

# Clinical analysis of moderate-to-deep-sedation by nonmedical sedation practitioners in 597 patients undergoing gastrointestinal endoscopy: a retrospective study

## Authors

Hermanus Vaessen, Elisabeth Bruens, Johannes Knape

## Institution

Department of Anesthesiology, Intensive Care and Emergency Medicine, University Medical Centre Utrecht, the Netherlands

## submitted:

2. November 2015

## accepted after revision:

8. February 2016

## Bibliography

**DOI** <http://dx.doi.org/10.1055/s-0042-103238>  
Published online: 8.4.2016  
Endoscopy International Open 2016; 04: E564–E571  
© Georg Thieme Verlag KG  
Stuttgart · New York  
E-ISSN 2196-9736

## Corresponding author

**H. H. B. (Paul) Vaessen, RNA, PSA Specialist**

University Medical Centre  
Utrecht  
Department of Anesthesiology,  
Intensive Care and Emergency  
Medicine  
Heidelberglaan 100  
Huispostnr.: F02.811  
3584 CX Utrecht  
The Netherlands  
Fax: + 31-30-7555442  
H.H.B.Vaessen@umcutrecht.nl

**Background and study aim:** The purpose of this study was to evaluate whether moderate-to-deep sedation with propofol and alfentanil can be administered safely by nonmedical sedation practitioners, and the outcomes of this practice in the Netherlands. We retrospectively analyzed the occurrence of sedation-related complications in patients undergoing gastrointestinal endoscopic procedures.

**Patients and methods:** In this study, 597 adult patients consecutively underwent upper gastrointestinal endoscopic procedures. The health status of the patients was screened according to a standardized protocol, and the patients were sedated by trained nonmedical sedation practitioners. Their vital signs were continuously monitored and recorded. All patients received oxygen, and the depth of sedation was continuously assessed and recorded. Mild and severe complications were recorded and analyzed.

## Introduction

Diagnostic and therapeutic gastrointestinal (GI) endoscopic procedures have become standard tools for the investigation and surveillance of GI disease. These often-complex procedures may be uncomfortable and painful for patients. Moderate-to-deep sedation is frequently used to relieve discomfort and improve working conditions for endoscopists [1].

Sedation is considered to be a risky medical procedure [2,3]. Traditionally, benzodiazepines, such as midazolam [4], have frequently been used for that purpose, often in combination with fentanyl [5] or meperidine [6]. However, many patients report bad experiences [7] and unpleasant memories of their procedures, refusing to undergo similar sedation during later endoscopic procedures. Sedation with propofol (2,6-diisopropylphenol) and a short-acting opioid is found to be comfortable by many patients, improves operational effi-

**Results:** All patients recovered uneventfully, and no mortality occurred. Overall, of the 597 sedated patients, 85 had mild and 4 had severe complications. Hypoxemia and upper airway obstruction, which were easily managed by trained nonmedical sedation practitioners, were the most common events. Hypotension was rare. No signs or symptoms suggestive of aspiration were reported.

**Conclusion:** Moderate-to-deep sedation has been and continues to be a risky medical procedure. Serious complications of propofol/opioid-based sedation, especially respiratory and cardiovascular adverse events, may occur. These complications need to be recognized rapidly and appropriately managed. Our study shows that well-trained nonmedical sedation practitioners can be entrusted to take responsibility for the safe administration of moderate-to-deep sedation.

ciency, results in a short recovery time [8], and is more easily controlled than sedation with midazolam-based regimens [9].

The shortage of medical practitioners who can undertake the direct, personal, specialist-based supervision of moderate-to-deep sedation in a significant number of patients in the Netherlands [10] has led to initiatives to transfer responsibilities for such sedation to health care personnel other than anesthesiologists. Therefore, a pilot program for sedation skills training was developed in the departments of anesthesiology and gastroenterology at the University Medical Centre Utrecht (UMCU) and the Amsterdam Medical Centre (AMC) as part of an effort to shift or reshuffle certain tasks, in which a task normally performed by a physician is transferred to a health care professional with a different, usually lower, level of education and training. Such programs may result in the creation of new types of health care personnel, such as nonmedical sedation

## License terms



practitioners, whose function is to assist physicians or to perform specific tasks independently. Selected nurse anesthetists have been trained and certified to accept responsibility for the decisions they make while safely administering propofol/alfentanil sedation under the indirect supervision of an anesthesiologist. The primary aim of this 30-month retrospective study was to evaluate the clinical outcomes of moderate-to-deep sedation administered by trained nonmedical sedation practitioners using a propofol/opioid technique during GI endoscopy, with a particular emphasis on adverse events related to ventilation and circulation complications.

## Patients/materials and methods

### Study population and design

On September 11, 2013, the UMCU Medical Ethical Committee approved the protocol (No.13-467/C) for this retrospective study, which was registered as reference No.WAG/om/13069604. Selected patients were offered sedation because of the earlier failure of light sedation administered by a gastroenterologist and/or because of their medical condition. A total of 597 patients consecutively underwent diagnostic and therapeutic GI endoscopic procedures with moderate-to-deep sedation administered by five trained nonmedical sedation practitioners during a period of 30 months, from September 2013 to July 2014; these patients were included in a database that was retrospectively analyzed. The nonmedical trained sedation practitioners had experience in administering propofol for moderate-to-deep sedation in the department of gastroenterology; they also had experience of at least 150 cases in administering moderate-to-deep sedation during (interventional) cardiology and pulmonary diagnostic procedures.

The patients were divided into four groups based on increasing procedural complexity: group I, colonoscopy; group II, combined gastroscopy and colonoscopy; group III, esophagogastroduodenoscopy (EGD), defined as upper GI endoscopy and/or a single-balloon endoscopic procedure; and group IV, endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS) (Table 1).

The medical status of each patient was screened and approved by the trained sedation practitioner. In the case of a patient with American Society of Anesthesiologists (ASA) physical status class III or IV, an anesthesiologist was consulted to determine the most appropriate strategy. The ASA physical status class [11] of each patient was assessed in accordance with the hospital procedural sedation and analgesia screening protocol. The Mallampati clinical scoring system [12,13] was used to predict difficult airway management. Demographic data, duration of the procedures, complications (e.g., hypoventilation, apnea, arterial desaturation,

hypotension, rhythm disturbances, decreased awareness), and data from the recovery period were assessed. Clinical outcomes were analyzed according to the complication list of the Netherlands Society of Anesthesiology (Table 2).

Following screening, all patients gave informed consent for the sedation. Inclusion criteria for moderate-to-deep sedation were age of 18 years or older and compliance with fasting guidelines before the procedure. Exclusion criteria were allergy to soy, eggs, or peanuts; pregnancy; acute GI bleeding; and mental disability [14].

Trained nonmedical sedation practitioners of the department of anesthesiology screened the health status of the patients, monitored them, provided procedural sedation and analgesia, and recorded their data. These professionals had no concomitant responsibilities at the time. All patients were briefed before the sedation procedure, with an anesthesiologist immediately available by phone for consultation and/or intervention, as documented in a hospital protocol.

### Sedation protocol and monitoring

The depth of sedation was assessed continuously and recorded at least every 5 minutes with the Observer's Assessment of Alertness/Sedation (OAA/S) scale [15], based on a combination of observation of the resting patient and the patient's responses to verbal commands of increasing intensity. The score ranges from 1 (does not respond) to 5 (alert). Before the GI procedure, an intravenous infusion was initiated for fluid administration. The vital signs of all patients were continuously observed and monitored (cube Compact Monitor; Spacelabs Healthcare, Snoqualmie, Washington, USA), and all data were recorded every 5 minutes with AnStat, an anesthesia information management system. Heart activity was monitored with three-lead electrocardiography (ECG) and oxygen saturation with pulse oximetry (SpO<sub>2</sub>). Noninvasive blood pressure (NIBP) measurements were taken at 5-minute intervals, and capnography readings (Smart CapnoLine Plus; Oridion Capnography, Needham, Massachusetts, USA) were continuously recorded. All patients received supplemental oxygen (2L/min) by nasal cannula. Procedural sedation and anesthesia started with the intravenous administration via infusion pump (Alaris Medical UK) of 5 mg/kg/hrs of propofol (Lipuro 1% [10mg/mL]; B. Braun) per hour and 200µg of alfentanil (Janssen-Cilag) as a bolus. Additional intravenous boluses of 10 or 20 mg of propofol were titrated until the desired level of moderate-to-deep sedation (OAA/S sedation score of 4 or 3) was achieved. Our goal was to maintain a sedation level between moderate (patient responds to verbal or tactile stimulus) and deep (patient not aroused easily but responds to painful stimuli). Depending on the clinical signs or symptoms of pain, additional intravenous boluses of 100 to 200µg of alfentanil were given.

The primary outcome was to investigate the incidence of adverse events affecting the patient's ventilation and circulation. Unintended disruption of the patient's ventilation was defined as the observation of hypoxemia, aspiration, or laryngospasm. Hypoxemia was defined as oxygen saturation of 92% or lower for at least 5 minutes and aspiration of gastric contents confirmed by aspiration of fluid in the trachea with a suction catheter. Laryngospasm was defined as stridor or upper airway obstruction associated with a decrease in arterial oxygen saturation, requiring an intervention such as chin lift, jaw thrust, insertion of an oral airway, placement of a laryngeal mask, or even orotracheal intubation. A ventilation complication was defined as mild if an unintended disruption lasted for no longer as 30 seconds and was self-limit-

**Table 1** Endoscopic procedures grouped according to complexity.

Group	Procedure
I	Colonoscopy
II	Combined gastroscopy and colonoscopy
III	Esophagogastroduodenoscopy (EGD)
	Percutaneous endoscopic gastrostomy (PEG)
	Endoscopic mucosal resection (EMR)
IV	Zenker's diverticulum
	Endoscopic retrograde cholangiopancreatography (ERCP)
	Endoscopic ultrasonography (EUS)

**Table 2** The national modified complication list of the Netherlands Society of Anaesthesiology.

Baseline characteristics of the study population	Measurements
<b>Patient identification</b>	Baseline first measured systolic NIBP, mean, mmHg
<i>Gastrointestinal endoscopy</i>	Baseline first measured diastolic NIBP, mean, mmHg
Group I	Baseline lowest measured systolic NIBP, mean, mmHg
Colonoscopy	Baseline lowest measured diastolic NIBP, mean, mmHg
Group II	Baseline first measured heart rate, mean, beats/min
Combined gastroscopy and colonoscopy	Baseline highest measured heart rate, mean, beats/min
Group III	Baseline lowest measured heart rate, mean, beats/min
Esophagogastroduodenoscopy	Baseline first measured SpO <sub>2</sub> , mean, %
Percutaneous endoscopic gastrostomy	Baseline lowest measured SpO <sub>2</sub> , mean, %
Endoscopic mucosal resection	Baseline last measured SpO <sub>2</sub> , mean, %
Zenker's diverticulum	Baseline first measured end-tidal CO <sub>2</sub> , mean, %
Group IV	Last measured end-tidal CO <sub>2</sub> , mean, %
Endoscopic retrograde cholangiopancreatography	Overall OAA/S score
Endoscopic ultrasonography	5
<i>Baseline characteristics</i>	4
Age, y	3
Male	2
Female	1
<i>American Society of Anesthesiologists (ASA) classification</i>	<i>Recovery care</i>
I	First VAS score in recovery room: 0, no pain; 10, maximum pain
II	First Aldrete score in recovery room
III	<i>Events associated with sedation and intervention</i>
IV	Systolic hypotension (> 25 % from baseline), mmHg
<i>Mallampati score</i>	Systolic hypertension (> 25 % from baseline), mmHg
I	Bradycardia (> 25 % from baseline), beats/min
II	Tachycardia (> 25 % from baseline), beats/min
III	Hypoxemia (SpO <sub>2</sub> ≤ 92 %)
IV	Chin lift
<i>Monitoring</i>	Aspiration
ECG, SpO <sub>2</sub> , capnography, O <sub>2</sub> supply, NIBP	Airway obstruction
Procedure time, min	Oral Guedel airway
Intravenous cannula, 20 gauge	Bag valve mask – assisted ventilation
<i>Medication during procedure</i>	Oral tracheal intubation
Alfentanil dose, mg	Aborted procedure
Propofol dose, mg	Anesthesiologist advice required
Atropine	<i>Complication due to endoscopic procedure</i>
Ephedrine	Perforation
Lidocaine	Bleeding
Others	

ECG, electrocardiography; SpO<sub>2</sub>, oxygen saturation as measured with pulse oximetry; NIBP, noninvasive blood pressure; OAA/S, observer's assessment of alertness/sedation; VAS, Visual Analog Scale.

ASA class	Group I: Colonoscopy	Group II: Combined gastroscopy and colonoscopy	Group III: EGD, PEG, EMR, Zenker's diverticulum	Group IV: ERCP, EUS
I	47	3	24*	1
II	97	30	244	54
III	12	3	30	47
IV	0	0	3	1

EGD, esophagogastroduodenoscopy; PEG, percutaneous endoscopic gastrostomy; EMR, endoscopic mucosal resection; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasonography.

\* In one case, the patient's ASA class was not reported.

**Table 3** Study results according to American Society of Anesthesiologists (ASA) physical status class of patients.

ing; otherwise, the complication was considered severe. Unintended disruption of the circulation was defined as the registration of hypotension or hypertension. Hypotension was defined as a mean NIBP measurement of 60 mmHg or less for at least 5 minutes and was treated with vasopressors. Hypertensive periods were defined when the diastolic NIBP was above 110 mmHg and/or the systolic NIBP was above 180 mmHg for at least 5 minutes, requiring pharmacologic intervention. A circulation compli-

cation was defined as severe if the given drug did not have the desired effect within 30 seconds.

### Recovery

After the procedure, all patients stayed in the recovery room for at least 1 hour and were continuously observed and monitored (ECG, NIBP, and SpO<sub>2</sub>). The modified Aldrete score [16] was recorded on arrival and every 10 minutes in the recovery room.

**Table 4** Age of the patients (Part 1).

Age	Group I		Group II		Group III		Group IV	
	Colonoscopy		Combined gastroscopy and colonoscopy		EGD, PEG, EMR, Zenker's diverticulum		ERCP, EUS	
	Male	Female	Male	Female	Male	Female	Male	Female
Count	44	112	16	20	160	142	39	64
Mean	54.8	52.9	47.6	46.6	56.4	54.8	55.4	52.8
Minimum	19	20	18	23	19	20	15	15
Maximum	80	89	79	75	86	90	75	88
Standard deviation	17.93	17.09	16.78	16.87	15.5	15.29	12.23	16.88

**Table 4** Age of the patients (Part 2).

ANOVA						
Age	Sum of squares	df	Mean square	F	Significant	
Between groups	2,574,123	3	858,041	3.366	.018	
Within groups	151,151,144	593	254,892			
Total	153,725,266	596				

**Table 4** Age of the patients (Part 3).

Bonferroni multiple comparisons							
Age							
(I) Group	(J) Group	Mean difference (I-J)	Standard error	Significant	95%CI		
					Lower boundary	Upper boundary	
1	2	6.419	2.952	.180	-1.40	14.23	
	3	-2.178	1.574	1.000	-6.34	1.99	
	4	-.302	2.027	1.000	-5.67	5.06	
2	1	-6.419	2.952	.180	-14.23	1.40	
	3	-8.597*	2.815	.014	-16.05	-1.15	
	4	-6.721	3.091	.180	-14.90	1.46	
3	1	2.178	1.574	1.000	-1.99	6.34	
	2	8.597*	2.815	.014	1.15	16.05	
	4	1.876	1.822	1.000	-2.95	6.70	
4	1	.302	2.027	1.000	-5.06	5.67	
	2	6.721	3.091	.180	-1.46	14.90	
	3	-1.876	1.822	1.000	-6.70	2.95	

EGD, esophagogastroduodenoscopy; PEG, percutaneous endoscopic gastrostomy; EMR, endoscopic mucosal resection; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasonography; ANOVA, analysis of variance; df, degrees of freedom; F, F statistic; CI, confidence interval.

\* Significant at  $P=0.05$ .

This score describes patient motor activity, oxygen saturation, blood pressure, respiratory function, and consciousness. Pain scores were recorded and evaluated every 10 minutes with a Visual Analog Scale (VAS) [17]. The VAS score ranged from 0 (no pain) to 10 (extreme pain). Patients were discharged when full consciousness had been regained, when their vital signs (heart rate, oxygen saturation, NIBP) were within normal limits, when the pain score was 3 or lower [18], and when the modified Aldrete score was 9 or higher and stable for a minimum of 60 minutes.

### Statistical analyses

Statistical analyses were performed with IBM SPSS Statistics, Version 23 (IBM, Armonk, New York, USA). The four endoscopy groups were compared with one-way analysis of variance (ANOVA). This test determines if there is any significant difference be-

tween groups by age, duration of the procedure, or gender. The Bonferroni method, as a follow-up test to ANOVA, is used to determine significant differences between groups. For age,  $P=0.05$  was considered statistically significant.

### Results

#### ▼ Safety

All endoscopic procedures in the 597 patients were carried out efficiently according to plan, and no failures were recorded. An acute intervention by the indirectly supervising anesthesiologist was not required in any of the cases. No mortality and no serious morbidity occurred. The anesthesiologist who conducted the briefing before the sedation procedure decided that moderate-to-deep sedation was not indicated in 5 of the 597 patients, in

**Table 5** Mild and severe cases of unintended disruption of ventilation and circulation.

	Group I: Colonoscopy				Group II: Combined gastroscopy and colonoscopy				Group III: EGD, PEG, EMR, Zenker's diverticulum				Group IV: ERCP, EUS			
	ASA I	ASA II	ASA III	ASA IV	ASA I	ASA II	ASA III	ASA IV	ASA I	ASA II	ASA III	ASA IV	ASA I	ASA II	ASA III	ASA IV
<b>Unintended disruption of ventilation</b>																
Aspiration	n = 0															
Laryngospasm																
Intubation	n = 2 (0.3%)															
Mask ventilation	n = 7 (1.1%)															
Chin lift	n = 17 (2.8%)															
Guedell	n = 4 (0.7%)															
<b>Unintended disruption of circulation</b>																
NIBP																
Mean <60 mmHg	n = 7 (1.2%)															
Diastolic >110 mmHg, systolic >80 mmHg	n = 7 (1.2%)															

EGD, esophagogastroduodenoscopy; PEG, percutaneous endoscopic gastrostomy; EMR, endoscopic mucosal resection; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasonography; ASA, American Society of Anesthesiologists; SpO<sub>2</sub>, oxygen saturation as measured by pulse oximetry; NIBP, noninvasive blood pressure.

\* Severe complication.

whom sedation was converted to general anesthesia by an anesthesia team.

### Demographic data

The distribution of the ASA physical status scores was as follows: ASA I, 75 patients (13%); ASA II, 426 patients (71%); ASA III, 92 patients (15%); and ASA IV, 4 patients (<1%). In one case, the ASA classification score was not reported (● **Table 3**).

### Patient age and procedure duration

The mean age of the patients between the four groups varies significantly ( $P=0.018$ , ● **Table 4**). Groups II and III appear to differ significantly from each other ( $P=0.014$ ), whereas there is no significant proof of a difference for the other groups ( $P>0.1$ ). A linear regression with  $P<0.001$  indicating significance shows a positive correlation between patient age and procedure duration.

### Incidence of hypoxemia, hypotension, and hypertension

Mild complications (● **Table 5**) were recorded in 85 of the 597 patients, and severe complications in 4 of the 597 patients. Hypoxemia was a severe complication (desaturation lasting longer than 5 minutes and requiring intubation of the trachea) in 2 patients (0.3%) and a mild complication in 43 patients (7.2%). Laryngospasm, which was treated with chin lift, mask ventilation, or insertion of an oral airway, was characterized as a mild complication in 28 patients (4.7%) and as a severe complication in 2 patients (0.3%).

No signs or symptoms suggestive of aspiration were reported.

Mild blood pressure-related complications were as follows: hypotension in 7 patients (1.2%), which was treated with vasopressors; hypertension in 7 patients, which was managed by increasing the dose of the sedative and/or opioid. All procedures were successfully completed.

Moderate-to-deep sedation provided by trained sedation practitioners resulted in efficient endoscopic GI procedures in all cases.

Among the 597 patients, 11 with a sedation score of OAA/S 3 or 4 spontaneously reported awareness as a sign of an insufficient level of sedation during the procedure.

### Recovery and discharge

Upon arrival in the recovery room, 177 patients (29.6%) had the maximum Aldrete score of 10. There were 168 patients (28.1%) with a score of 9, 134 patients (22.4%) with a score of 8, and 74 patients (12.3%) with a score of 7. Fewer than 10% of all patients had an Aldrete score between 6 and 2. Furthermore, upon arrival in the recovery room, 246 patients (41%) had a minimum VAS score of 0, 114 patients (19%) had a score of 1, and 69 patients (12%) had a score of 2 (● **Table 6**).

### Discussion

As a result of the exponential increase in the number of diagnostic and therapeutic GI endoscopic procedures being performed in the last few decades, there is a great demand for sedation services, which in most countries cannot be met by anesthesiologists because of a shortage of these specialists. Meanwhile, endoscopists have been looking for alternative solutions to increase the efficiency of endoscopic procedures and to improve their working conditions with the use of sedative drugs, often in uncontrolled or moderately controlled conditions.

Quality and safety usually have not been primary considerations in the development of these solutions, which rapidly became popular because of their ease of application. A number of articles have discussed the use of propofol by clinicians [19, 20], mostly gastroenterologists, who have no training in anesthesia or resuscitation. In contrast, anesthesiologists, in particular in the United States, abide by the official Food and Drug Administration (FDA) standpoint that propofol should be administered only by persons trained in general anesthesia [21]. However, an increasing num-

Aldrete scoring system		First Aldrete score after each procedure	
Respiration	Score	Score	Patient data
Able to take deep breath and cough	2	10	n = 177 (30 %)
Dyspnea/shallow breathing	1	9	n = 168 (28 %)
Apnea	0	8	n = 134 (22 %)
Activity		7	n = 74 (12 %)
Able to move 4 extremities	2	6	n = 23 (4 %)
Able to move 2 extremities	1	5	n = 11 (2 %)
Able to move 0 extremities	0	4	n = 6 (1 %)
Circulation		3	n = 2 (< 1 %)
NIBP 20 mmHg before sedation	2	2	n = 2 (< 1 %)
NIBP 20 – 50 mmHg before sedation	1	1	n = 0
Consciousness		VAS score before release/recovery	
Fully awake	2	Score	Patient data
Arousable on calling	1	0	n = 246 (41 %)
Not responding	0	1	n = 114 (19 %)
SpO <sub>2</sub> on room air		2	n = 69 (12 %)
100 % – 98 %		3	n = 18 (3 %)
97 % – 95 %		4	n = 28 (5 %)
< 95 %		5	n = 24 (4 %)
Total score		6	n = 21 (4 %)
		7	n = 8 (1 %)
		8	n = 8 (1 %)
		9	n = 2 (< 1 %)
		10	n = 1 (< 1 %)

**Table 6** Modified Aldrete score and visual analog scale (VAS) score.

NIBP, noninvasive blood pressure; VAS, Visual Analog Scale; SpO<sub>2</sub>, oxygen saturation as measured by pulse oximetry.

ber of published reports [22,23] show a very good safety record for sedation administered by clinicians other than anesthesiologists, even nonmedical practitioners. These findings are in contrast with data from a study published in 2002 [24]. We hereby report on our first experiences with 597 consecutive patients undergoing GI endoscopic procedures with moderate-to-deep sedation administered by trained anesthesia nurses. The patients eligible for moderate-to-deep sedation during endoscopy were clustered and treated in a full-day program.

In our retrospective study, all GI endoscopic procedures (100%) were completed successfully with the patients under moderate-to-deep sedation administered by nonmedical sedation practitioners. None of our procedures, even technically difficult and time-consuming ones such as ERCP and EUS, had to be interrupted because of insufficient cooperation or unrest of the patient or because of severe complications.

In our 597 procedures, mild hypoxemia occurred in 7.2% of the cases and mild laryngospasm in 4.7% of the cases, and both complications could be managed easily by the trained sedation practitioners. Endotracheal intubation was required in only 2 patients (0.3%), in one because of increasing stridor and in the other because of blood loss from the upper GI tract as a complication of the endoscopic procedure. In these two cases, the assistance of an anesthesiologist was required.

Hypotension was observed in 1.2% of the patients and hypertension in another 1.2%, both considered mild cardiovascular complications.

Berzin [25] reported 140 events in 109 patients (20.6%) during 528 ERCP procedures in which sedation was administered by anesthesiologists. The events were often a combination of hypotension (38), arrhythmia (20), oxygen desaturation to less than 85% (66), and unplanned intubation (16) that could occur during one procedure. Our rate of mild complications was lower. This under-

scores the need for good patient selection, well-trained sedation practitioners, careful monitoring, and the practitioner's undivided attention for each patient. Wehrmann and Riphaus [26], in a 6-year study of 9547 patients, reported a total of 135 adverse events (1.4%) during endoscopic procedures conducted with the patients under propofol sedation. In their study, the events were mainly assisted ventilation (0.4%) and endotracheal intubation (0.09%), and 4 patients died (mortality rate of 0.04%). Agostoni et al. [27], in an 8-year study, reported adverse events in 4.5% of 17,999 patients undergoing target-controlled propofol sedation for GI endoscopic procedures. There were 6 complications (arterial hypotension, desaturation, bradycardia, arterial hypertension, arrhythmia, and aspiration) occurring in more than 0.1% of the patients, and 3 patients died (0.017%). In both studies, the overall incidence of adverse events was lower than that in our study, although differences in definitions may play a role.

We agree with the findings and the conclusion of Wehrmann and Riphaus that interventional endoscopy under propofol sedation is not risk-free, and that monitoring of the patient's vital parameters during GI interventions is necessary.

Because several studies [28,29] have shown a variety of moderate-to-deep sedation-related complications in GI endoscopy, it is mandatory, in our opinion, that moderate-to-deep sedation be administered by a well-trained practitioner who is competent in handling acute respiratory and circulatory events [30]. This is especially true for some subcategories of patients. We observed a trend toward a greater incidence of unwanted side effects in a specific group of patients – namely, those undergoing EGD, defined as upper GI endoscopy and/or a single-balloon endoscopy procedure; this was particularly noted in ASA class I and II patients more than in ASA class III patients.

It has also been shown by other investigators [31,32] that propofol-based sedation can be administered safely to patients by well-

trained nonmedical sedation practitioners whose attention is solely devoted to administering sedation and who are not participating in the endoscopic procedure itself [33]. Propofol-based sedation is characterized by a narrow therapeutic window [34, 35]. In our study, the nonmedical sedation practitioners had no responsibility other than to administer sedation and to observe and monitor the patients.

We provided sedation to our patients with a continuous infusion of propofol (5 mg/kg/h) followed by intermittent titrated doses of alfentanil (100–200 µg). This strategy in relation to the severity of the stress response has been shown to contribute to cardiovascular stability during sedation.

Capnography was used to monitor respiratory activity [36], as an early warning system for hypoventilation and impending hypoxemia. In our experience, this mode of monitoring, which now is easily applied as a result of newly developed sampling techniques in combination with disposable pulse oximeter sensors, contributes significantly to the early detection of impending hypoxemia and may improve patient safety during procedural sedation and analgesia in GI endoscopy. Our experience is in contrast to the study of van Loon et al. [37], in which 100 mg of propofol was given as an initial dose to 427 patients and no alveolar plateau appeared in the capnogram before hypoxemia occurred. Therefore, use of the OAA/S scale, which assesses the patient's level of alertness, is also mandatory during moderate-to-deep sedation. These findings are in agreement with those of Lera dos Santos et al. [38], who evaluated the use of OAA/S scores determined every 2 minutes and found an overall rate of deep sedation of 18% as a result of using the observational alertness tool.

## Conclusion

For a risky medical procedure such as moderate-to-deep sedation during GI endoscopic procedures, strict safety conditions have to be met. Improvement in the quality of sedation care achieved by coordinating practices will contribute to quality, safety, and patient comfort. Our study shows that in the Netherlands, well-trained nonmedical sedation practitioners can be entrusted with the responsibility of safely administering propofol/opioid-based moderate-to-deep sedation in selected patients undergoing GI endoscopic procedures.

Serious complications with propofol-based sedation, especially respiratory and cardiovascular adverse events, may occur but were rare in our safety setting. These complications need to be recognized rapidly by pro-active monitoring and could be appropriately managed by skilled practitioners. Our data may be useful for the future planning of new clinical strategies in this setting in Europe.

**Competing interests:** None

## References

- Hazeldine S, Fritschi L, Forbes G. Predicting patient tolerance of endoscopy with conscious sedation. *Scand J Gastroenterol* 2010; 45: 1248–1254
- Zakko SF, Seifert HA, Gross JB. A comparison of midazolam and diazepam for conscious sedation during colonoscopy in a prospective double-blind study. *Gastrointest Endosc* 1999; 49: 684–689
- Qadeer MA, Lopez AR, Dumot JA et al. Hypoxemia during moderate sedation for gastrointestinal endoscopy: causes and associations. *Digestion* 2011; 84: 37–45
- Girdler NM, Fairbrother KJ, Lyne JP et al. A randomised crossover trial of post-operative cognitive and psychomotor recovery from benzodiazepine sedation: effects of reversal with flumazenil over a prolonged recovery period. *Br Dent J* 2002; 192: 335–339
- Stanley TH. The history and development of the fentanyl series. *J Pain Symptom Manage* 1992; 7 Suppl 3: 3–S7
- Patel S, Vargo J, Khandwala F et al. Deep sedation occurs frequently during elective endoscopy with meperidine and midazolam. *Am J Gastroenterol* 2005; 100: 2689–2695
- Heuss LT, Sughanda SP, Degen LP. Endoscopy teams' judgment of discomfort among patients undergoing colonoscopy – how bad was it really? *Swiss Med Wkly* 2012; 142: w13726
- Cohen LB, Wechsler JS, Gaetano JN et al. Endoscopic sedation in the United States: results from a nationwide survey. *Am J Gastroenterol* 2006; 101: 967–974
- Jung M, Hofmann C, Kiesslich R et al. Improved sedation in diagnostic and therapeutic ERCP: propofol is an alternative to midazolam. *Endoscopy* 2000; 32: 233–238
- Knappe JTA, van Everdingen JJE. Consensus sedatie en analgesie door artsen-niet-anesthesiologen. *Ned Tijdschr Geneeskde* 1999; 143: 1098–1102
- Mak PH, Campbell RC, Irwin MG. American Society of Anesthesiologists. The ASA Physical Status Classification: inter-observer consistency. *American Society of Anesthesiologists. Anaesth Intensive Care* 2002; 30: 633–640
- Mallampati SR. Clinical sign to predict difficult tracheal intubation (hypothesis). *Can Anaesth Soc J* 1983; 30: 316–317
- Mallampati SR, Gatt SP, Gugino LD et al. A clinical sign to predict difficult tracheal intubation: a prospective study. *Can Anaesth Soc J* 1985; 32: 429–434
- Dripps RD. New classification of physical status. *Anesthesiology* 1963; 24: 111
- Chernik DA, Gillings D, Laine H et al. Validity and reliability of the observer's assessment of alertness/sedation scale: study with intravenous midazolam. *J Clin Psychopharmacol* 1994; 10: 244–251
- Aldrete JA. The post-anesthesia recovery score revisited. *J Clin Anesth* 1995; 7: 89–91
- Frieling T, Heise J, Kreysel C et al. Sedation-associated complications in endoscopy prospective multicentre survey of 191142 patients. *Z Gastroenterol* 2013; 51: 568–572
- McCaffery M, Pasero C. Using the 0-to-10 pain rating scale. *Am J Nurs* 2001; 101: 81–82
- Kim SG. The elderly also deserves to undergo therapeutic endoscopy safely under sedation with propofol by gastroenterologists. *Gut Liver* 2015; 9: 1–2
- García-Suárez C, López-Rosés L, Olivencia P et al. Sedation with propofol controlled by endoscopists during percutaneous endoscopic gastrostomy. *Rev Esp Enferm Dig* 2010; 102: 249–256
- Garewal D, Waikar P. Propofol sedation for ERCP procedures: a dilemma? Observations from an anesthesia perspective *Diagn Ther Endosc* 2012; 2012: 639190
- Frieling T, Heise J, Kreysel C et al. Sedation-associated complications in endoscopy – prospective multicentre survey of 191142 patients. *Z Gastroenterol* 2013; 51: 568–572
- Killing D, Orlandi M, Inauen W. Propofol sedation during endoscopic procedures: how much staff and monitoring are necessary? *Gastrointest Endosc* 2007; 66: 443–449
- Eisen M, Baron T, Dominitz J et al. Complications of upper GI endoscopy. *Gastrointest Endosc* 2002; 55: 784–793
- Berzin TM, Sanaka S, Barnett SR 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: 710–717
- Wehrmann T, Riphaut A. Sedation with propofol for interventional endoscopic procedures: a risk factor analysis. *Scand J Gastroenterol* 2008; 43: 368–374
- Agostoni M, Fanti L, Gemma M et al. Adverse events during monitored anesthesia care for GI endoscopy: an 8-year experience. *Gastrointest Endosc* 2011; 74: 266–275
- Amorniyotin S, Chalayonnawin W, Kongphlay S. Deep sedation for endoscopic retrograde cholangiopancreatography: a comparison between clinical assessment and Narcotrend(TM) monitoring. *Med Devices (Auckl)* 2011; 4: 43–49
- Nayar DS, Guthrie WG, Goodman A et al. Comparison of propofol deep sedation versus moderate sedation during endoscopy. *Dig Dis Sci* 2010; 55: 2537–2544

- 30 *Amornyotin S, Chalayonnavin W, Kongphlay S.* Propofol-based sedation does not increase rate of complication during percutaneous endoscopic gastrostomy procedure. *Gastroenterol Res Pract* 2011; 2011: 134819
- 31 American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. *Anesthesiology* 2002; 96: 1004–1017
- 32 *Yusof F, Raymond G, Sahai AV.* Endoscopist administered propofol for upper-GI EUS is safe and effective: a prospective study in 500 patients. *Gastrointest Endosc* 2004; 60: 356–360
- 33 *Deenadayalu VP, Eid EF, Goff JS et al.* Non-anesthesiologist administered propofol sedation for endoscopic procedures: a worldwide safety review. *Gastrointest Endosc* 2008; 67: AB107
- 34 *Faigel DO, Baron TH, Goldstein JL et al.* Guidelines for the use of deep sedation and anesthesia for GI endoscopy. *Gastrointest Endosc* 2002; 5: 613–617
- 35 *Nelson DB, Barkun AN, Block KP et al.* Propofol use during gastrointestinal endoscopy. *Gastrointest Endosc* 2001; 7: 876–879
- 36 *Qadeer MA, Vargo JJ, Dumot JA et al.* Capnographic monitoring of respiratory activity improves safety of sedation for endoscopic cholangiopancreatography and ultrasonography. *Gastroenterology* 2009; 136: 1568–1576
- 37 *van Loon K, van Rheineck Leyssius AAT, van Zaane B et al.* Capnography during deep sedation with propofol by non-anesthesiologists: a randomized controlled trial. *Anesth Analg* 2014; 119: 49–55
- 38 *Lera dos Santos ME, Maluf-Filho F, Chaves DM et al.* Deep sedation during gastrointestinal endoscopy: propofol-fentanyl and midazolam-fentanyl regimens. *World J Gastroenterol* 2013; 19: 3439–344