0 vs. 5.3%; \( P = 0.006 \)) [31*]. Patients were moderately sedated with midazolam and fentanyl, with the more elderly group requiring lower doses; propofol use for deeper sedation was rare. The findings for elderly patients undergoing ERCP with midazolam/opioid sedation were similar, with elderly patients requiring lower sedative doses; however, no difference in complication rates were reported [32]. Given the differential risk profile compared with younger patients, the decision to proceed with endoscopy in elderly, frail patients must be carefully considered and in keeping with overall goals of care.

Concern exists in providing anesthesia for patients with obstructive sleep apnea (OSA) because of the increased risk for airway loss and postprocedure respiratory complications. Reassuringly, a study comparing 248 patients with moderate or severe OSA to 252 patients without OSA undergoing sedation for a spectrum of endoscopic procedures did not find any respiratory complications. However, those receiving propofol-based deep sedation were specifically excluded [33*]. In the large prospective audit of safety where deep propofol-based sedation was administered by anesthesiologists, OSA was not a predictor for either unplanned intra-procedure events or 30-day mortality [30*].

**CONCLUSION**

Demand for deep, propofol-based sedation for endoscopy is likely to increase to facilitate advanced endoscopic procedures. Reported rates of adverse events during sedation for endoscopy vary widely, depending on study methodology. However, there is strong evidence that indicates patients who are older and have more comorbidities are at increased risk. Whether sedation for endoscopy by anesthesia personnel promotes safety is controversial.

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**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES AND RECOMMENDED READING**

Papers of particular interest, published within the annual period of review, have been highlighted as:

* of special interest
** of outstanding interest

Non-operating room anesthesia


11. This article highlights current sedation for endoscopy practice in Europe and emphasizes that sedation practices are highly variable.


15. This study reveals that Australian anesthesiasts very commonly use propofol for endoscopy sedation and routinely target deep levels of sedation.


18. This study reveals that intensive preadmission triage can correctly allocate the vast majority of patients undergoing simple endoscopy to appropriate sedation providers (endoscopist or anesthesiologist).


20. Despite capnography being advocated as a routine respiratory monitor during endoscopy sedation, this study failed to show that capnography improved outcomes in low-risk patients.


22. This is an in-depth economic analysis of the use of capnography during endoscopy sedation. Compiling cost savings are demonstrated for both moderate and deep sedation. Note, however, the authors’ affiliations to industry, particularly a company which supplies capnography monitors.


24. This article reveals a promising system to alert the sedation provider to deeper than intended sedation and hypoxemia, allowing for more timely corrective action to be applied.


28. This study demonstrates the well tolerated and effective use of a standardized sedation regimen that relies on clinical and bispectral index data to direct propofol sedation for advanced endoscopic procedures.


31. This study shows that patient-controlled propofol sedation is feasible and well tolerated for use during complex endoscopic procedures when suitable patients are selected, and there are anesthesia personnel available to provide rescue.


33. This article summarizes the results of a trial comparing desmedetomidine–ketamine vs. propofol–fentanyl for deep sedation for advanced endoscopy. The authors report effective sedation with no major respiratory events using the desmedetomidine–ketamine combination.


36. This is a very large database study comparing serious adverse event rates with anesthesiast-directed compared with endoscopist-directed sedation. American Society of Anesthesiologists and age were significant predictors of adverse events. After properly matching, anesthesiast-directed sedation was associated with an increased odds of serious adverse events during esophagogastroduodenoscopy. However, there was no report of the actual sedative medications administered nor the reason for anesthesia provider involvement.


38. This is a closed claims analysis comparing adverse events during colonoscopy sedation where anesthesia providers were present or not. This administrative data study found increased risk where anesthetic services were present but no information on why anesthetic services were needed in particular cases was reported.


40. This is a small, prospective study demonstrating that minor adverse events are very common during endoscopy. The study highlights that some very serious events may occur but may not be captured if patient outcome is the only reported endpoint.


42. This large prospective audit of endoscopy safety found a high rate of unplanned events (23%). The reported 90-day mortality for endoscopy was 0.2% elective for elective cases and 6% for emergency cases. These rates are much higher than the adverse events reported in large database studies of sedation side effects.


44. This study concluded that elderly patients are at increased risk of cardiorespiratory side effects of sedation.


47. This study concluded that moderate sedation for endoscopy is generally well tolerated in patients with obstructive sleep apnea.