

Factors Affecting Recovery Time after Sedation for Upper Gastrointestinal Endoscopy

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The purpose of this study was to investigate factors affecting recovery time after sedation for upper gastrointestinal endoscopy. The study population included 1310 patients in the national gastric cancer screening program who received sedation for upper gastrointestinal endoscopy from April 15, 2015 to December 31, 2018. Multivariate regression analysis was performed to identify factors related to recovery time. The mean recovery time after examination was 51.2 minutes (SD=13.3). Patients with a history of hypertension had a recovery time 2.59 minutes shorter than that of patients without hypertension ($p=0.006$, Bonferroni-corrected $p=0.108$). Patients with a history of stroke had a recovery time 9.41 minutes longer than that of patients without stroke ($p=0.007$, Bonferroni-corrected $p=0.124$). Patients who received 3 mg midazolam had a recovery time 2.99 minutes longer than that of patients received 2 mg ($p=0.001$, Bonferroni-corrected $p=0.010$), and patients who received less than 6 cc of propofol had a recovery time 2.90 minutes longer than those that of patients received 7-12 cc of propofol ($p<0.001$, Bonferroni-corrected $p=0.005$). These results suggest that receiving high doses of midazolam and having a history of stroke are associated with longer recovery times. Patients meeting these criteria should be managed carefully after sedation for upper gastrointestinal endoscopy.

Key Words: *Conscious Sedation; Endoscopy; Gastrointestinal; Midazolam*

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INTRODUCTION

Gastrointestinal endoscopy (GIE) is a diagnostic tool used for direct observation of the gastric mucosa. It is a highly sensitive test that is essential to diagnosing gastrointestinal diseases.¹ GIE is increasingly being used because of government support for cancer screening and growing interest in preventive medicine.²

Sedation is used for GIE to reduce patient's anxiety and discomfort while increasing patient satisfaction. Sedation also minimizes the risk of patient injury during GIE and provides ideal working conditions for the endoscopist, thereby increasing patient satisfaction with the procedure.³⁻⁵ As a result of these advantages, the frequency with which sedation is used for GIE is gradually increasing worldwide and also in Korea.⁵⁻⁸ In the United States, most GIEs are performed under sedation to control pain and reduce an-

xiety.^{4,9}

Sedation can be classified into four levels: minimal sedation (anxiolysis), conscious sedation, deep sedation, and general anesthesia.¹⁰ When sedating a patient for endoscopy, the aim is moderate sedation.^{11,12} However, the level of patient consciousness may vary by operator and patient because the depth of sedation depends on the quantity of sedatives used and the patient's response.^{11,13}

It is very important to maintain an appropriate level of sedation.¹⁴ If sedation is too light, the patient may make unconscious movements and make the exam difficult for the endoscopist. If sedation is too deep, respiratory distress, hypotension, or other adverse events can occur.¹⁵ Since sedation for GIE reduces the patient's level of consciousness, a recovery period is required.¹⁶⁻¹⁸ It is important to prevent these adverse events and provide a safe examination for patients. Also, it is necessary to shorten

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the length of stay in the recovery room by reducing the recovery time to increase economic efficiency.

The identification of factors related to recovery time after sedation can help reduce adverse effects, ensure patient safety during GIE and increase economic efficiency.

Some studies have suggested that age, pulmonary function, alcohol intake, and gender are the factors most related to recovery time after sedation.¹⁹⁻²¹ However, most previous studies have focused on evaluating sedative drugs rather than identifying factors related to recovery time. The aim of this study is to investigate the factors affecting recovery time after sedation for GIE in order to manage patients safely and provide adequate assistance during the recovery period.

MATERIALS AND METHODS

1. Study population

In total, 1409 patients were sedated for GIE during gastric cancer screenings by the National Health Insurance Service at Chonnam National University Bitgoeul Hospital from April 15, 2015 to December 31, 2018. Of them, 1310 were included in the final study analysis; the other 99 patients were excluded for the following reasons: not having a general checkup (66 patients); having incomplete medical records (17 patients); receiving a single drug except midazolam or propofol (10 patients); or using antagonists for changes in condition during sedation or for other reasons (6 patients). This study's protocol was approved by the Institutional Review Board of Chonnam National University Hospital (IRB No. CNUH-2019-233). The requirement to obtain participant consent was waived because of the retrospective nature of the study.

2. Data collection

Data was collected using electronic medical records. We recorded the following data for each patient: gender, age, body mass index (BMI), smoking status, alcohol intake, physical activity, medical history, liver function, kidney function, and anemia. BMI was defined as weight (kg) divided by height squared (m^2), and obesity was defined as a BMI of $25 \text{ kg}/m^2$ or more. Smoking status, alcohol intake, and physical activity were recorded as binary variables (yes/no). We also recorded history of stroke, heart disease (myocardial infarction, angina pectoris), hypertension, diabetes, and history of sedation. History of hypertension was defined as "yes" if the patient had been diagnosed previously based on health checkup questionnaire. Liver function was considered abnormal when aspartate amino transferase (AST) was higher than 40 U/L or alanine amino transferase (ALT) was higher than 40 U/L. Anemia was defined as a hemoglobin level below 13 g/dL in men and 12 g/dL in women. Kidney function was evaluated using an estimated glomerular filtration rate (eGFR), which was calculated with the Modification of Diet in Renal Disease (MDRD) formula. Patients with a GFR $<60 \text{ mL}/\text{min}/1.73 \text{ m}^2$ for 3 months are defined as having chronic kidney disease

(CKD). Examination time was defined as the time from the start of sedation to the end of the examination.

3. Measurement of recovery time after examination

Recovery time was defined as the time from the removal of the endoscopic device at the end of the examination, to the time of the patient's departure from the recovery room. The criteria for exiting the recovery room were based on the Modified Aldrete Score. This measure assessed recovery from anesthesia using objective information about the patient's physical condition. The higher the score, the better the recovery. Five items are used to evaluate of recovery: reflex ability, oxygen saturation, breathing, circulation, and consciousness. Patients can be given a maximum of two points per item. Patients included in this study were permitted to leave when they had reached a score of 10 points (the highest possible score). A recovery score of 10 means that fully recovered, and able to move all limbs spontaneously, breathe deeply, maintain a blood pressure within $\pm 20\%$ of their blood pressure before sedation, and maintain oxygen saturation of 92% or greater in atmosphere.

4. Statistical analysis

Multivariate linear regression analysis was performed to evaluate factors related to recovery time after GIE.

TABLE 1. General characteristics of study participants according to the gender

	Men	Women	Total
N	468 (35.7)	842 (64.3)	1310 (100.0)
Age	57.3 \pm 10.4	56.9 \pm 10.1	57.1 \pm 10.2
Obese (BMI \geq 25kg/m ²)	202 (43.2)	285 (33.8)	487 (37.2)
Current smoking	119 (25.4)	14 (1.7)	133 (10.2)
Alcohol intake	245 (52.4)	136 (16.2)	381 (29.1)
Physical activity	207 (44.2)	338 (40.1)	545 (41.6)
History of hypertension	132 (28.2)	201 (23.9)	333 (25.4)
History of diabetes mellitus	82 (17.5)	90 (10.7)	172 (13.1)
History of stroke	10 (2.1)	5 (0.6)	15 (1.1)
History of ischemic heart disease	24 (5.1)	35 (4.2)	59 (4.5)
Elevated liver function ¹	101 (21.6)	84 (10.0)	185 (14.1)
Anemia ²	25 (5.3)	92 (10.9)	117 (8.9)
Chronic kidney disease ³	36 (7.7)	51 (6.1)	87 (6.6)
History of sedation	443 (94.7)	790 (93.8)	1233 (94.1)
Midazolam			
Low ($\leq 2 \text{ mg}$)	151 (32.3)	505 (60.0)	656 (50.1)
High (3 mg)	317 (67.7)	337 (40.0)	654 (49.9)
Propofol			
Low ($\leq 6 \text{ cc}$)	179 (38.2)	423 (50.2)	602 (46.0)
Moderate (7-12 cc)	277 (59.2)	404 (48.0)	681 (52.0)
High ($\geq 13 \text{ cc}$)	12 (2.6)	15 (1.8)	27 (2.1)
Recovery time, minutes	51.6 \pm 13.3	50.9 \pm 13.2	51.2 \pm 13.3
Examination time, minutes	9.0 \pm 3.2	8.4 \pm 2.8	8.6 \pm 2.9

Values are mean (SD) or number (%).

BMI: body mass index. ¹AST or ALT $>40 \text{ U}/\text{L}$, ²Hemoglobin men $<13 \text{ g}/\text{dL}$, women $<12 \text{ g}/\text{dL}$, ³MDRD e-GFR $\leq 60 \text{ mL}/\text{min}/1.73 \text{ m}^2$.

Independent variables included age, gender, obesity, smoking, alcohol intake, physical activity, hypertension, diabetes, stroke, ischemic heart disease, liver function, anemia, chronic kidney disease, history of sedation, amount of midazolam and propofol, and examination time.

Patient groups were divided based on the dose of midazolam and propofol: 3 mg vs. ≤ 2 mg (midazolam), ≤ 6 cc vs. 7-12 cc vs. ≥ 13 cc (propofol). In addition, the Bonferroni-corrected p-value was presented to account for multiple comparison in the multivariate linear regression. Statistical analyses were performed using STATA/SE 15.0 (StataCorp, College Station, TX, USA).

RESULTS

1. Patient characteristics

In total, 1310 patients were included in the analyses. Table 1 lists their characteristics by gender. The proportion of women was high, with 842 females (64.3 %) versus 468 males (35.7%). The mean age was 57.1 years; (men: 57.3 years; women: 56.9 years). After sedation for GIE, the mean recovery time was 51.2 ± 13.3 minutes (men: 51.6 ± 13.3 minutes; women: 50.9 ± 13.3 minutes) (Fig. 1). Recovery time for patients with a history of hypertension was 2.59 minutes shorter than that of patients without hypertension ($p=0.006$, Bonferroni-corrected $p=0.108$) and patients with a history of stroke had a recovery time 9.41 minutes longer than that of patients without stroke ($p=0.007$, Bonferroni-corrected $p=0.124$) (Table 2).

2. Sedative dose and recovery time

Recovery time for patients receiving a higher dose of midazolam (3 mg) was 2.99 minutes longer than recovery time for patients receiving a lower dose of midazolam (≤ 2 mg) ($p=0.001$, Bonferroni-corrected $p=0.010$). Patients who received less than 6 cc propofol had a recovery time 2.90 minutes longer recovery time than that of those who received 7-12 cc propofol ($p<0.001$, Bonferroni-corrected $p=0.005$). Patients who received more than 13 cc propofol had a recov-

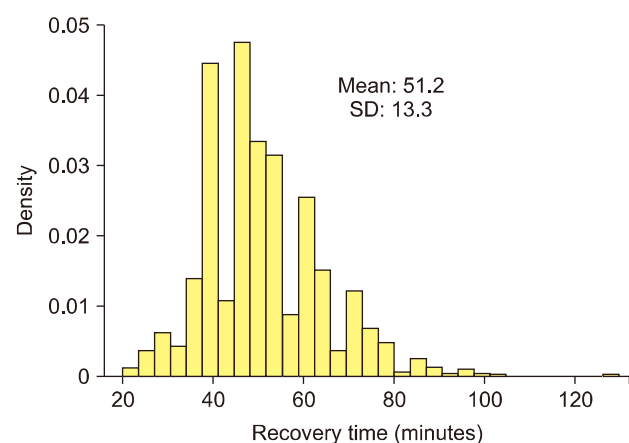


FIG. 1. Histogram of recovery time (minutes) after sedation gastroscopy.

ery time 1.86 minutes longer than that of those who received 7-12 cc propofol ($p=0.477$, Bonferroni-corrected $p=1.000$) (Table 2).

3. Factors related to recovery time

Patient characteristics and sedative dose were investigated and analyzed. Patients with a history of hypertension had a recovery time 2.59 minutes shorter than that of patients without hypertension ($p=0.006$, Bonferroni-corrected $p=0.108$). Patients with a history of stroke had a recovery time 9.41 minutes longer than that of patients without a history of stroke ($p=0.007$, Bonferroni-corrected $p=0.124$) (Table 2). Patients receiving a higher dose of midazolam (3 mg) had a recovery time 2.99 minutes longer than that of patients receiving a lower dose of midazolam (≤ 2 mg) ($p=0.001$, Bonferroni-corrected $p=0.010$). Patients who received less than 6 cc propofol had a recovery time 2.90 minutes longer than that of those who received 7-12 cc propofol ($p<0.001$, Bonferroni-corrected $p=0.005$).

This analysis revealed that a history of hypertension and stroke history had a tendency to be related to recovery time. However, there was no statistical significance in multiple comparisons of the multivariate linear regression. Dose of midazolam and propofol are factors related to recovery time.

DISCUSSION

The purpose of this study was to identify factors related to recovery time after sedation for GIE in patients in the national gastric cancer screening by the National Health Insurance Service. Two factors had a tendency to affect recovery time after sedation for GIE: history of hypertension and history of stroke. Dose of sedative also affected recovery time after sedation for GIE with statistical significance. Patients who had a history of hypertension ($p=0.006$, Bonferroni-corrected $p=0.108$) had shorter recovery times. Patients who had a history of stroke ($p=0.007$, Bonferroni-corrected $p=0.124$) or received high doses of midazolam (3 mg vs. ≤ 2 mg, $p=0.001$, Bonferroni-corrected $p=0.010$) had longer recovery times.

A previous study involving 103 patients used a stepwise regression analysis to identify factors affecting recovery. It found that recovery time was longer for patients with poor pulmonary function, and that alcohol intake was associated with shorter recovery time.²⁰ In an Israeli study of 405 people, age was the only factor affecting recovery time. The authors reported that age accounted for approximately 2% of the variation in recovery time.¹⁹ Another study related to prolonged recovery time included 31,442 patients and found that women had longer recovery times.²¹

In the present study, however, alcohol intake, age, and gender were not related to recovery time after sedation.

Previous studies have not found an association between recovery time and a history of hypertension or stroke.¹⁹⁻²¹ In our study population, recovery time after sedation for upper GIE was 2.59 minutes shorter in patients with a his-

TABLE 2. Factors affecting recovery time (minutes) after sedation gastroscopy by the multivariate linear regression analysis

	Regression coefficient (95% CI)	p-value	Bonferroni-corrected p-value
Age (one year)	0.05 (−0.05-0.14)	0.345	1.000
Gender (women vs men)	−0.54 (−2.33-1.25)	0.557	1.000
Obese (BMI \geq 25 kg/m ² vs BMI $<$ 25 kg/m ²)	1.22 (−0.36-2.79)	0.130	1.000
Current smoking (yes vs no)	−0.37 (−3.00-2.24)	0.780	1.000
Alcohol intake (yes vs no)	−1.04 (−2.80-0.72)	0.247	1.000
Physical activity (yes vs no)	−0.77 (−2.24-0.70)	0.36	1.000
History of hypertension (yes vs no)	−2.59 (−4.44−0.74)	0.006	0.108
History of diabetes mellitus (yes vs no)	0.50 (−1.76-2.77)	0.662	1.000
History of stroke (yes vs no)	9.41 (2.59-16.22)	0.007	0.124
History of ischemic heart disease (yes vs no)	1.85 (−1.66-5.37)	0.302	1.000
Elevated liver function ¹ (yes vs no)	−0.13 (−2.25-1.99)	0.905	1.000
Anemia ² (yes vs no)	0.30 (−2.26-2.86)	0.820	1.000
Chronic kidney disease ³ (yes vs no)	−0.06 (−3.12-2.99)	0.967	1.000
History of sedation (yes vs no)	2.65 (−0.39-5.68)	0.087	1.000
Midazolam (3 mg vs \leq 2 mg)	2.99 (1.30-4.68)	0.001	0.010
Propofol			
\leq 6 cc vs 7-12 cc	2.90 (1.35-4.45)	$<$ 0.001	0.005
\geq 13 cc vs 7-12 cc	1.86 (−3.27-7.00)	0.477	1.000
Examination time (one minute)	−0.186 (−0.431-0.06)	0.136	1.000

BMI: body mass index.

¹AST or ALT $>$ 40 U/L, ²Hemoglobin men $<$ 13 g/dL, women $<$ 12 g/dL, ³MDRD e-GFR \leq 60 mL/min/1.73 m².

tory of hypertension (p=0.006, Bonferroni-corrected p=0.108) and 9.41 minutes longer in patients with a history of stroke (p=0.007, Bonferroni-corrected p=0.124). However, because we considered only history of hypertension and did not assess the use of hypertension medications, a more detailed analysis of the relationship between hypertension and recovery time could not be conducted.

Furthermore, in the present study, higher doses of midazolam (3 mg) were associated with longer recovery times compared with lower doses of midazolam (\leq 2 mg) (p=0.001, Bonferroni-corrected p=0.010). This is consistent with the findings of a previous study reporting that patients who received higher doses of sedative needed more recovery time.²²

However, patients who received less propofol (\leq 6 cc) had a recovery time 2.90 minutes longer than that of those who received 7-12 cc propofol (p $<$ 0.001, Bonferroni-corrected p=0.005). Patients who received 7-12cc propofol had generally been given additional propofol because the initial level of sedation was unsatisfactory. Therefore, it is possible that propofol was not an effective sedative in the group that received high doses of propofol. Recovery time tended to be longer with higher doses of propofol, although the difference was not significant (\geq 13 cc, p=0.477, Bonferroni-corrected p=1.000). This finding suggests that recovery time increases at a certain dosage of propofol, even when it is used in patients in whom propofol tends to be ineffective.

The mean recovery time after sedation in our study was 51.2 minutes. Recovery time after sedation for GIE is generally considered to be 30 minutes or more, because serious

side effects tend to occur within 25 minutes of the last administration of sedative drugs.^{17,22}

Unlike previous studies evaluating sedative drugs, the present study investigated factors related to recovery time after sedation for GIE and identified factors associated with long recovery times. However, the study had some limitations. First, investigation of the relationship between short recovery times and a history of hypertension was limited by our inability to include information on hypertension medication. The biological mechanism of the association between hypertension and recovery time is uncertain, and further studies are needed. Second, previous studies have found a relationship between alcohol intake and short recovery time.²⁰ Our study included patient alcohol intake as a binary variable (yes/no). Patients' level of alcohol intake was not analyzed because the data was not available. Further studies of the relationship between alcohol intake and recovery time are needed.

Overall, we found that factors related to recovery time related factors after sedation for upper GIE included having a history of stroke or hypertension and receiving a high dose of midazolam. Patients meeting these criteria should be carefully managed. To respond effectively to dangerous situations and avoid complications, factors relevant to recovery time after sedation for GIE should be identified before the procedure is performed. Safe and appropriated patient management is required after endoscopic examination to ensure proper recovery.

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CONFLICT OF INTEREST STATEMENT

None declared.

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