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Original Article

Safety of propofol/midazolam sedation for upper gastrointestinal endoscopy in patients with co-morbidities

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Abstract: Propofol sedation has been increasingly applied in upper gastrointestinal (GI) endoscopy, but its application in patients with co-morbidities needs deep investigation. The aim of the present study was to explore the safety of propofol/midazolam sedation for upper gastrointestinal endoscopy in patients with co-morbidities. Collected data from 96,583 patients who underwent sedative upper GI endoscopy with propofol and midazolam were analyzed. Saturation of peripheral oxygen, blood pressure, and pulse rate were monitored, and patient discomfort, adverse events, drug dosages, and recovery time were recorded. The occurrence rates of hypoxemia, hypotension, hypertension, tachycardia, bradycardia, and arrhythmia were 0.888%, 0.243%, 0.019%, 0.277%, 0.286%, and 0.006%, respectively. Reductions in blood pressure and pulse rate were transient, requiring no treatment, and values returned to normal rapidly after endoscopic procedures. The overall rate of adverse events and that of hypoxemia were associated with age, weight, alcohol consumption, smoking, American Society of Anesthesiology (ASA) physical status, co-morbidities and sedation method. These rates were higher in patients with cardiovascular, respiratory, or hepatic disease, sleep apnea, or severe anemia than in patients without co-morbidities ($P < 0.005$), and the rates were significantly higher with continuous sedation than with stepwise sedation ($P < 0.005$). The administration of propofol combined with midazolam for upper GI endoscopy is practicable and safe, but patients with cardiovascular, respiratory, or hepatic disease, sleep apnea, or severe anemia are more likely to experience decreased SpO_2. Stepwise sedation can reduce the drug dosage, incidence of hypoxemia and overall rate of adverse events.

Keywords: Apper gastrointestinal endoscopy, sedation, propofol, midazolam, adverse event

Introduction

Upper gastrointestinal (GI) endoscopy is important for the reliable diagnosis of upper GI diseases. Due to practitioners' inadequate experience with the application of sedation technology during endoscopy in past decades, patients have typically undergone routine endoscopic procedures without a sedative, and have received only local pharyngeal anesthesia with lidocaine before endosco [1, 2]. However, this technique can have various adverse effects, including fear, nausea and vomiting, tachycardia, hypertension, angina, myocardial infarction, arrhythmia, and even cardiopulmonary arrest and death [3-5]. Moreover, the risk of adverse effects is greater in patients with co-morbidities [6, 7]. These issues render patients reluctant to undergo endoscopy, delaying the diagnosis and treatment of alimentary system diseases.

In recent years, the sedative endoscopic technique has become a popular option for patients and gastroenterologists [8, 9]. However, the use of sedatives during endoscopy remains controversial due to safety concerns. For example, Agostoni et al reported that the endoscopic procedures performed at the S. Raffaele Hospital (Milan, Italy) between October 2001 and December 2009 led to 3 deaths in 17,999 patients (mortality rate = 0.017%) [10]. We took the lead in using sedatives during endoscopic procedures in China in 1999 [11]. In this study, we collected data from 96,583 patients who

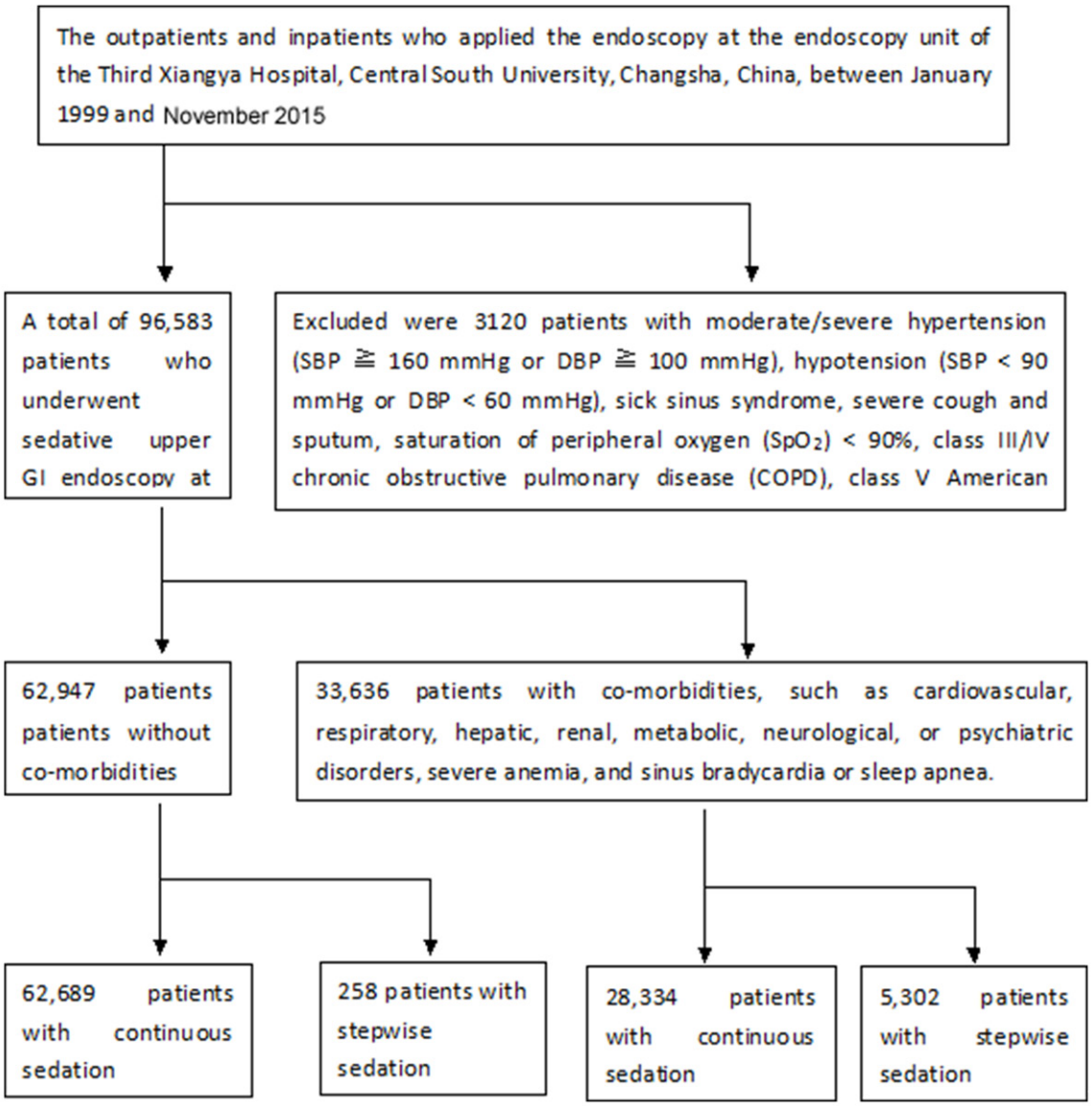

Figure 1. Flowchart of the inclusion and exclusion of the studied patients. The patients were included and exclude in this study according to the standard and procedure.

underwent sedative upper GI endoscopy with propofol and midazolam, and analyzed the safety of this sedation technique in patients with co-morbidities.

Materials and methods

Patients

A database of outpatients and inpatients who applied the sedative upper GI endoscopy at the endoscopy unit of the Third Xiangya Hospital, Central South University, Changsha, China, between January 1999 and November 2015 was recorded for the study. A part of patients (n = 3120) were excluded and did not undergo the sedative endoscopy. The exclusion criteria included moderate/severe hypertension (SBP ≥ 160 mmHg or DBP ≥ 100 mmHg), hypotension (SBP < 90 mmHg or DBP < 60 mmHg), sick sinus syndrome, severe cough and sputum, saturation of peripheral oxygen (SpO_2) < 90%, class III/IV chronic obstructive pulmonary disease (COPD), class V American Society of Anesthesiology (ASA) physical status, or allergy to the sedatives. A total of 96,583 patients underwent the sedative upper GI endoscopy, including 62,947 patients without co-morbidities and 33,636 patients with co-morbidities,

Table 1. Demographic and clinical characteristics of the study population

Parameter	Patients without co-morbidities (*n* = 62,947)	Patients with co-morbidities (*n* = 33,636)	*P* value
Sex (male/female)	34,411/28,536	20,182/13,454	0.082
Age [years; mean ± SD (range)]	44.6 ± 4.6 (2-88)	52.7 ± 4.9 (8-98)	0.543
ASA classification			0.001
I	62,947	1392	
II	0	26,293	
III	0	3644	
IV	0	2307	
Co-morbidities	0	33,636	0.000
Cardiovascular disease[a]	0	10,186	
Respiratory disease[b]	0	2886	
Hepatic disease[c]	0	3764	
Renal disease[d]	0	241	
Metabolic disease[e]	0	3452	
Neurological/psychiatric disease[f]	0	235	
Severe anemia (Hb < 60 g/L)	0	1625	
Sinus bradycardia[g]	0	5594	
Sleep apnea	0	5653	
Major endoscopic findings[h]			0.001
Normal gastric mucosa	226	68	
Acute gastritis	45	18	
Chronic gastritis	42,623	22,959	
Gastric ulcer	5864	2751	
Duodenal ulcer	4365	3366	
Gastroduodenal ulcer	402	211	
Gastric cancer	385	140	
Gastric polyp	4436	2258	
Esophageal cancer	341	175	
Esophagitis	3612	1344	
Esophageal/gastric varices	604	316	
Esophageal/gastric foreign bodies	19	17	
Duodenal carcinoma	4	3	
Gastric calculus	21	10	
Endoscopic diagnosis	61,005	32,173	
Endoscopic therapy	1942	1463	

[a]Hypertension (controlled preoperative blood pressure < 160/100 mmHg), coronary heart disease, rheumatic heart disease, dilated cardiomyopathy, New York Heart Association (NYHA) functional classification 1-2, and cardiac arrhythmia (ventricular extrasystole, atrial fibrillation). [b]Chronic bronchitis, chronic obstructive pulmonary disease, cor pulmonale (NYHA 1-2), bronchial asthma (remission stage), pulmonary tuberculosis, and lung cancer. [c]Cirrhosis, hepatic carcinoma, and chronic hepatitis; grading of liver (Child-Pugh): A (*n* = 2080), B (*n* = 1620), C (*n* = 64). [d]Chronic nephritis and chronic renal insufficiency. [e]Diabetes mellitus and hyperthyroidism. [f]Cerebral infarction, Parkinson's disease, epilepsy, and schizophrenia. [g]Sick sinus syndrome was excluded by atropine test in patients with sinus bradycardia. [h]e.g. variceal ligation, stiffening agent injection, electric coagulation of polyps/malignant tumor, mucosal resection, foreign body extraction, esophageal stenting. Diagnoses of conditions indicating endoscopy and co-morbidities were made according to the 8th edition of the Cecil Essentials of Medicine.

such as cardiovascular, respiratory, hepatic, renal, metabolic, neurological or psychiatric disorders, severe anemia, and sinus bradycardia or sleep apnea. Diagnoses of conditions indicating endoscopy and co-morbidities were made according to the 8th edition of the Cecil Essentials of Medicine [12]. Before endoscopic procedures, all participants provided written informed consent. **Figure 1** shows the flowchart of the patients. **Table 1** provides the sociode-

Table 2. Adverse events occurring in the study population

Adverse event	Patients without co-morbidities (*n* = 62,947)	Patients with co-morbidities (*n* = 33,636)	Risk Ratio*	*P* value
Hypoxemia (SpO_2 < 90%)	25 (0.040)	833 (2.477)[a]	62	0.013
SpO_2 80-89%	20 (0.032)	378 (1.124)[a]	35	
SpO_2 60-79%	5 (0.008)	381 (1.133)[a]	142	
SpO_2 40-59%	0	46 (0.137)[a]	86	
SpO_2 < 40%	0	28 (0.083)[a]	52	
Hypotension	42 (0.067)	193 (0.574)[a]	9	0.056
Hypertension	7 (0.011)	11 (0.033)[b]	3	
Tachycardia (> 100 bpm)	99 (0.157)	169 (0.502)[a]	3	0.044
Bradycardia (< 60 bpm)	118 (0.187)	158 (0.470)[a]	3	
Arrhythmia	0	6 (1.018)[a]	11	
Other adverse events				0.253
Extrapyramidal reaction	5 (0.008)	7 (0.021)	3	
Drug allergy	3 (0.005)	4 (0.012)	2	
Hiccups	8 (0.013)	10 (0.030)	2	
Somnolence	156 (0.248)	408 (1.213)[a]	5	
Dizziness	104 (0.165)	284 (0.844)[a]	5	
Cardiac arrest	0	1 (0.003)	2	
Hemorrhage	12 (0.019)	18 (0.054)[a]	3	
Perforation	0	0		
Death	0	0		
Overall rate of adverse events	579 (0.920)	2102 (6.249)[a]		

Data are presented as *n* (%). SpO_2 = saturation of peripheral oxygen. Hypoxemia: SpO_2 < 90% for ≥ 15 s; Hypotension: SBP < 90 mmHg or DBP < 60 mmHg. Moderate/severe hypertension: SBP ≥ 160 mmHg or DBP ≥ 100 mmHg. *The risk ratio is defined as the ratio of adverse event percentage in patients with co-morbidities to that in patients without co-morbidities. For certain adverse event, if no case of appears in patients without co-morbidities, we give number "1" to it for the calculation for comparison. [a]*P* < 0.005, [b]*P* < 0.05 *vs* patients without co-morbidities.

mographic and clinical characteristics of the study population, and the co-morbidities are defined in the footnote. The experiment was approved by the Medical Ethics Council of the Third Xiangya Hospital of Central South University. All participants signed informed consent after told study details.

Administration of sedation

The gastroenterologists among us with specific expertise in GI endoscopy performed all the endoscopic procedures. All patients were given lidocaine *via* throat spray before the endoscopic procedures, and received nasal oxygen insufflation at a rate of 2 L/min during endoscopy. Continuous sedation was given to 90,923 patients, initially by an intravenous injection of midazolam (technical concentration of 5 g/L diluted to 0.25 g/L with normal saline), then placing a mouthpiece in the patient's mouth, and next by an intravenous injection of propofol (technical concentration of 10 g/L diluted to 5 g/L with normal saline) at 1.0 mg/kg/min until the Ramsay Sedation Scale score reached 5-6 so that the endoscopic procedure was carried out. Stepwise sedation was given to 5,615 patients because of cough, phlegm, sleep apnea or above 70 years old, by following steps. Step 1: Initial administration of an intravenous injection of midazolam at 0.015 mg/kg (with a maximum dose of 1.0 mg). The Ramsay Sedation Scale score here was 1, and after 3-5 min, a mouthpiece was placed in the patient's mouth for the start of step 2. Step 2: Administration of 15-40 mg propofol *via* intravenous injection until the Ramsay Sedation Scale score was 2-3. Then the endoscope was passed through the patient's throat. Step 3: Administration of an additional intravenous injection of propofol at 1.0 mg/kg/min until the Ramsay Sedation Scale score was 5-6 (when retardation or loss of eyelash reflex was achieved) [13, 14]. At this point, the endoscopic procedure was carried

out. If necessary, propofol was administered again to prevent the patient from experiencing discomfort during long-lasting endoscopic procedures.

Collecting of data

We recorded each patient's age, sex, COPD and ASA classifications, SpO_2, blood pressure, pulse rate, adverse events, midazolam and propofol dosages, and recovery time (interval between the termination of propofol injection and the patient's ability to open his/her eyes at the doctor's prompting and answer questions). The SpO_2, blood pressure, and pulse rate of all patients were continuously monitored using a multifunctional monitor (Dinamap Pro 1000; GE Medical Systems Co., Ltd., Wuxi, China).

Statistical analysis

Data are presented as means ± standard deviations. Statistical analyses were performed using SPSS software (version 17.0 for Windows; SPSS Inc., Chicago, IL, USA). Measurements were compared between patients with and without co-morbidities, using the two-sample *t*-test for normally distributed variables and the Mann-Whitney test for non-normally distributed variables. Quantitative data were expressed as *n* (%) and compared using the χ^2 test. A two-sided *P* value < 0.05 was considered to indicate statistical significance.

Results

Overview of endoscopic procedure

The average SpO_2, systolic blood pressure, diastolic blood pressure, and pulse rate decreased immediately after propofol administration during endoscopic procedures ($P < 0.001$) with the reductions ranging from 0-92.9%, 4.4-18.9%, 2.5-19.7%, and 0-16.9%, respectively. The reductions in blood pressure and pulse rate were transient, and values returned to normal rapidly after the endoscopic procedures.

Adverse events

Table 2 lists adverse events occurring in association with procedures performed in patients with and without co-morbidities. The overall rate of adverse events in patients with co-morbidities was significantly higher than in those without co-morbidities (6.249% *vs* 0.920%, $P < 0.005$), and that also was significantly higher in patients with continuous sedation than in those with stepwise sedation (2.817% *vs* 2.120%, $P < 0.005$). From the risk ratio column, we can see that hypoxemia (SpO_2 60-79%) is the most possible adverse event in patients with co-morbidities after the propofol/midazolam sedation, and next are arrhythmia, hypotension, somnolence and dizziness.

Hypoxemi

Hypoxemia (SpO_2 < 90% for ≥ 15 s) occurred in 0.888% of patients. The occurrence of hypoxemia was significantly higher in patients with than in those without co-morbidities (2.477% *vs* 0.040%, $P < 0.005$), and that also was significantly higher in patients with continuous sedation than in those with stepwise sedation (0.905% *vs* 0.623%, $P < 0.05$). In 781 patients who experienced slight hypoxemia (SpO_2 ≥ 60%), SpO_2 quickly returned to normal after the endoscopist held the mandible with two hands, patted the patient on the back, and increased oxygen flow through the nasal catheter; endoscopic procedures were completed in all of these patients. In 74 patients who developed severe hypoxemia (SpO_2 < 60%), including three patients with SpO_2 values of 3-5%, SpO_2 returned to normal after the endoscopist removed the endoscope, held the mandible with two hands, pressed the chest, suctioned sputum, administered oxygen through a mask, and intravenously injected the benzodiazepine antagonist flumazenil (0.5 mg). After these patients awakened, endoscopic procedures were restarted and completed with no obvious patient discomfort.

Hypotension and hypertension

The occurrence rates of hypotension (SBP < 90 mmHg or DBP < 60 mmHg) and moderate/severe hypertension (SBP ≥ 160 mmHg or DBP ≥ 100 mmHg) were 0.243% and 0.019%, respectively. These rates were significantly higher in patients with than in those without co-morbidities (0.574% vs 0.067% and 0.033% vs 0.011%, respectively, P < 0.005 or P < 0.05).

Tachycardia, bradycardia, and arrhythmia

Patients' pulse rates declined slightly (by 1-15 bpm), did not change, or increased slightly (by

Table 3. Clinical parameters of patients in whom serious adverse events occurred

	n	All adverse events	Hypoxemia	Hypotension
Age (years)				
≤ 14	523	16 (3.059)	3 (0.574)	0
15-44	49,282	1190 (2.415)	266 (0.540)	118 (0.239)
45-64	35,602	897 (2.520)	225 (0.574)	85 (0.239)
65-74	10,205	514 (5.037)[a]	326 (3.195)[a]	29 (0.284)
≥ 75	971	64 (6.591)[a]	38 (3.913)[a]	3 (0.309)
P		0.000	0.000	0.697
Sex				
Male	54,593	1498 (2.744)	491 (0.899)	133 (0.244)
Female	41,990	1153 (2.746)	367 (0.874)	102 (0.243)
P		0.985	0.677	0.982
Weight				
Normal	95,427	2638 (2.764)	830 (0.870)	232 (0.243)
Underweight	384	12 (3.125)	4 (1.042)	1 (0.260)
Obese	772	31 (4.016)[b]	24 (3.109)[a]	2 (0.259)
P		0.099	0.000	0.676
Alcohol consumption				
No	84,052	2235 (2.659)	708 (0.842)	205 (0.244)
Yes	12,531	446 (3.559)[a]	150 (1.197)[a]	30 (0.239)
P		0.000	0.000	0.924
Smoking				
No	80,575	1951 (2.421)	570 (0.707)	197 (0.244)
Yes	16,008	730 (4.560)[a]	288 (1.799)[a]	38 (0.237)
P		0.000	0.000	0.868
ASA classification				
I-II	90,632	2378 (2.624)	772 (0.852)	211 (0.233)
III-IV	5951	303 (5.092)[a]	86 (1.415)[a]	24 (0.403)
P		0.000	0.000	0.010
Patients without co-morbidities	62,947	579 (0.920)	25 (0.040)	151 (0.240)
Patients with co-morbidities	33,636	2102 (6.249)[a]	833 (2.477)[a]	84 (0.250)
P		0.000	0.000	0.767
Cardiovascular disease	10,186	1007 (9.886)[a]	274 (2.769)[a]	25 (0.245)
Respiratory disease	2886	348 (12.058)[a]	197 (6.826)[a]	7 (0.243)
Hepatic disease	3764	114 (3.029)[a]	58 (1.541)[a]	9 (0.239)
Renal disease	241	4 (1.660)	0	1 (0.415)
Metabolic disease	3452	38 (1.100)	3 (0.087)	8 (0.232)
Neurological/psychiatric disease	235	3 (1.277)	0	1 (0.426)
Severe anemia (Hb < 60 g/L)	1623	66 (4.067)[a]	45 (2.773)[a]	4 (0.246)
Sleep apnea	5653	464 (8.208)[a]	251 (4.440)[a]	15 (0.265)
Sinus bradycardia	5596	58 (1.036)	5 (0.089)	14 (0.250)
P		0.000	0.000	0.971
Patients with stepwise sedation	5660	120 (2.120)	35 (0.618)	13 (0.230)
Patients with continuous sedation	90,923	2561 (2.817)[a]	823 (0.905)[b]	222 (0.244)
P		0.002	0.026	0.830
Endoscopic diagnosis	93,178	2562 (2.750)	820 (0.880)	230 (0.247)
Endoscopic therapy	3405	89 (2.614)	38 (1.116)	5 (0.147)
P		0.634	0.146	0.245

Data are presented as *n* (% in each corresponding index group). [a]*P* < 0.005, [b]*P* < 0.05 *vs* 15-44 for age, normal for weight, no alcohol consumption, non-smoking, ASA classification I-II, without co-morbidities, and with stepwise sedation, respectively.

Table 4. Propofol dosage of patients with different co-morbidities (mean ± SD)

	n	Propofol dosage (mg)	*P* value
Common patients (without co-morbidities)	62,947	77.9 ± 18.1	
Patients with cardiovascular disease	10186	75.9 ± 18.2	0.063
Patients with respiratory disease	2886	66.7 ± 22.3	0.008
Patients with hepatic disease	3764	76.3 ± 22.8	0.052
Patients with renal disease	241	76.6 ± 22.9	0.068
Patients with metabolic disease	3452	75.9 ± 21.8	0.074
Patients with nervous or psychiatric disease	235	77.9 ± 23.4	0.089
Patients with serious anaemia	1625	55.7 ± 15.8	0.009
Patients with snoring disease	5653	65.5 ± 21.0	0.007
Patients with sinus bradycardia	5594	75.6 ± 18.5	0.056

SD, standard deviation; *P* value *vs* common patients.

1-10 bpm) during the procedure. The occurrence rates of tachycardia (> 100 bpm), bradycardia (< 60 bpm), and arrhythmia in all patients were 0.277%, 0.286%, and 0.006%, respectively; these rates in patients with co-morbidities were significantly higher than in those without co-morbidities (P < 0.005).

Other adverse events

During propofol injection, 12 patients exhibited extrapyramidal signs (abnormal involuntary limb movements, opisthotonus), which disappeared after 30-60 s. Propofol induced facial erythema and rash in 7 patients, which quickly disappeared after intravenous administration of dexamethasone (5 mg). Eighteen patients developed hiccups, which disappeared after the endoscopic procedures. Five hundred and sixty-four (0.584%) and 388 (0.402%) patients experienced somnolence and dizziness, respectively, which disappeared within 10-50 min after completion of the endoscopic procedures; these effects occurred significantly more possibly in patients with than without co-morbidities (P < 0.005). One outpatient with dilated cardiomyopathy had a cardiac arrest 2 min after endoscopy and was hospitalized after resuscitation. This patient was discharged from our hospital after 1 week and had no sequela. Thirty patients had hemorrhage after biopsies and stopped bleeding by spraying norepinephrine. The hemorrhage rate in patients with co-morbidities was significantly higher than in those without co-morbidities (P < 0.005). No gastrointestinal perforation or even death occurred in the patients of the study population.

The overall rate of adverse events and that of hypoxemia were associated with age, ASA physical status, co-morbidities and sedation method. These rates were higher in patients with cardiovascular, respiratory or hepatic disease, sleep apnea, or severe anemia than in patients without co-morbidities (all *P* < 0.005), and those also were significantly higher in patients with continuous sedation than in those with stepwise sedation (*P* < 0.005 or *P* < 0.05, **Table 3**).

Recovery time

The mean recovery time was 4.8 ± 1.3 (range, 2.0-21.0) min. Average recovery times in patients with and without co-morbidities were 4.4 ± 0.9 (range, 2.0-12.0) and 5.5 ± 1.0 (range, 3.0-21.0) min, respectively. Recovery times were significantly longer in patients with than in those without co-morbidities (*P* < 0.005). All patients were fully conscious and able to answer questions accurately within 21 min after endoscopy. They were able to walk normally when they left the endoscopy unit 30-60 min after endoscopy.

Drug dosage

The mean midazolam and propofol dosages were 1.15 ± 0.58 (range, 0.3-2.0) and 76.5 ± 20.8 (range, 12.0-240.0) mg, respectively. Individual differences in propofol dosage showed no evident linear correlation with weight (r = 0.068, P > 0.05), but were associated with sex, age (P < 0.05). Propofol dosage in common patients without co-morbidities was 77.8 ± 18.4 mg. And that in patients with cardiovascular, hepatic, renal, metabolic, neurologic or psychiatric diseases and sinus bradycardia had no significant difference with that in common patients, whereas propofol dosage in patients

with respiratory disease, snoring disease and serious anemia was lower than that in common patients without co-morbidities (**Table 4**). Propofol dosage in patients with stepwise sedation was significantly lower than that in patients with continuous sedation (68.9 ± 10.2 mg and 75.7 ± 9.8 mg, respectively, $P < 0.05$).

Discussion

Many patients with co-morbidities do not undergo endoscopic procedures due to patients' and gastroenterologists' concerns about associated risks. The results of this study indicate that sedative endoscopic procedures can be completed successfully in patients with cardiovascular, respiratory, hepatic, metabolic, neurological, or psychiatric diseases, and sinus bradycardia, and sleep apnea. Patients and gastroenterologists have gradually accepted the sedative endoscopic technique. This method reduces the range of contraindications in upper GI endoscopy, contributing to its wide use for the diagnosis and treatment of alimentary system diseases.

Midazolam and propofol are generally used in sedative endoscopic procedures [15, 16]. However, selection of the most suitable and safest drug(s) for special patient groups, such as elderly individuals and patients with co-morbidities, is an important issue that must be addressed [17, 18]. At hypnotic concentrations, propofol is a potent airway reflex depressant [19]. Patients with cardiovascular, respiratory, or hepatic disease, sleep apnea, or severe anemia are more likely to experience decreased SpO_2 during sedated endoscopy. These conditions are commonly associated with a higher risk of adverse events during GI endoscopy. For patients with cough, phlegm, and sleep apnea, or above 70 years old, we recently designed a stepwise sedation method involving three-stage administration of propofol combined with midazolam to gradually approach the sedation depth. This method reduced the propofol dosage, as well as the incidence of hypoxemia and the overall rate of adverse events. It was shown to be safer than the continuous sedation method in elderly patients with mild or moderate COPD during upper GI endoscopy [20]. With the in-depth study of the sedative regimen in respect of various physiological parameters, this will contribute to the wider use of upper GI endoscopy in diagnosis and treatment of alimentary system diseases [21, 22].

In conclusion, the findings of this study showed that the use of propofol combined with midazolam for upper GI endoscopy is practicable and safe. However, patients with cardiovascular, respiratory, or hepatic disease, sleep apnea, or severe anemia are more likely to experience decreased SpO_2. The stepwise sedation method can reduce the drug dosage, incidence of hypoxemia and overall rate of adverse events.

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Disclosure of conflict of interest

None.

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References

[1] Orel R, Brecelj J, Dias JA, Romano C, Barros F, Thomson M, Vandenplas Y. Review on sedation for gastrointestinal tract endoscopy in children by non-anesthesiologists. World J Gastrointest Endosc 2015; 7: 895-911.

[2] Nkuize M, De Wit S, Muls V, Pirenne C, Buset M. The role of upper gastrointestinal endoscopy in the era of modern antiretroviral therapy. Eur J Gastroenterol Hepatol 2015; 27: 1459-1465.

[3] Izanloo A, Fathi M, Izanloo S, Vosooghinia H, Hashemian A, Sadrzadeh SM, Ghaffarzadehgan K. Efficacy of conversational hypnosis and propofol in reducing adverse effects of endoscopy. Anesth Pain Med 2015; 5: e27695.

[4] Elmunzer BJ. Increasing the impact of randomized, controlled trials in gastrointestinal endoscopy. Gastroenterology 2015; 149: 521-525.

[5] Effenberger M, Steinle H, Offner FA, Vogel W, Millonig G. Holes in gastric mucosa in upper

gastrointestinal endoscopy. Eur J Gastroenterol Hepatol 2014; 26: 676-678.
[6] Romagnuolo J, Cotton PB, Eisen G, Vargo J, Petersen BT. Identifying and reporting risk factors for adverse events in endoscopy: cardiopulmonary events (Part 1). Gastrointest Endosc 2011; 73: 579-585.
[7] Jałocha L, Wojtuń S, Gil J. Incidence and prevention methods of complications of gastrointestinal endoscopy procedures. Pol Merkur Lekarski 2007; 22: 495-498.
[8] Correia LM, Bonilha DQ, Gomes GF, Brito JR, Nakao FS, Lenz L, Rohr MR, Ferrari AP, Libera ED. Sedation during upper GI endoscopy in cirrhotic outpatients: a randomized, controlled trial comparing propofol and fentanyl with midazolam and fentanyl. Gastrointest Endosc 2011; 73: 45-51.
[9] Ferreira AO, Torres J, Dinis-Ribeiro M, Cravo M. Endoscopic sedation and monitoring practices in portugal: a nationwide web-based survey. Eur J Gastroenterol Hepatol 2015; 27: 265-270.
[10] Agostoni M, Fanti L, Gemma M, Pasculli N, Beretta L, Testoni PA. Adverse events during monitored anesthesia care for GI endoscopy: an 8-year experience. Gastrointest Endosc 2011; 74: 266-275.
[11] Wang F, Shen SR, Xiao DH, Xu CX, Tang WL. Sedation, analgesia, and cardiorespiratory function in colonoscopy using midazolam combined with fentanyl or propofol. Int J Colorectal Dis 2011; 26: 703-708.
[12] Baysal B, Kayar Y, Danalıoğlu A, Özkan T, Kayar NB, Ünver N, Bozkurt S, İnce AT. The importance of upper gastrointestinal endoscopy in morbidly obese patients. Turk J Gastroenterol 2015; 26: 228-231.
[13] Lucendo AJ, Arias Á, González-Castillo S, Angueira T, Guagnozzi D, Fernández-Fuente M, Serrano-Valverde M, Sánchez-Cazalilla M, Chumillas O, Fernández-Ordóñez M, Tenías JM. Same-day bidirectional endoscopy with non-anesthesiologist administration of propofol: safety and cost-effectiveness compared with separated exams. Eur J Gastroenterol Hepatol 2014; 26: 301-308.
[14] Kawano S, Okada H, Iwamuro M, Kouno Y, Miura K, Inokuchi T, Kanzaki H, Hori K, Harada K, Hiraoka S, Kawahara Y, Yamamoto K. An effective and safe sedation technique combining target-controlled infusion pump with propofol, intra venous pentazocine, and bispectral index monitoring for peroral double-balloon endoscopy. Digestion 2015; 91: 112-116.
[15] Licker M, Diaper J, Tschopp JM. Propofol: is it really worse than midazolam in medical thoracoscopy? Respiration 2015; 89: 436.
[16] Kiriyama S, Naitoh H, Kuwano H. Propofol sedation during endoscopic treatment for early gastric cancer compared to midazolam. World J Gastroenterol 2014; 20: 11985-11990.
[17] Kerker A, Hardt C, Schlief HE, Dumoulin FL. Combined sedation with midazolam/propofol for gastrointestinal endoscopy in elderly patients. BMC Gastroenterol 2011; 10: 11.
[18] Haq MM, Faisal N, Khalil A, Haqqi SA, Shaikh H, Arain N. Midazolam for sedation during diagnostic or therapeutic upper gastrointestinal endoscopy in cirrhotic patients. Eur J Gastroenterol Hepatol 2012; 24: 1214-1218.
[19] Ludtke KA, Stanley KS, Yount NL, Gerkin RD. Retrospective review of critically ill patients experiencing alcohol withdrawal: dexmedetomidine versus propofol and/or lorazepam continuous infusions. Hosp Pharm 2015; 50: 208-213.
[20] Xu CX, Chen X, Jia Y, Xiao DH, Zou HF, Guo Q, Wang F, Wang XY, Shen SR, Tong LL, Cao K, Liu XM. Stepwise sedation for elderly patients with mild/moderate COPD during upper gastrointestinal endoscopy. World J Gastroenterol 2013; 19: 4791-4798.
[21] Tanaka N, Horiuchi A, Nakayama Y, Katsuyama Y, Isobe M, Aoyama T, Tanaka E, Ohmori S. Safety and effectiveness of low-dose propofol sedation during and after esophagogastroduodenoscopy in child A and B cirrhotic patients. Dig Dis Sci 2013; 58: 1383-1389.
[22] Kwon JS, Kim ES, Cho KB, Park KS, Park WY, Lee JE, Kim TY, Jang BK, Chung WJ, Hwang JS. Incidence of propofol injection pain and effect of lidocaine pretreatment during upper gastrointestinal endoscopy. Dig Dis Sci 2012; 57: 1291-7.