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Risk factors for sedation-related adverse events during endoscopic ultrasound

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Abstract

Background Complex endoscopic procedures such as endoscopic ultrasound (EUS) require higher doses of sedation, and thus carry a higher risk of adverse events compared to conventional endoscopy. This prospective cohort study assessed the safety of propofol sedation administered by non-anesthesiologists, and identified factors associated with sedation-related adverse events during EUS.

Methods A total of 2986 examinations were performed between January 2011 and May 2019. We collected data on patient characteristics (including age, body mass index and American Society of Anesthesiologists [ASA] class), procedural details, and sedation-related outcomes. Procedure characteristics and sedation-related adverse events were compared, firstly between interventional and diagnostic EUS, and then based on body mass index, ASA class and age. Logistic regression was performed to search for independent risk factors for sedation-related adverse events.

Results Sedation-related complications occurred in 4.8% of patients, hypoxemia being the most frequent (3.8%). Obese patients exhibited the highest rates of hypoxemia, early discontinuation and bag-mask ventilation (29.6%, 22.2% and 11.1%, respectively). Multivariate analysis revealed that obesity (odds ratio [OR] 8.57, 95% confidence interval [CI] 3.62-20.28) and comorbidities (ASA III/IV) (OR 2.04, 95%CI 1.44-3.01) were independently associated with sedation-related adverse events, while age was not significant.

Conclusions Propofol sedation administered by non-anesthesiologists during EUS was safe, with low rates of adverse events, the vast majority of which were clinically insignificant. Comorbidities and obesity, but not age, were independent risk factors for sedation-related complications during EUS. Appropriate patient selection and adequate training of endoscopists are warranted to minimize the risks associated with sedation during EUS.

Keywords Endoscopic ultrasound, sedation-related complications, obesity, American Society of Anesthesiologists class, propofol

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Introduction

Endoscopic ultrasound (EUS) is an endoscopic procedure with both diagnostic and therapeutic capacities, focused on the gastrointestinal (GI) wall and on surrounding organs [1]. However, the procedure is invasive, and causes discomfort to patients, related to the width of the probe; it also has an impact on airway management and the procedure's duration, both necessitating sedation [2].

Different levels of sedation are possible, based on ventilatory capacity and response to stimuli. Moderate sedation is the goal in GI endoscopy, but deep sedation often occurs, leading to more adverse effects [3]. These can be divided into cardiovascular events (arrhythmias, hypotension, bradycardia or shock) and respiratory events (hypoxemia, respiratory arrest, upper airway obstruction or pulmonary aspiration) [4].

Over the past few decades, the use of propofol for endoscopic procedures has increased. Despite its rapid onset of action, propofol has a narrow therapeutic index, which can potentially increase the risk of cardiovascular and airway-related adverse events [5].

Previous studies showed that gastroenterology-guided propofol sedation (non-anesthesiologist-administered propofol sedation [NAAPS]) may have a similar rate of adverse events as sedation administered by anesthesiologists, while reducing costs [6-8]. In complex endoscopic procedures, such as endoscopic retrograde cholangiopancreatography (ERCP) or EUS, higher doses of sedation are required for patient comfort and compliance, thus increasing the risk of sedation-related adverse effects. Although some studies support sedation by gastroenterologists in advanced endoscopy [5,9] data from large patient cohorts and analyses of factors that may influence sedation-related adverse effects are still lacking.

Age, obesity, comorbidity, endoscopist's experience, propofol dose and procedure time are the main factors that have been associated with the development of adverse events during sedation in gastrointestinal endoscopy. Most studies have examined the occurrence of these complications in non-advanced endoscopic procedures, such as gastroscopy or colonoscopy [10,11], or have assessed complex procedures collectively, but few have specifically focused on EUS, and these have yielded conflicting results [12,13].

Thus, the aim of our study was to assess the safety of gastroenterologist-guided sedation in different EUS procedures (diagnostic or interventional) and to identify the main factors associated with sedation-related adverse events.

Material and methods

Study design

We performed a prospective cohort study in the gastroenterology department of a tertiary center between January 2011 and May 2019, aiming to assess complications and adverse effects occurring during or after the procedure, as well as the predictive factors associated with them. The STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines were followed to ensure accurate reporting of the methods, results and discussion.

Sample size estimation

Sample size was estimated using a 2-step procedure. First, a single proportion formula was applied to calculate overall sample size, assuming a pooled prevalence of sedation-related adverse events of 5%, with a desired margin of error of ±5%, a power of 80%, and a confidence level of 95%. This step determined the overall sample size required to evaluate sedation-related adverse events in EUS. Secondly for subgroup comparisons, a 2-proportion formula was used to ensure sufficient power, including age (≥65 vs. <65 years), American Society of Anesthesiologists (ASA) status (ASA III/IV vs. ASA I/II), and obesity (obese vs. non-obese). These calculations accounted for potential differences in sedation-related adverse events between subgroups, based on previously reported rates. To address potential missing data, variability in subgroup proportions, and the inclusion of both interventional and diagnostic cases, the total sample size was increased to ensure robust statistical power across all analyses. Detailed calculations and assumptions are provided in the Supplementary material.

Data collection

Patients older than 18 years old, referred to the endoscopy unit for either a diagnostic or interventional EUS, were included. Patients who refused to sign informed consent, patients with conditions that prevented sedation by the endoscopist (severe sleep apnea, severe chronic obstructive pulmonary disease, airway management difficulty predictors and those with body mass index [BMI] >35 kg/m^2), those sedated by the anesthesiologists, or those who presented with allergy to propofol, or any other medication used for sedation, were excluded. Given the large sample size and the fact that data collection was performed immediately after the EUS procedure, a minimal amount of missing data was anticipated. For any missing data, a complete case analysis was performed to maintain the accuracy and consistency of the results.

Procedures were performed by 2 experienced endoscopists (ERC and JGMC) who perform more than 400 EUS per year and have more than 10 years' experience. Linear and radial echoendoscopes were used (UCT-GF180-AL5; UCT-GF160-AL5, Olympus, Japan). A systematic EUS evaluation was performed in each patient.

Data regarding age, sex, comorbidities, BMI and ASA class, heart rate, oxygen saturation while breathing room air, indication, type of EUS (diagnostic or interventional) and procedure were collected prior to the procedure, while recovery time and complications were routinely documented after the technique.

After data collection, 3 divisions were established in the key variables to compare sedation-related complications and the actions performed in relation to these complications: age <65 years vs. ≥65 years, BMI <30 vs. ≥30 kg/m^2, and ASA class I/II vs. III/IV. The ASA division was established in order to differentiate low- and high-risk patients. In the former group NAAPS is widely accepted and safe, but in the latter the evidence is not so clear and patient selection is critical. Complications, baseline heart rate and baseline oxygen saturation, initial and total amount of propofol used, sedation induction time and recovery time were also compared in all these groups.

Sedation procedure

Sedation was administered by the endoscopist and trained nursing staff. Only those patients with multiple comorbidities,

predictors of a difficult airway, hemodynamic instability or sepsis, and severe obesity (grades II and III) were sedated by an anesthetist, and were therefore excluded from the study. Moreover, only selected obese patients, with no other predictors of a difficult airway, underwent NAAPS.

Deep sedation was performed in nearly all cases with propofol alone. An initial propofol bolus (0.5-1 mg/kg) and repeated boluses (10-20 mg), based on the patient's condition, were administered by protocol. In most patients 0.5-1 mg of atropine were also administered prior to the technique, primarily because of its antisialagogue effect, which helps reduce salivary and airway secretions, minimizing the risk of airway obstruction or aspiration during sedation [14]. During the procedure, the degree of deep sedation was assessed using the Ramsay sedation scale and it was only performed when a level of 4 or more was reached. Once the technique was completed, the patient was observed for 15-30 min and, after regaining a good level of consciousness (Ramsay 3 or lower), and in the absence of abnormal vital signs, the patient was discharged.

All patients were monitored with continuous electrocardiography, pulse oximetry and blood pressure every 5 minutes. Supplemental oxygen flow (5 L/min) through a nasal cannula was administered in all patients, as well as an intravenous saline infusion (250 mL). All procedures were carried out with the patient in the left lateral decubitus position. All medications used for sedation (including their induction and total doses) as well as all sedation-related complications were documented after the procedure.

Definitions

Sedation-related complications were defined as hypoxemia (<90% oxygen saturation for more than 10 s, registered on the pulsometer by the attending physician or nurse), hypotension (systolic blood pressure <90 mmHg), any cardiac rhythm abnormalities, or death. All actions that were necessary in the presence of adverse events, such as jaw thrust or chin lift maneuvers, cardiopulmonary resuscitation, bag and mask ventilation or tracheal intubation, were recorded. Early discontinuation was defined as an interruption of the procedure due to an adverse event. Other procedure-related complications, such as hemorrhage, postprocedure pancreatitis, vomiting or perforation were reported. We differentiated between diagnostic EUS procedures and those involving tissue acquisition via fine-needle aspiration (FNA) or fine-needle biopsy (FNB).

Statistical analysis

Statistical analysis was carried out using the software PAWS Statistics 17.0 (SPSS Inc., Chicago, IL, USA). Initially, procedure characteristics and sedation-related adverse events were compared between interventional diagnostic EUS and EUS FNA/FNB. Statistical significance was defined as a P-value <0.05. Differences were assessed using the chi-square test or Student t-test as appropriate. The baseline characteristics were compared based on BMI, age and ASA class, as mentioned above. After the bivariate analysis, multivariate analysis, based on multiple backward stepwise regression, was performed to identify risk factors for sedation-related adverse events. Variables with P-values <0.20 were included in the multivariate analysis. To account for potential confounding factors, a sensitivity analysis was conducted for obese patients, evaluating the impact of ASA classification on sedation-related adverse events within this subgroup.

Statement of ethics

The study was approved by Virgen de las Nieves university hospital Ethics Committee in November 2010, and is in accordance with the World Health Organization Declaration of Helsinki. Patients gave informed consent to their participation in the study and the disclosure of the results.

Results

Patient's characteristics

Between January 2011 and May 2019, 3217 EUS examinations were performed in our department. Of these, 227 were conducted with sedation by an anesthesiologist and 4 had incomplete data; all of these cases were excluded. Consequently, 2986 EUS examinations were included in the analysis (Fig. 1). EUS FNA/FNB was conducted in 755 cases (25.28%). The demographic characteristics of the sample are presented in Table 1.

The mean age of the patients was 61.22±15.03 years, and 46.6% were over 65 years old. Nearly 1% had a BMI >30 kg/m^2 and up to 25% were classified as ASA III/IV. Patients' characteristics and the most usual indications are depicted in Table 1.

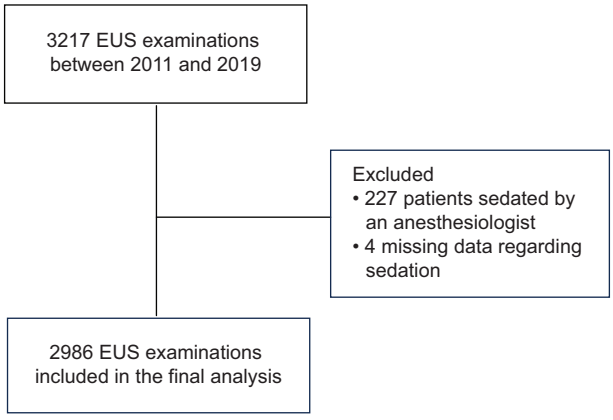

Figure 1 Study flowchart illustrating patient inclusion
EUS, endoscopic ultrasound

Table 1 Patients' characteristics

Characteristics	Value
Age (years), mean±SD	61.22±15.03
Age groups	
<65 years	1593 (53.3%)
>65 years	1393 (46.6%)
Sex	
Male	1452 (48.6%)
Female	1534 (51.4%)
BMI	
BMI <30 kg/m^2	2959 (99.1%)
BMI >30 kg/m^2	27 (0.9%)
ASA class	
ASA score I/II	2242 (75.1%)
ASA score III/IV	744 (24.9%)
Most common indications	
Suspected choledocholithiasis or cholelithiasis	524 (17.5%)
Staging esophagogastric neoplasms	336 (11.2%)
Chronic pancreatitis	276 (9.2%)
Acute pancreatitis of unknown etiology	239 (8%)
Cystic lesion of the pancreas	232 (7.8%)
Pancreatic mass	201 (6.7%)
Jaundice or cholestasis	198 (6.6%)
Submucosal lesions	163 (5.5%)
Abdominal pain	135 (4.6%)
Other indications	682 (22.84%)

Values are given as n (%) unless otherwise indicated
SD, standard deviation; BMI, body mass index; ASA, American Society of Anesthesiologists

Sedation-related complications

There were 145 cases with sedation-related adverse events, which represented 4.8% of the procedures. Hypoxemia was the most frequent complication (3.8%). The bivariate analysis showed that ASAIII/IV patients (5.33% vs. 3.33%; P=0.022), and in particular obese patients (29.6% vs. 3.6%; P=0.007) suffered hypoxemia more frequently, but not older patients.

Regarding resuscitation techniques, the differences were especially notable in obese patients (18.5% vs. 1.95%; P<0.001), who also needed mask ventilation more frequently (11.1% vs. 0.6%; P<0.001). Furthermore, they were the only group in which the need for an early discontinuation of the procedure showed significant differences (22.2% vs. 2.1%: P<0.001). There were no deaths in any group.

Adverse events in diagnostic vs. EUS FNA/FNB

The main features of EUS performance and sedation-related adverse events, comparing diagnostic EUS and EUS with tissue acquisition, are shown in Table 2. No significant differences in the development of sedation-related complications between patients undergoing diagnostic EUS or EUS FNA/FNB were found; however, other procedure-related complications, such as acute pancreatitis or hemorrhage, were slightly more frequent in patients undergoing FNA/FNB (P<0.001).

Risk factors for sedation-related adverse events

Data concerning the endoscopic and sedation aspects, as well as sedation-related adverse events, in relation to age, ASA class and BMI are shown in Table 3. The average total propofol dose was 207±97 mg, and dosages were significantly lower in older people (172 vs. 238 mg; P<0.001), and ASA III/IV (107 vs. 150 mg; P<0.001). In obese patients, only the induction dose was different with respect to leaner patients (68 vs. 85 mg; P<0.001), but not the reinjection doses.

The overall median procedure duration was 16±9 minutes. In obese patients only, the procedure time was statistically significantly shorter than in lean patients (11 vs. 17 minutes; P<0.002). No differences were found in recovery time between groups.

When all complications related with sedation (hypoxemia, bradycardia and hypotension) were considered in a multivariate analysis, BMI, comorbidities, age, sex, propofol dose, FNA during EUS and examination time were included as potential risk factors (Table 4). We found that obesity (odds ratio [OR] 7.66, 95% confidence interval [CI] 3.17-18.46; P<0.001) and comorbidities (ASAIII/IV) (OR 1.89, 95%CI 1.24-2.87; P=0.003) but not age, when corrected for the 2 other risk factors, independently increased the risk of sedation-related adverse events.

Sensitivity analysis

To evaluate the potential interaction between ASA III/IV status and obesity, a sensitivity analysis was conducted. A balanced random dataset of non-obese patients was created to match the sample size of obese patients, ensuring a comparable basis for analysis. The ORs of ASA III/IV status for sedation-related adverse events were assessed independently within each group (obese and non-obese). Additionally, in view of the small sample size, an interaction term between ASA III/IV status and obesity was included in the logistic regression model to evaluate potential synergistic effects. The results of the sensitivity analysis are presented in Table 5. In both obese and non-obese subgroups, ASA III/IV status was associated with a greater risk for sedation-related adverse events (OR 3.75, 95%CI 0.63-22.04 and OR 5.42, 95%CI 0.42-69.67, respectively), though these differences did not reach statistical significance. Furthermore, the inclusion of the interaction term suggested a potential synergistic effect (OR 3.5, 95%CI 0.43-28.44), but this, too, was not statistically significant.

Discussion

Our study is one of the few analyses specifically focused on NAAPS in the context of EUS, demonstrating a low rate of sedation-related adverse events when the procedure is performed by a trained gastroenterologist in large cohort of

Table 2 Main aspects of the EUS procedures

Aspects	Total EUS (N=2986)	Diagnostic EUS (N=2272)	EUS FNA/FNB (N=624)	P-value
Procedure duration, minutes (median, range)	16 (7-25)	14 (7-21)	27 (17-37)	<0.001
Propofol doses total, mg (median, range)	207 (110-304)	187 (110-264)	282 (162-402)	<0.001
Induction dose, mg (median, range)	68 (46-80)	68(45-91)	67 (46-88)	0.502
Reinjection, mg (median, range)	140 (51-229)	119(50-188)	215 (103-327)	<0.001
Recuperation time, minutes (median, range)	7 (3-11)	7(3-11)	8 (4-12)	0,014
Complications	145 (4.8%)	115 (5%)	30 (4.8%)	0.816
Hypoxemia	114 (3.8%)	96 (4.2%)	18 (2.8%)	0.053
Bradycardia	8 (0.26%)	7 (0.3%)	1 (0.16%)	0.501
Gastrointestinal bleeding	10 (0.3%)	0 (0%)	10 (1.6%)	<0.001
Acute pancreatitis	3 (0.1%)	0 (0%)	3 (0.4%)	<0.001
Gastrointestinal perforation	2 (0.06%)	0 (0%)	2 (0.3%)	<0.001
Vomiting during the procedure	3 (0.1%)	0 (0%)	3 (0.4%)	<0.001
Early discontinuation	69 (2.3%)	63 (2.77%)	6 (0.96%)	0.006
Airway modifications (chin lift, modified face mask ventilation, and nasal airway)	63 (2.1%)	51 (2.44%)	12 (1.92%)	0.523
Bag-mask ventilation	21 (0.7%)	17(0.74%)	4 (0.64%)	0.714

EUS, endoscopic ultrasound; FNA, fine-needle aspiration; FNB, fine-needle biopsy

patients. We identified comorbidities, particularly obesity, as independent risk factors for these events. Additionally, our findings confirm that gastroenterologist-guided sedation with propofol monotherapy in EUS (FNA/FNB) is safe, showing no greater risk of sedation-related complications compared to diagnostic EUS. However, when tissue acquisition was needed, higher total doses of propofol were required, resulting in longer procedure times.

We found an overall sedation-related complication rate of 4.8%, with early discontinuation of the procedure occurring in 2.3% of cases. The most common complication was hypoxemia (3.8%), while hemodynamic complications were rare. All hypoxemia cases were transient and resolved with minor interventions; urgent endotracheal intubation was not required. This aligns with previous studies that reported complication rates of 3-4.5%, with the need for assisted ventilation or intubation ranging from 1.1-1.7% [15,16]. Although Coté *et al* reported hypoxemia rates 3 times higher, with 3.6% of patients requiring mask ventilation, their study involved high-risk patients and complex procedures such as ERCP, which probably explains the disparity [13]. Conversely, Razpotnik *et al* reported a lower rate of sedation-related adverse events (1.8%) when analyzing diagnostic and interventional EUS, although their study involved a smaller sample size than ours [12]. Our study provides comprehensive data exclusively on sedation-related adverse events in EUS, analyzing one of the largest sample sizes to date. The results demonstrate a low rate of adverse events, the vast majority with no clinical relevance. These findings strongly support the use of trained gastroenterologist-guided sedation for both diagnostic EUS and EUS FNA/FNB in most cases.

Regarding comorbidities, almost 25% of patients were ASA III/IV, and we observed a higher rate of respiratory and cardiovascular complications and a lower dose of propofol required than in ASA I/II patients, but no differences in examination times or premature discontinuation of the procedure. Some other studies have shown similar results, reporting and ASA score >II as an independent risk factor for complications associated with sedation [12,13,17].

The association of obesity and sedation-related outcomes in patients undergoing advanced endoscopy has scarcely been explored. Several studies have shown higher rates of complications among obese patients [18,19]. In our study, similar findings were observed, with patients classified as obese (BMI >30 kg/m^2) exhibiting the highest rates of hypoxemia, need for airway maneuvers such as mask ventilation, and instances of early procedure discontinuation. However, the key point for our results is careful patient selection, in which individuals with extreme central or cervical obesity, predictors for a difficult airway, or severe cardiorespiratory comorbidities were referred for anesthesiologist-guided sedation or general anesthesia. To further investigate the potential confounding role of ASA III/IV status in obesity-related outcomes, we conducted a sensitivity analysis comparing obese patients with a matched dataset of non-obese patients. No significant differences were identified between the groups, suggesting that ASA III/IV status alone may not fully explain the observed outcomes. Additionally, while our analysis suggested a possible interaction between obesity and high ASA status, the results were not statistically significant. This finding highlights the need for future studies with larger cohorts of obese patients to better elucidate the

Table 3 Patients' characteristics, procedural data and sedation related complications based on ASA class, age and body mass index

Variable	ASA class			AGE			BMI		
	I/II (n=2242)	III/IV (n=744)	P-value	<65 (n=1593)	>65 (n=1393)	P-value	<30 (n=2959)	>30 (n=27)	P-value
Male sex	1163 (51.8%)	289 (38.8%)	<0.001	n: 798 (50%)	n: 654 (46.9%)	0.09	n: 1434 (48.4%)	n: 18 (66.6%)	0.059
Age >65 years	830 (37%)	563 (75.6%)	<0.001				n: 1386 (46.8%)	n: 7 (25.9%)	0.03
ASA class	-	-	-	n: 181 (11.36%)	n: 563 (40.41%)	<0.001	n: 736 (24.8%)	n: 8 (29.6%)	0.569
BMI >30 kg/m^2	19 (0.8%)	8 (1.07%)	0.569	n: 20 (1.25%)	n: 7 (0.50%)	0.03	-	-	-
Heart rate (median, range)	77 (63-91)	76 (60-90)	<0.001	78 (64-92)	75 (61-86)	<0.001	77 (63-91)	82 (65-99)	0.069
Oxygen saturation (median, range)	98 (95-100)	96 (94-98)	<0.001	98 (96-100)	97 (94-100)	<0.001	97 (94-100)	97 (95-99)	0.958
Procedural data									
Induction propofol dose, mg (median, range)	71 (50-93)	56 (35-76)	<0.001	77 (55-99)	57 (40-74)	<0.001	68 (46-90)	85 (53-97)	<0.001
Total propofol dose, mg (median, range)	150 (58-243)	107 (36-177)	<0.001	238 (137-339)	172 (93-251)	<0.001	207 (111-303)	217 (103-331)	0.626
Sedation induction time, seconds (median, range)	38 (19-57)	40 (20-60)	0.038	39 (17-60)	37 (19-55)	0.002	38 (19-57)	42 (14-70)	0.272
Endoscopy time, min (median, range)	16 (7-25)	17 (8-26)	0.704	16 (7-25)	17 (8-26)	0.008	17 (8-26)	11 (3-19)	0.002
Recovery time, (median, range)	7 (3-11)	7 (3-11)	0.887	7 (3-11)	7 (3-11)	0.603	7 (3-11)	6 (3-9)	0.315
Sedation-related complications									
Total complications	92 (4.1%)	53 (7.1%)	0.005	n: 69 (4.3%)	n: 76 (5.4%)	0.133	136 (4.5%)	9 (33,3%)	0.009
Hypoxemia	74 (3.33%)	40 (5.3%)	0.022	n: 56 (3.5%)	n: 58 (4.16%)	0.354	n: 106 (3.58%)	n: 8 (29.6%)	0.007
Bradycardia	3 (0.13%)	5 (0.67%)	0.082	n: 2 (0.125%)	n: 6 (0.43%)	0.121	n: 8 (0.27%)	n: 0 (0%)	>0.99
Early discontinuation	45 (2.01%)	24 (3.25%)	0.053	n: 36 (2.25%)	n: 33 (2.37%)	0.843	n: 63 (2.1%)	n: 6 (22.22%)	<0.001
Any airway maneuver	37 (1.65%)	26 (3.52%)	0.002	n: 24 (1.5%)	n: 39 (2.8%)	0.014	n: 58 (1.95%)	n: 5 (18.5%)	<0.001
Bag-mask ventilation	12 (0.53%)	n :9 (1.21%)	0.055	n: 8 (0.50%)	n: 13 (0.93%)	0.161	n: 18 (0.6%)	n: 3 (11.1%)	0.001

ASA, American Society of Anesthesiologists; BMI, body mass index

potential synergistic effects of obesity and ASA status on sedation-related adverse events.

We did not find age to be an independent risk factor for sedation-related complications, although lower doses of propofol were required in elderly patients [20]. Razpotnik *et al* reported a twofold higher rate of sedation-related complications in patients over 75 years, but their smaller sample size and definition of elderly (we included patients over 65 years) could explain these disparities [12].

The main limitations of our study are: (I) the low proportion of obese patients in our cohort compared to the prevalence of obesity in the Spanish population [21]. The reason could be that obese patients preferentially undergo other diagnostic methods, such as magnetic resonance imaging, to avoid invasive techniques and their complications, or anesthesiologist-guided sedation; (II) patients with higher comorbidity, or those undergoing longer procedures such as EUS + ERCP, were sedated by an experienced anesthesiologist

Table 4 Multivariate analysis of risk factors for sedation-related adverse events

Risk factor	OR	95%CI	P-value
Obesity	7.66	3.18-18.46	<0.001
Age	0.99	0.98-1.01	0.17
ASA	1.89	1.24-2.88	0.003
Sex	1.08	0.75-1.57	0.42
Propofol dose	0.99	0.98-1	0.89
Examination time	0.96	0.94-0.99	0.007
Fine needle aspiration/biopsy	1.43	0.86-2.36	0.52

OR, odds ratio; CI, confidence interval; NS, non-significant; ASA, American Society of Anesthesiologists

Table 5 Subgroup analysis of ASA III/IV and its interaction with obesity in sedation-related adverse events

Subgroup	OR	95%CI	P-value
Obese (n=27)			
ASA III/IV	3.75	0.63-22.04	0.37
Non-obese (n=29)			
ASA III/IV	5.42	0.42-69.47	0.41
Overall (n=56)			
ASA III/IV	1.94	0.31-12.11	0.73
Interaction Obesity - ASAIII/IV	3.5	0.43-28.44	0.81

OR, odds ratio; CI, confidence interval; NS, non-significant; ASA, American Society of Anesthesiologists

and so were excluded from our study. However, most guidelines recommend anesthesiologist-guided sedation in high-risk patients, and we also followed this principle [22]. The main strength of our study is the large sample size, which confers considerable power on the results found, as well as its prospective nature. Furthermore, the fact that it was a single-center study also means that data collection was adequately protocolized and uniform.

In conclusion, our study demonstrates a low rate of sedation-related adverse events in patients undergoing EUS when sedation is administered by a trained gastroenterologist, with most events being of minimal clinical relevance. Comorbidities, particularly obesity, emerged as independent risk factors for adverse events during EUS sedation, whereas patients aged over 65 did not exhibit a higher risk of complications. Notably, the observed rates of hypoxemia and early discontinuation among obese patients highlight the importance of careful patient selection and suggest that the involvement of anesthesiologists may be advisable for the management of complex procedures in this population.

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Summary Box

What is already known:

- Endoscopic ultrasound (EUS) is an invasive procedure requiring sedation such as propofol; the latter possesses a narrow therapeutic index, which could potentially elevate the risk of cardiovascular and airway-related adverse events
- Propofol administered by gastroenterologists may have a comparable rate of adverse events to sedation administered by anesthesiologists, while also reducing costs
- Factors such as age, obesity, comorbidities, endoscopist's experience, propofol dose and procedure time have been associated with the development of adverse events during sedation in gastrointestinal endoscopy

What the new findings are:

- Propofol sedation administered by non-anesthesiologists during EUS was found to be safe, with low rates of adverse events (4.8%), the vast majority of which were clinically insignificant
- Comorbidities (American Society of Anesthesiologists grade III/IV) and obesity (body mass index >30 kg/m^2) were identified as independent risk factors associated with sedation-related adverse events during EUS
- Unlike comorbidities and obesity, age was not found to be an independent risk factor for sedation-related complications in patients undergoing EUS
- Obese patients exhibited the highest rates of hypoxemia (29.6%), early procedure discontinuation (22.2%), and need for bag-mask ventilation (11.1%)

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Supplementary material

RISK FACTORS OF SEDATION-RELATED ADVERSE EVENTS IN ENDOSCOPIC ULTRASOUND

Annals of Gastroenterology

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Supplementary 1

Sample size was calculated based on the expected overall rate of sedation-related adverse events (SRAV) and subgroup comparisons. Previous studies reported SRAV rates of 1.4–12.8%, often including complex procedures such as ERCP and enteroscopy. Based on our experience, we anticipate lower SRAV rates in endoscopic ultrasound (EUS), including both diagnostic and interventional procedures. We estimate an overall SRAV rate of 5%, with slightly higher rates (~9%) in high-risk groups (ASA III/IV, obese, and older patients). To ensure robust statistical power, the sample size was calculated using the following parameters:

1. Overall Adverse Event Rate: 5%, with a margin of error of ±5%, a power of 80% and a 95% confidence level.
2. The expected comparison between the following groups:
   - Older than 65 years vs younger
   - ASA III/IV vs ASA I/II
   - Obese vs non-obese

First of all, based in an adverse event rate of 5% of all EUS cases, we used the single proportion formula:

$$n = \frac{Z^2 * P(1-P)}{E^2}$$

Where:

- n= sample size
- Z = Z-value (for 95% confidence level, Z = 1.96)
- P = estimated proportion (5% = 0.05)
- E = margin of error (5% = 0.05)

$$n = \frac{1.96^2 * 0.05(1-0.05)}{0.05^2} = 73$$

Then, for the subgroup analyses (older vs younger, ASA III/IV vs ASA I/II, and obese vs non-obese), we calculated the sample size required for each of these comparisons using the two proportion formula:

$$n = \frac{(Z1+Z2)^2 * \left[P1*\left(1-P1\right)+P2*(1-P2)\right]}{(P1-P2)^2}$$

Where:

- n= sample size
- Z1 = 1.96 for 95% confidence level
- Z2 = 0.84 for 80 of power
- P1 and P2 are the estimated proportion or sedated related adverse events in each group: (9% for ASA III/IV, > 65 years and obese = 0.09; and 5% for ASA I/II, < 65 years old and non-obese = 0.05)
- E = margin of error (5% = 0.05)

$$n = \frac{1.96+0.84^2 * \left[0.09*\left(1-0.09\right)+0.05*(1-0.05)\right]}{(0.09-0.05)^2} = 1282$$

So, we should need at least 1282 patients per group for age, body mass index and ASA comparison, in total 2564 patients. To account for potential missing data, variability in obesity rates, and the inclusion of both interventional and diagnostic cases, the total sample size was increased to 2900 patients. This ensures sufficient power to detect differences in SRAV across all subgroups.