North Clin Istanb 2019;6(4):321–326
doi: 10.14744/nci.2019.93763

Original Article ANESTHESIOLOGY & REANIMATION

The effects of obesity on sedation-related outcomes of advanced endoscopic procedures

Ebru Tarikci Kilic,[1] Suleyman Sayar,[2] Resul Kahraman,[2] Kamil Ozdil[2]

[1]Department of Anesthesiology and Reanimation, Health Sciences University, Umraniye Training and Research Hospital, Istanbul, Turkey
[2]Department of Gastroenterology, Health Sciences University, Umraniye Training and Research Hospital, Istanbul, Turkey

ABSTRACT

OBJECTIVE: Current literature covers limited data on the safety of sedation in advanced endoscopic procedures in obese patients. The present study aims to evaluate the association between obesity and the frequency of sedation-related complications in patients who were undergoing advanced endoscopic procedures.

METHODS: A retrospective chart analysis of 1172 consecutive patients, meeting the inclusion and exclusion criteria for this study and undergoing intravenous ketamine-propofol (ketofol) sedation for endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP) procedures were evaluated. The patients were classified into three groups according to their body mass index (BMI) (kg/m2). Group I comprised patients with a BMI between 25 and 30, group II with a BMI between 30 and 35, and group III with a BMI between 35-40. The sedation-related outcomes in the form of adverse events, and airway interventions were compared between the groups.

RESULTS: For analysis, out of the 1172 available records, 289 patients had a BMI between 35-40 and were predominantly male patients. The total adverse events were more common in obese patients, with apnea (in 5.5% patients in group I, 5.7% in group II, 22.8% in group III p<0.000), oxygen desaturation (in 7.7% patients in group I, 9.4% in group II, and 27.7% in group III p<0.000), and airway obstruction (in 4.9% patients in group I, 5.4% in group II, 22.8% in group III, p<0.000). Moreover, the obese patients more frequently required airway interventions, including airway placement, suctioning and bag-mask ventilation.

CONCLUSION: Higher BMI was associated with an increased frequency of sedation-related complications. However, we concluded that ketofol sedation regimen could be used safely in obese patients during advanced endoscopic procedures by skilled anesthesia providers.

Keywords: Advanced endoscopic procedures; airway interventions; ketofol; obesity; sedation.

Cite this article as: *Tarikci Kilic E, Sayar S, Kahraman R, Ozdil K. The impact of obesity on sedation related outcomes of advanced endoscopic procedures.* 2019;6(4):321–326.

Sedation has become common for advanced endoscopic procedures, such as endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP) in semiprone position. EUS and ERCP, are partly invasive-procedures, causing discomfort and pain to the patients; therefore, analgesics and sedatives are notably requested for these procedures [1, 2]. However, the choice of optimal sedation regimen in overweight and obese patients undergoing these advanced procedures remains unclear [3].

Obese patients pose a high-risk group of patients, and for them, the pharmacokinetics of drugs cannot be predicted; as the volume of distribution increases, a higher dose of the lipid-soluble agents is needed to achieve the

Received: May 22, 2019 *Accepted:* June 28, 2019 *Online:* October 24, 2019

Correspondence: Dr. Ebru TARIKCI KILIC. Saglik Bilimleri Universitesi, Umraniye Egitim ve Arastirma Hastanesi, Anesteziyoloji ve Reanimasyon Anabilim Dali, Istanbul, Turkey.
Tel: +90 506 330 66 40 e-mail: ebru.tarkc@yahoo.com

target level of sedation [4, 5].

Obesity has been defined as one of the major predictors of sedation-related adverse events in patients undergoing advanced procedures. Thus, sedation in these patients becomes more challenging with reduced lung volume, functional residual capacity, and vital capacity. The lung volumes decrease exponentially with an increase in the body mass index (BMI). Moreover, the ventilation-perfusion mismatch can frequently occur in obese patients. Events, such as obstructive sleep apnea and airway collapse, are frequently detected during deep sedation in obese adults. They have an increased risk of airway obstruction and critical airway events, along with other cardiopulmonary adverse events [6, 7].

A combination of ketamine and propofol for sedation was proved to be safe and effective by minimizing the side effects of each of the drugs, simultaneously preserving the sedation efficacy [8].

In the background of an ongoing obesity epidemic, in the present study, we aimed to evaluate the sedation-related complications in obese patients undergoing advanced endoscopic procedures.

MATERIALS AND METHODS

In this study, in a retrospective study design, patients undergoing advanced endoscopic procedures in a single tertiary referral medical center, from January 2016 to December 2018, were enrolled. This study was approved by the Ethics Committee of the local hospital (22/03/2019 B.10.1.TKH.4.34.H.GP.0.01/58).

Patients between 18 and 60 years of age; categorized as American Society of Anesthesiologists physical status classification (ASA) I–III: with BMI between 25-30, BMI between 30-35, and BMI between 35-40 were included in this study. However, patients categorized as ASA IV–V or patients with severe chronic obstructive pulmonary disease, cardiorespiratory failure, baseline oxygen saturation <90, or known to have an allergy to the drugs used in this study and patients with BMI <25 were excluded from this study.

All the procedures were performed by the same gastroenterologist team, holding an experience of more than five years. A single anesthesiologist participated in this study, holding an experience of more than 10 years. All the patients meeting the inclusion criteria were classified into three groups according to the BMI.

Appropriate monitoring was performed using continuous electrocardiography, while heart rate and non-invasive blood pressure monitoring, pulse oximetry, and end-tidal CO_2 were measured using capnography during the procedure. Patients undergoing the procedures were kept in a left lateral decubitus position.

Bolus induction was performed with 0.5 mg/kg ketamine and 0.5 mg/kg propofol intravenously, followed by a ketofol (1:1) infusion, prepared with 2 ml ketamine (50 mg/ml) and 10 ml propofol 1% (10 mg/ml) with 8 ml normal saline containing 5 mg ketamine 5 mg propofol for each ml was titrated to maintain Ramsay Sedation Scale (RSS) value of 4 or more. Supplemental oxygen by nasal cannula at the rate of 4 liters/min was administered to all the patients at the onset of sedation. Additional doses of ketofol were administered when vital signs demonstrated significant sympathetic stimulation (elevated heart rate and blood pressure) during the procedures, depending on the discretion of the anesthesiologist. In case of apnea, the anesthesiologist performed the necessary airway modifications involving chin-lift, jaw- thrust, and stimulation of the patient using noxious stimuli. Bag-mask ventilation was allowed when the stimuli were not adequate for respiration. Apnea was defined as no spontaneous breathing for at least 20 seconds.

The demographic parameters, BMI, Mallampati score, and ASA classification were assessed before endoscopy by the anesthesiologist. The procedure and sedation factors, efficacy, adverse events, and required therapeutic interventions were recorded. Recovery after procedures was assessed according to the Modified Aldrete Score (MAS), and the patients were discharged from the unit when they achieved a MAS ≥ 9. The anesthesiologist checked for the MAS in the post-operative care unit during the follow-up period.

In this study, the primary objectives were [1] analysis of the association of the frequency of sedation-related complications and airway interventions in the obese patients and [2] comparison of the patients' characteristics and pharmacological data.

Statistical Analysis

Nominal and ordinal parameters were described with frequency analysis. Scale parameters were described with mean and standard deviations. Kolmogorov–Smirnov test was carried out for normality of the scale parameters. Since all the parameters were found to be non-nor-

mal in distribution, non-parametric tests were applied. Differences between the groups were analyzed using the chi-square and Kruskal–Wallis tests. All the analyses were performed by SPSS 17.0 for Windows (Operating System) at a 95% confidence interval.

RESULTS

A total of 1172 patients were enrolled for this study. Among them, 950 patients (81.05%) for ERCP and 222 (18.95%) for EUS. The demographic characteristics have been highlighted in Table 1. The mean age did not differ statistically between the groups (p=0.090).

A total of 289 patients had a BMI between 35-40, and were predominantly male. However, the distribution of gender did not differ statistically (p=0.306). Mallampati score was significantly higher in the group of patients with BMI between 35-40 (p=0.000) (Table 1).

The duration of endoscopy, the time required to achieve RSS >4, total ketofol dose, and the duration of ketofol infusion were significantly higher in the group with the BMI 35-40 (p<0.000). No response to endoscopic intubation was significantly higher in the group with the BMI between 25- 30 (p=0.000) (Table 2).

All other comorbidities were more common in the group with the BMI between 35-40. The distributions of events like allergic rhinitis, vomiting, agitation or delirium, and aspiration were not significantly different (p=0.949), while other comorbidities distributions were significantly different (p=0.000) (Table 3).

Jaw-thrust, airway placement, bag–mask ventilation, and suctioning were more common in the group with the BMI between 35-40, with statistically significant differences (p=0.000), whereas repositioning was higher in the group with the BMI between 30 and 35 (Table 4).

Time to achieve RSS >4 was 2.78±0.31 min. in BMI between 25-30 group, 4.04±0.43 min. in BMI between 30 and 35 group, 6.00±0.40 min in BMI between 35-40 group (p=0.000) (Table 5).

Aldrete scores did not differ between the groups (Table 6).

Apnea, Desaturation <80% and airway obstruction were statistically common in the group BMI between 35-40, as shown in Figure 1.

Table 1. Patient demographics and clinical presentation

	25-30 (n=182)	30-35 (n=701)	35-40 (n=289)	p
Age	55.06±0.84	55.25±1.67	55.05±1.63	0.090[a]
Male	32 (17.6)	131 (18.7)	65 (22.5)	0.306[b]
Mallampati score	0.54±0.01	0.61±0.03	1.74±0.07	0.000[a]

[a]Kruskal Wallis Test; [b]Chi-Square Test.

DISCUSSION

Overweight and obesity are significant health problems and continue to rise at epidemic proportions among adults aged older than 20 years [9]. Defining the safety of advanced endoscopic procedures performed under sedation and deciding the best sedative regimen for such high-risk patients have paramount importance, as there is limited data in the literature.

Table 2. Procedural and pharmacologic data

	25-30 (n=182)	30-35 (n=701)	35-40 (n=289)	p
Endoscopy time	30.11±0.55	30.60±0.77	31.83±0.63	0.000[a]
No response to end intubation	72 (39.6)	86 (12.3)	81 (28.0)	0.000[b]
Time to achieve RSS>4	2.78±0.31	4.04±0.43	6.00±0.40	0.000[a]
Aldrete score	9 (100.0)	9 (100.0)	9 (100.0)	N/A
Total Ketofol dose	1.11±0.05	1.37±0.05	1.90±0.06	0.000[a]
Ketofol infusion time	30.10±0.49	31.17±0.37	32.20±0.40	0.000[a]

[a]Kruskal Wallis Test; [b]Chi-Square Test; RSS: Ramsay Sedation Scale.

Table 3. Sedation related complications

	25-30 (n=182)	30-35 (n=701)	35-40 (n=289)	p
Apnea	10 (5.5)	40 (5.7)	66 (22.8)	0.000[a]
Allergic rhinitis	6 (3.3)	22 (3.1)	10 (3.5)	0.966[a]
Coughing	33 (18.1)	182 (26.0)	114 (39.4)	0.000[a]
Desaturation <80% for 3 min.	14 (7.7)	66 (9.4)	80 (27.7)	0.000[a]
Prolonged recovery time	14 (7.7)	80 (11.4)	100 (34.6)	0.000[a]
Secretions requiring treatment	4 (2.2)	135 (19.3)	93 (32.2)	0.000[a]
Vomiting	1 (0.5)	10 (1.4)	3 (1.0)	0.558[b]
Wheezing	12 (6.6)	68 (9.7)	44 (15.2)	0.006[a]
Agitation-Delirium	-	3 (0.4)	1 (0.3)	0.500[b]
Airway obstruction	9 (4.9)	38 (5.4)	66 (22.8)	0.000[a]
Inability to complete procedure	1 (0.5)	3 (0.4)	5 (1.7)	0.137[b]
Laryngospasm	7 (3.8)	31 (4.4)	50 (17.3)	0.000[a]
Stridor	7(3.8)	31 (4.4)	50 (17.3)	0.000[a]
Aspiration	1 (0.5)	3 (0.4)	1 (0.3)	0.949[b]

[a]Chi-Square Test; [b]Chi-Square with likelihood ratio.

Table 4. Airway maneuvers

	25-30 (n=182)	30-35 (n=701)	35-40 (n=289)	p
Jaw thrust	9 (4.9)	40 (5.7)	66 (22.8)	0.000[a]
LMA	-	-	1 (0.3)	N/A
Airway placement	9 (4.9)	40 (5.7)	66 (22.8)	0.000[a]
BM Vent	7 (3.8)	30 (4.3)	40 (13.8)	0.000[a]
Suctioning	44 (24.2)	100 (14.3)	100 (34.6)	0.000[a]
Repositioning	84 (46.2)	501 (71.5)	100 (34.7)	0.000[a]

[a]Chi-Square Test; BM: Bag mask ventilation; LMA: Laryngeal mask.

Even though obese patients have increased risk of sedation-related side effects and require airway interventions, we have not observed any life-threatening and/or major adverse events in the present study.

The optimal dose to achieve deep sedation in obese patients remains unclear. In obese individuals, the pharmacokinetics of sedative drugs mostly used, such as propofol, may not be predictable, and higher doses may be needed to reach the target level of sedation and a prolonged elimination [4, 5]. Propofol is a strong anesthetic causing respiratory depression, apnea, and fall in blood pressure in patients with no property of internal analgesia. Using opioids or midazolam with propofol may have a synergistic action, such as increasing the frequency of respiratory depression while reducing the amount of propofol used. Ketamine is a safe sedo-analgesic agent, which can be mixed with propofol without causing respiratory depression, while its sympathetic effects raise the blood pressure and heart rate [10]. Recent studies have highlighted combining propofol and ketamine at lowest doses to maintain the hemodynamical stability and to avoid adverse side effects which may occur when either drug is administered in large doses individually.

Many studies have reported the comparison of

TABLE 5. Ramsay Sedation Scale

Ramsay Sedation Scale
i. Patient is anxious and agitated or restless, or both.
ii. Patient is co-operative, oriented, and tranquil.
iii. Patient responds to commands only.
iv. Patient exhibits brisk response to light glabellar tap or loud auditory stimulus.
v. Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus.
vi. Patient exhibits no response.

TABLE 6. Modified Aldrete score

Criteria	Score
1. Activity	
Moves all extremities	2
Moves two extremities	1
Unable to move extremities	0
2. Respiration	
Breathes deeply, coughs freely	2
Dyspenic, shallow or limited breathing	1
Apneic	0
3. Circulation(blood pressure)	
20% ± preanaesthetic level	2
20–49% ± preanaesthetic level	1
50% ± preanaesthetic level	0
4. Consciousness	
Fully awake	2
Arousable on calling	1
Not responding	0
5. Oxygen saturation	
SpO_2 >92% on room air	2
Supplemental oxygen requirement to maintain SpO_2 >90%	1
SpO_2 <90% with oxygen supplementation	0

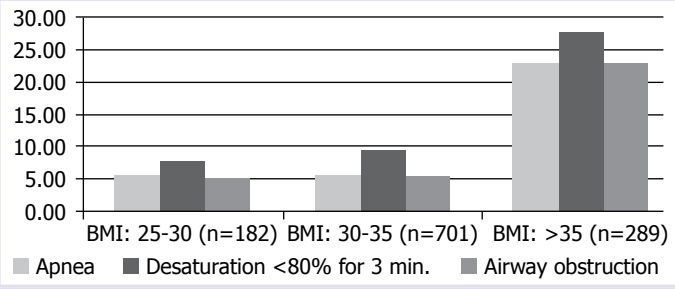

FIGURE 1. The distribution of apnea, desaturation, airway obstruction.

Jaw thrust, Airway placement, Bag Mask Vent., Suctioning were more common in BMI 35-40 group with statistically significant differences ($p<0.05$).

propofol used alone and in combination with other sedative drugs, with the combination group exhibiting to be more beneficial due to lesser side effects [11, 12]. Similar to our study, these reports excluded high-risk patients. Here, we excluded the ASA IV–V patients having serious comorbidities and included patients categorized to be at average-risk for analysis of the complications associated with sedation alone. Consistent with several reports in the literature, the increased risk of respiratory and cardiopulmonary events starts getting exhibited at ASA physical status III [13]. Higher BMI with ASA scores is directly associated with sedation-related adverse effects because of the higher number of life-threatening comorbidities. This study showed a higher frequency of airway maneuvers, hypoxemia, apnea, and airway obstruction in obese patients; however, early termination of the procedure was seen less in this group. This can be justified by the management by trained anesthesiologists together with the team of gastroenterologists and the proper use of capnography in this study. Capnography has been proven to decrease the incidence of apnea and hypoxemia in obese patients in this setting.

Wani et al. [14] conducted a prospective cohort study on 1,016 consecutive patients undergoing advanced endoscopic procedures with propofol alone and combination with benzodiazepines. They reported that increasing BMI was associated with a higher frequency of airway modifications; however, with trained professionals, sedation could be used in obese patients.

Scherrer et al. analyzed 28.792 records and compared sedation-related adverse events between obese and non-obese children. They reported that the total adverse events were more common in obese children. However, such events were rare when sedation was performed by a trained and experienced team with robust capability like represented in many other similar studies [15–17].

Quadeer et al.'s findings are consistent with our results reported hypoxemia occurring in about 50% of ASA I and II patients who were undergoing ambulatory gastrointestinal endoscopy. They found BMI correlated with the number of hypoxemic episodes and that hypoxemia was numerically more frequent in obese patients (BMI >30) compared with nonobese patients (BMI<30) [18].

During the procedures, we used RSS for monitoring the depth of sedation. Based on this scale, obese patients required more ketofol usage compared with the overweight ones. Likewise, the time needed to achieve RSS >4 was longer in the obese patients than the overweight ones.

A significant strength of our study is a large number of available patients for analysis, despite a single-centered approach, and the findings could outline the sedation-related outcomes. We should note that we have several limitations in our study. The therapeutic endoscopy unit at our hospital includes an experienced team, and the sedation-related complications cannot be generalized to all the other centers, as some of the centers prefer endotracheal intubation or gastric laryngeal mask, based on general anesthesia for advanced endoscopic procedures.

In conclusion, despite the increased frequency of airway maneuvers and complications associated with sedation in obese patients, these procedures are safe, and ketofol with its sedo-analgesic properties can be used routinely for sedation by skilled sedation providers. However, further prospective studies are needed to evaluate the effects of obesity on the risks associated with the comorbidities.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions: Design – S.S., R.K.; Supervision – R.K., K.Ö.; Materials – S.S.; Data collection and/or processing – E.T.K.; Analysis and/or interpretation – E.T.K.; Writing – E.T.K.; Critical review – K.Ö.

REFERENCES

1. Adler DG, Baron TH, Davila RE, Egan J, Hirota WK, Leighton JA, et al. ASGE guideline: the role of ERCP in diseases of the biliary tract and the pancreas. Gastrointest Endosc 2005;62:1–8. [CrossRef]
2. Raymondos K, Panning B, Bachem I, Manns MP, Piepenbrock S, Meier PN. Evaluation of endoscopic retrograde cholangiopancreatography under conscious sedation and general anesthesia. Endoscopy 2002;34:721–6. [CrossRef]
3. Coté GA, Hovis RM, Ansstas MA, Waldbaum L, Azar RR, Early DS, et al. Incidence of sedation-related complications with propofol use during advanced endoscopic procedures. Clin Gastroenterol Hepatol 2010;8:137–42. [CrossRef]
4. Berzin TM, Sanaka S, Barnett SR, Sundar E, Sepe PS, Jakubowski M, et al. A prospective assessment of sedation-related adverse events and patient and endoscopist satisfaction in ERCP with anesthesiologist-administered sedation. Gastrointest Endosc 2011;73:710–7. [CrossRef]
5. Kern SE, Xie G, White JL, Egan TD. A response surface analysis of propofol-remifentanil pharmacodynamic interaction in volunteers. Anesthesiology 2004;100:1373–81. [CrossRef]
6. Tishler PV, et al. Incidence of sleep-disordered breathing in an urban adult population: the relative importance of risk factors in the development of sleep-disordered breathing. Jama. 2003;289(17):2230–7.
7. Hillman DR, Walsh JH, Maddison KJ, Platt PR, Kirkness JP, Noffsinger WJ, et al. Evolution of changes in upper airway collapsibility during slow induction of anesthesia with propofol. Anesthesiology 2009;111:63–71. [CrossRef]
8. Akin A, Guler G, Esmaoglu A, Bedirli N, Boyaci A.A comparison of fentanyl-propofol with a ketamine-propofol combination for sedation during endome-trial biopsy. J Clin Anesth 2005;17:187–90. [CrossRef]
9. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999-2008. JAMA 2010;303:235–41.
10. VanNatta ME, Rex DK. Propofol alone titrated to deep sedation versus propofol in combination with opioids and/or benzodiazepines and titrated to moderate sedation for colonoscopy. Am J Gastroenterol 2006;101:2209–17. [CrossRef]
11. Mortero RF, Clark LD, Tolan MM, Metz RJ, Tsueda K, Sheppard RA. The effects of small-dose ketamine on propofol sedation: respiration, postoperative mood, perception, cognition, and pain. Anesth Analg 2001;92:1465–9. [CrossRef]
12. Messenger DW, Murray HE, Dungey PE, van Vlymen J, Sivilotti ML. Subdissociative-dose ketamine versus fentanyl for analgesia during propofol procedural sedation: a randomized clinical trial. Acad Emerg Med 2008;15:877–86.
13. Donoghue TJ. Assessing Fraility and its implication on Anesthesia care and postoperative outcomes in Surgical Patients. AANA J.2019;87:152–9.
14. Wani S, Azar R, Hovis CE, Hovis RM, Cote GA, Hall M, et al. Obesity as a risk factor for sedation-related complications during propofol-mediated sedation for advanced endoscopic procedures. Gastrointest Endosc 2011;74:1238–47. [CrossRef]
15. Scherrer PD, Mallory MD, Cravero JP, Lowrie L, Hertzog JH, Berkenbosch JW, et al. The impact of obesity on pediatric procedural sedation-related outcomes; results from the Pediatric Sedation Research Consortium. Pediatr Anesth 2015;25:689–97. [CrossRef]
16. Baker S, Yagiela JA. Obesity: acomplicating factor for sedation in children. Pediatr Dent 2006;28:487–93.
17. Mallory MD, Baxter AL, Kost SI; Pediatric Sedation Research Consortium. Propofol vs pentobarbital for sedation of children undergoing magnetic resonance imaging: results from the Pediatric Sedation Research Consortium. Paediatr Anaesth 2009;19:601–11. [CrossRef]
18. Qadeer MA, Rocio Lopez A, Dumot JA, Vargo JJ. Risk factors for hypoxemia during ambulatory gastrointestinal endoscopy in ASA I-II patients. Dig Dis Sci 2009;54:1035–40. [CrossRef]