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# Patient satisfaction after endoscopic submucosal dissection under propofol-based sedation: a small premedication makes all the difference

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**Abstract**
*Background* Ideal sedation for endoscopic submucosal dissection (ESD) aims to satisfy both the endoscopist and patient. However, previous studies show that a satisfactory procedure for the endoscopist does not equal higher patient satisfaction. This study attempted to find a sedation protocol that is able to increase patient satisfaction during propofol-based sedation by adding low-dose midazolam as premedication.
*Methods* Seventy-two adult patients were randomly allocated to receive either 0.02 mg/kg midazolam (Midazolam Group) or placebo (Control Group) as premedication before ESD. Sedation was done by targeting Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale of 3 or 4 with continuous propofol infusion and bolus doses of fentanyl. Satisfaction scores of the endoscopists and patients, and whether the patient was willing to receive the same sedation method in the future was assessed. Interim analysis was done after enrollment of 50 % of patients.
*Results* This study was prematurely terminated when interim analysis showed that patients willing to receive the same sedation method in the future were significantly lower in the Control Group compared to the Midazolam Group ($P = 0.001$). There was no difference in sedation time, procedure and recovery time, drug requirements and adverse events between the two groups. Endoscopist and overall patient satisfaction scores, patient pain scores and degree of recall were also similar between groups.
*Conclusions* A small dose of midazolam given as premedication before propofol-based sedation is able to reduce patient reluctance to repeat the same procedure in the future, without affecting procedural performance, recovery time or endoscopist satisfaction.

**Keywords** Endoscopy · Gastrointestinal · Midazolam · Satisfaction · Sedation · Conscious

The search for the ideal sedation regimen for interventional gastrointestinal (GI) procedures has been an ongoing mission for the past several decades. While the need for sedation during brief, diagnostic procedures may depend on cultural, economic and legislative factors, it is generally accepted that invasive interventional endoscopy procedures should be performed under proper sedation and analgesia [1]. A nonoperative approach for the treatment of early gastric cancer [2] endoscopic submucosal dissection (ESD) is commonly performed interventional procedure which is now accepted as standard care for removal of GI epithelial lesions [3]. Being technically demanding and invasive,

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ESD usually takes a substantial amount of time and also causes significant pain and discomfort in the patient [3]. Sedation and analgesia is considered an essential component of a successful ESD procedure [1], and many clinical studies have been undertaken to find a better sedation protocol for ESD.

As a high-volume center for ESDs, many interdepartmental efforts have been made at our hospital in order to find an ideal sedation regimen for this procedure. We found in our recent series of studies [4–6] that continuous propofol infusion combined with adequate pain control by an opioid was an appropriate sedation regimen for ESD in terms of endoscopist satisfaction, events interfering with the procedure and recovery times. However, in our most recent randomized controlled study, patient satisfaction scores were significantly lower with continuous propofol infusion and opioid injections done by an anesthesiologist, when compared to the conventional method of intermittent midazolam, propofol and meperidine injections done by an endoscopist. Moreover, this result was contradictory to the satisfaction scores of the endoscopists and procedural stability [6]. We found it interesting that a stable, satisfactory procedure in the eyes of the endoscopist did not necessarily translate to patient satisfaction, and hypothesized that a low dose of midazolam as premedication before ESD may enhance patient satisfaction without affecting endoscopic performance with propofol-based sedation.

## Materials and methods

### Patients and study design

Patients diagnosed with early gastric cancer or adenoma and scheduled for ESD between September 2014 and December 2015 were included in this prospective trial. Enrolled patients were American Society of Anesthesiologists (ASA) physical status I–III, Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1. Exclusion criteria included history of subtotal gastrectomy, gastrotomy or previous ESDs, known drug allergies, patients with three or more synchronous lesions and those that received sedation for other procedures within 24 h prior to ESD. The study protocol was approved by the Institutional Review Board and Hospital Research Ethics Committee of Severance Hospital (Ref: 4-2014-0310), and registered at http://clinicaltrials.gov (Ref: NCT 02504164). Written informed consent was obtained from all patients.

Enrolled patients were allocated to either the Midazolam Group or the Control Group in a 1:1 ratio by using a computer-generated random number table with sealed envelopes. Patients of the Midazolam Group received midazolam (Midazolam, Bukwang Pharm. Co. Ltd., Seoul, Korea) 0.02 mg/kg and those of the Control Group received placebo (saline) intravenously as premedication just before the procedure. The study drugs were prepared in a 5-mL syringe at fixed volumes of 3 mL in unmarked syringes by a nurse that was not involved in the study. Patients, endoscopists and attending anesthesiologists were blinded to group assignment until discharge.

ESD procedures of this study were performed by four attending gastroenterologists, and sedation was provided by board certified anesthesiologists that were qualified for procedural sedation. The targeted depth of sedation was Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale (Table 1) 3 or 4 in all patients [7]. Patients were given initial bolus doses of 1 μg/kg of fentanyl (Fentanyl®, HANA Pharm. Co. Ltd., Seoul, Korea) and 0.5 mg/kg of propofol (Pofol, Dong Kook Pharmaceutical Co. Ltd., Seoul, Korea), followed by continuous infusion of propofol at 2 mg/kg/h by using an automated pump (Terufusion® Syringe Pump TE-331, Terumo Corporation, Tokyo, Japan). Patients presenting with insufficient sedation (MOAA/S score 5 or 6) were given 0.25 mg/kg propofol as a bolus, followed by an increase in infusion rate by 0.5 mg/kg/h to achieve deeper sedation. Patients at targeted depth of sedation but showing signs of discomfort or pain were given 0.5 μg/kg of fentanyl for additional analgesia, but not at intervals shorter than 10 min. Propofol infusion rates were decreased by 0.5 mg/kg/h when the patient's mean blood pressure (MBP) fell below 60 mmHg or decreased by more than 20 % from baseline, or when desaturation was observed.

### Patient monitoring

ESDs were performed at an endoscopy room equipped for advanced cardiac life support and used exclusively for upper gastrointestinal endoscopic procedures. Upon arrival at the endoscopy room, 2 L/min oxygen via a nasal prong was supplied and monitoring devices including noninvasive blood pressure, pulse oximetry ($SpO_2$), electrocardiography and respiratory activity via thoracic leads were applied to all patients. Patients were transferred to the

**Table 1** Modified observer's assessment of alertness/sedation scale

| Responsiveness | Score |
|---|---|
| Agitated | 6 |
| Responds readily to name spoken in normal tone (alert) | 5 |
| Lethargic response to name spoken in normal tone | 4 |
| Responds only after name is called loudly and/or repeatedly | 3 |
| Responds only after mild prodding or shaking | 2 |
| Does not respond to mild prodding or shaking | 1 |
| Does not respond to deep stimulus | 0 |

endoscopy recovery unit at the end of ESD and continuously monitored with noninvasive blood pressure, $SpO_2$ and electrocardiography until discharge. Full recovery was documented when they reached an Aldrete score of 10 [8] as assessed by dedicated nursing staff.

### Outcome measures, definitions and study endpoints

Lesion characteristics including lesion location and size were assessed, and outcomes and complications of ESD were observed and collected. Sedation-related events such as events interfering with the procedure, respiratory and hemodynamic events were also recorded. Endoscopist satisfaction scores were assessed at the end of the procedure on a verbally administered numerical rating scale (NRS) of 0–10. Patient satisfaction scores were assessed on the morning after the procedure, also on a verbal NRS of 0–10. Pain scores immediately after the procedure were assessed by using the Wong–Baker FACES pain rating scale. Pain scores at time of discharge from the recovery unit and on the morning after the procedure were assessed on a visual analog scale of 0–10, 0 meaning no pain and 10 meaning worst pain imaginable. How much the patient was able to recall of the procedure and whether the patient was willing to undergo another ESD procedure in the future with the same sedation method were also assessed on the morning after the procedure.

Time from marking to complete removal of the tumor was defined as procedure time. Belching, vomiting, spontaneous movement or patients requiring physical restraint due to lack of cooperation were recorded as events interfering with ESD. Apnea or desaturation ($SpO_2 < 90$ % for more than 10 s) requiring either a chin lift or jaw thrust maneuver, increase in $O_2$ flow or assisted mask ventilation were defined as respiratory events. An increase in MBP of more than 20 % from baseline was defined as a hypertensive event, while a drop in mean blood pressure under 60 mmHg or more than 20 % from baseline was defined as a hypotensive event. Heart rate >120 beats/min was noted as tachycardia and <50 beats/min as bradycardia. En bloc resection was defined as removal of the tumor in a single piece and complete resection as tumor-free lateral and vertical margins on histologic examination. When a lesion was removed en bloc with tumor-free margins and fulfilled the criteria of node-negative neoplasms with no lymphovascular infiltration, it was considered curative resection.

The primary endpoint of this study was to compare the satisfaction scores of the patients between the two groups. Satisfaction scores of the endoscopists, patient pain scores, recall of events during ESD and whether the patient was willing to receive the same sedation method for future examinations were assessed as secondary endpoints.

### Statistical analysis

Sample size calculation was performed based on the results of our previous study [6]. On the basis of a mean difference of 0.8 and SD of 1.7 in satisfaction scores of the patients, we calculated that 72 patients in each group, with a total of 144 patients, would be required to test the null hypothesis at a significance of 0.05 with a power of 0.8. A single interim analysis of the overall primary end point was planned after enrollment of 50 % of patients. The significance level of 0.005 was needed to terminate the study after interim analysis, and an alpha of 0.049 would have to be achieved at final analysis should the study continue.

Continuous variables with normal distribution were analyzed with the $t$ test, and categorical variables were analyzed by the Chi-square or Fisher's exact test. All statistical analyses were done with IBM SPSS Statistics 20.0 (IBM Corp., Armonk, NY, USA). $P < 0.05$ was considered as statistically significant.

## Results

The CONSORT flow diagram of this study is shown in Fig. 1. Among the 81 patients that were assessed for eligibility during the study period, 9 patients that did not meet the inclusion criteria were excluded. The remaining 72 patients were randomly assigned to either the Midazolam Group ($n = 36$) or the Control Group ($n = 36$), and none were excluded from analysis. When 36 patients (50 %) in each group completed the study, an interim analysis was performed at a significance level of 0.005.

An interim analysis performed after 50 % of patient enrollment revealed that patient satisfaction scores were similar between the Control Group and the Midazolam Group ($9.0 \pm 1.7$ vs. $9.5 \pm 0.7$, $P = 0.135$), and the predefined criteria for termination was not met. However, it was found that willingness of the patient to receive the same sedation method in the future was unexpectedly lower in the Control Group compared to the Midazolam Group (69.4 % vs. 97.2 %, $P = 0.001$). Due to this finding, the present study was stopped for possible harm in the Control Group after the enrollment of 72 patients.

### Patient characteristics, lesion characteristics and outcomes of ESD

Patient characteristics are shown in Table 2. There were no differences in patient age, sex, body mass index, smoking or snoring history and ASA physical status between the two groups. The numbers of lesions were 39 in both groups, and there was no difference in lesion location or size between

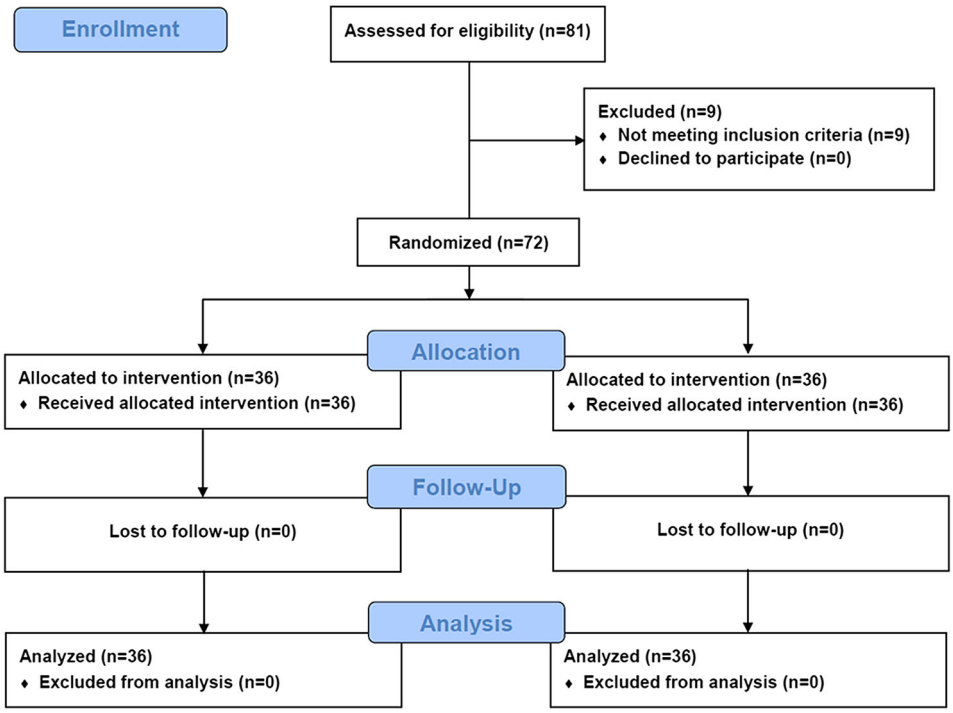


**Fig. 1** CONSORT flowchart of patient sample selection

**Table 2** Patient characteristics

| | Control group ($n = 36$) | Midazolam group ($n = 36$) | $P$ value |
|---|---|---|---|
| Age (years) | 64 (49–77) | 60 (45–78) | 0.097 |
| Male | 24 (66.7) | 26 (72.2) | 0.609 |
| Body mass index (kg/m$^2$) | 24.6 ± 3.2 | 24.3 ± 3.9 | 0.714 |
| Smoking history | | | 0.349 |
| Smoker | 6 (16.7) | 11 (30.6) | |
| Ex-smoker | 10 (27.8) | 7 (19.4) | |
| Nonsmoker | 20 (55.5) | 18 (50.5) | |
| Snoring history | | | 0.230 |
| Yes | 12 (33.3) | 17 (47.2) | |
| No | 24 (66.7) | 19 (52.8) | |
| ASA physical status | | | 0.707 |
| I | 7 (19.4) | 10 (27.8) | |
| II | 20 (55.6) | 18 (50.5) | |
| III | 9 (25.5) | 8 (22.2) | |

Values are mean (range), mean ± SD or n (%) of patients

the two groups. Outcomes and complications of ESD were also comparable between the two groups (Table 3).

## Sedation-related outcomes, drug requirements and adverse events

Table 4 shows data relevant to sedation-related outcomes, drug requirements and adverse events during the procedure. Sedation time, procedure and recovery time were all similar between the two groups. The required doses of propofol and fentanyl for sedation and the number of respiratory and hemodynamic events were also not different between the two groups.

## Satisfaction scores, pain scores, recall of procedure and willingness to receive same sedation method in the future

Endoscopist satisfaction was comparable between groups. Patient satisfaction scores regarding the overall ESD

**Table 3** Lesion characteristics and outcomes of endoscopic submucosal dissection

| | Control group ($n = 36$) | Midazolam group ($n = 36$) | $P$ value |
|---|---|---|---|
| Number of lesions | 39 | 39 | |
| Location of lesions | | | 0.936 |
| Upper third | 5 (12.8) | 4 (10.3) | |
| Middle third | 11 (28.2) | 11 (28.2) | |
| Lower third | 23 (59.0) | 24 (61.5) | |
| Lesion size | | | 0.082 |
| ≤10 mm | 13 (33.3) | 12 (30.8) | |
| 10–20 mm | 21 (53.9) | 14 (35.9) | |
| >20 mm | 5 (12.8) | 13 (33.3) | |
| Outcomes of endoscopic submucosal dissection | | | |
| En bloc resection | 39 (100.0) | 37 (94.9) | 0.152 |
| Complete resection | 37 (94.9) | 36 (92.3) | 0.644 |
| Curative resection | 35 (89.7) | 33 (84.6) | 0.498 |
| Complications of endoscopic submucosal dissection | | | |
| Post-procedural bleeding | 2 (5.1) | 2 (5.1) | 1.000 |
| Perforation | 0 (0.0) | 1 (2.7) | 0.314 |
| Pneumonia | 0 (0.0) | 0 (0.0) | N/A |

Values are $n$ (%) of patients

**Table 4** Sedation-related outcomes, drug requirements and adverse events

| | Control group ($n = 36$) | Midazolam group ($n = 36$) | $P$ value |
|---|---|---|---|
| Sedation time (min) | 48.1 ± 23.3 | 50.9 ± 30.4 | 0.668 |
| Procedure time (min) | 29.7 ± 16.0 | 35.3 ± 25.2 | 0.262 |
| Recovery time (min) | 23.5 ± 4.5 | 23.4 ± 5.4 | 0.924 |
| Drug requirements for sedation | | | |
| Midazolam (mg/kg) | – | 0.02 | N/A |
| Propofol (mg/kg/hr) | 6.3 ± 2.4 | 6.1 ± 1.7 | 0.647 |
| Fentanyl (μg/kg/hr) | 3.1 ± 2.4 | 2.5 ± 1.3 | 0.226 |
| Events interfering with procedure | | | |
| Belching | 14 (38.9) | 7 (19.4) | 0.070 |
| Vomiting | 0 (0.0) | 0 (0.0) | N/A |
| Spontaneous movement | 19 (52.8) | 15 (41.7) | 0.345 |
| Requiring physical restraint | 1 (2.8) | 2 (5.6) | 0.555 |
| Respiratory events | | | |
| Chin lift/jaw thrust maneuver | 5 (13.9) | 3 (8.3) | 0.453 |
| Increase in $O_2$ flow | 3 (8.3) | 2 (5.6) | 0.643 |
| Assisted mask ventilation | 0 (0.0) | 0 (0.0) | N/A |
| Desaturation | 0 (0.0) | 0 (0.0) | N/A |
| Hemodynamic events | | | |
| Hypertension | 10 (27.8) | 9 (25.0) | 0.789 |
| Hypotension | 1 (2.8) | 2 (5.6) | 0.555 |
| Tachycardia | 1 (2.8) | 0 (0.0) | 0.312 |
| Bradycardia | 0 (0.0) | 0 (0.0) | N/A |

Values are mean ± SD or $n$ (%) of patients

procedure as well as pain scores during the study period were also similar between the two groups. With regard to degree of recall during the endoscopic procedure, while the overall number of patients that reported recall of the procedure was not different between groups, 4 patients were able to remember most of the procedure in the Control Group compared to none in the Midazolam Group. The number of patients that were willing to receive the same sedation method for procedures in the future was significantly different between the two groups, with 11 patients refusing in the Control Group compared to only one patient in the Midazolam Group ($P = 0.001$) (Table 5).

## Discussion

The goal of endoscopic sedation needs to be approached from several different aspects, and optimal sedation should be able to allow comfort and satisfaction for both the endoscopist and the patient while preserving the safety of the procedure. The present study was able to suggest an improved sedation protocol employing propofol infusion combined with fentanyl as an analgesic and a small dose of midazolam before the procedure as premedication. This protocol was found to be safe and effective, and also able to significantly increase the number of patients willing to undergo endoscopy with the same sedation method in the future while maintaining high satisfaction of the endoscopists.

Sedatives and sedation protocols have evolved over time; propofol is now preferred over midazolam [9, 10], and the use of meperidine for analgesia is being criticized by many [11–13]. This change in sedatives is mainly due to the increase in sophisticated and interventional procedures and the need for more rapid yet stable endoscopic examinations while maintaining patient satisfaction. When endoscopic sedation by anesthesiologists was first started at our institution, the main drugs used for sedation were propofol combined with fentanyl or remifentanil. Midazolam was removed from the anesthesiologist's sedation protocol based on the logic that propofol would be able to replace its role, as both were sedatives that lacked analgesic properties. Our two earlier retrospective studies were able to confirm two important points regarding sedation for ESD; that continuous propofol infusion is superior to intermittent propofol and midazolam injections for stable sedation and better procedural performance [4]; and that adequate analgesia during sedation with propofol allows a lighter depth of sedation and lower respiratory complications [5]. This resulted in the general consensus that continuous propofol infusion combined with either fentanyl or remifentanil while targeting a sedation depth of MOAA/S scale 3 or 4 should be used when sedation for ESD was done by anaesthesiologists in our institution. While our latter retrospective analysis by Yoo et al. [5] suggested that a MOAA/S scale 5 was also feasible and safe with proper analgesia during ESD, some endoscopists had reservations against the patient being fully alert throughout the procedure. We therefore targeted a sedation depth of MOAA/S scale 3 or 4 during most of our following procedures. While this depth of sedation is within the scope of "moderate sedation," it only includes sedation depths where the patient responds to verbal stimulation but not mild prodding of shaking [14].

**Table 5** Satisfaction scores, pain scores, recall of procedure and willingness to receive same sedation method

| | Control group ($n = 36$) | Midazolam group ($n = 36$) | $P$ value |
|---|---|---|---|
| Endoscopist satisfaction score (NRS 0–10) | 8.5 ± 1.5 | 8.1 ± 1.7 | 0.307 |
| Patient satisfaction score (VAS 0–10) | 9.0 ± 1.7 | 9.5 ± 0.7 | 0.135 |
| Pain score | | | |
| Immediately after procedure[a] | 0.9 ± 1.3 | 1.0 ± 1.3 | 0.700 |
| Discharge from recovery unit (VAS 0–10) | 1.2 ± 2.0 | 1.4 ± 2.0 | 0.552 |
| POD #1 morning (VAS 0–10) | 1.7 ± 1.8 | 1.4 ± 1.7 | 0.503 |
| Recall of events during endoscopic procedure | | | 0.095 |
| No recall of procedure | 30 (83.3 %) | 35 (97.2 %) | |
| Cannot recall most of the procedure | 2 (5.6 %) | 1 (2.8 %) | |
| Can recall most of the procedure | 4 (11.1 %) | 0 (0.0 %) | |
| Willing to receive same sedation method in the future | | | 0.001 |
| Yes | 25 (69.4 %) | 35 (97.2 %) | |
| No | 11 (30.6 %) | 1 (2.8 %) | |

Values are mean ± SD or $n$ (%) of patients

*NRS* numerical rating scale; *VAS* visual analog scale

[a] Measured with Wong–Baker FACES scale (0–5)

Despite the change in choice of sedatives and the increasing popularity of propofol, patient satisfaction was not significantly increased by this new sedation method despite the relatively higher satisfaction levels of the endoscopists [15–17]. These findings were also seen in our recent study, where patient satisfaction scores after ESD did not always correspond to the degree of procedural stability and satisfaction scores of the endoscopists [6]. This aforementioned investigation was performed as an effort to refine our sedation protocol and improve outcomes of ESD, and to ultimately reach an agreement between the anesthesiologists and endoscopists regarding sedation protocol. Continuous propofol and remifentanil infusion by anesthesiologists was compared to intermittent midazolam/propofol injection by endoscopists with sedation depths targeted at MOAA/S score or 3 or 4 in both groups. Interestingly, despite more stable sedation and higher satisfaction of the endoscopists with propofol/remifentanil infusion, patients were significantly more satisfied with intermittent midazolam/propofol injections.

An interesting study done by Delius et al. [18] reported that German endoscopists rated midazolam as insufficient for sedation during endoscopy, with 98 % reporting that they felt that patients experienced pain during endoscopy. A staggering majority of the endoscopists (75 %) of this study reported the need to physically restrain the patient during examination, and 70 % wished to have soundproof examination rooms due to moaning and screaming of the patients. The authors of this study commented that their results were "disillusioning," considering that midazolam is still widely used by many endoscopists as the main sedative around the world. Moreover, despite all the commotion during the procedure, the amnesic qualities of midazolam will leave many patients to feel that all was well during endoscopy. This study shows that an effective sedation regimen should work for both the endoscopist and the patient. When only one side of the party is satisfied, the sedation regimen should be reconsidered. Premedication with orally administered midazolam has been reported to be safe and effective in patients undergoing esophagogastroduodenoscopy (EGD) [19]. Patients that received oral midazolam before EGD were more willing to repeat the procedure compared to those that did not take premedication. This previous study is similar in concept to the present study, and also shows similar results. However, the previous study was performed in patients undergoing diagnostic EGD that lasted less than 5 min and thus was able to sedate patients solely with midazolam. Had this study been performed in patient undergoing procedures such as ESD or endoscopic retrograde cholangiopancreatography (ERCP), the results would not have been as satisfying. Increased consciousness and greater recall is evident in patients that undergo longer procedures and therapeutic procedures compared to shorter diagnostic procedures [20]. In context with these previous studies and our past experience, we added a very small dose of midazolam in a form of premedication in the present study, but not as a main sedative.

The most interesting results of the present study seem to be the contradicting results of patient satisfaction scores and the willingness to repeat the procedure under the same sedation method. While there was no difference in patient satisfaction scores between the two groups, nearly one-third of the patients in the Control Group refused to undergo the same sedation method in the future, compared to only one patient in the Midazolam Group. One would speculate that a satisfied patient would probably be willing to say "yes" to the same procedure afterward. However, this was not the case in the present study, and the results should be carefully interpreted. Considering that the patients enrolled in the present study are those diagnosed with cancer, albeit treatable, the fact that they are able to remove the lesion with an endoscopic procedure rather than abdominal surgery may have played a significant role in the high satisfaction scores in both groups. The satisfaction scores do not refer only to sedation *per se*, but to the overall procedure and its outcome. This was why the present study was prematurely terminated when we found in our interim analysis that an alarming proportion of patients in the Control Group were refusing to undergo future procedures under the same sedation method. While these results should not discredit the previous studies that measured satisfaction levels after ESD on NRS scales, it may shed some light on how future studies should assess patient satisfaction regarding the sedation method itself.

The amnesic effect of midazolam is well known, and it is known to cause anterograde amnesia in a dose-dependent manner in the setting of sedation endoscopy [21]. However, the results of our study cannot be attributed to the amnesic effects of midazolam alone. While the number of patients with no recall of the procedure was slightly higher in the Midazolam Group, and none of the patients in this group reported complete recall of the procedure compared to 4 (11.1 %) in the Control Group, these results were not statistically significant. The small dose of midazolam used in this study seems to have worked synergistically with propofol and fentanyl to enhance hypnotic and sedative effects without delaying recovery or increasing complications, albeit not being large enough to decrease the overall dose of propofol or fentanyl.

The main limitation of the present study is that early termination after interim analysis was done due to an unexpected difference in results that had not been predefined as criteria for stopping. Despite the lack of difference in patient satisfaction scores, we identified the significant difference in "willingness to receive the same sedation

again" between groups as an indicator of potential harm to the patients in the Control Group relative to the Midazolam Group. We feel that the willingness to undergo the same sedation method, rather than overall satisfaction score, may truly reflect the degree of patient comfort during the procedure. A future study comparing patient willingness to undergo the same sedation method for future procedures as primary outcome will be able to further confirm the results of the present study. Secondly, it is unclear whether the positive effect of midazolam premedication is due to its amnesic properties or its synergistic sedative action with propofol. Although there is a trend of less recall of events in the Midazolam Group, the difference was not statistically significant. Moreover, the mechanism by which midazolam is effective is unlikely to be clear-cut, but rather a combination of the two aforementioned mechanisms. Also, whether the relatively small dose of midazolam used in this study will be as effective in other invasive procedures such as colonic ESD or ERCP is not clear. Colonic ESD and ERCP are both complex and painful procedures often requiring greater skill of the endoscopist, and may require a higher dose of midazolam for effective premedication.

As shown in the results of our series of previous studies [4–6] and those of other investigators [22–25], the safety issues of propofol have been largely overcome by efforts made by anesthesiologists and endoscopists alike. As a result, the controversy on whether or not to use propofol for endoscopic sedation seems to have winded down, with clinicians increasingly preferring propofol over other sedatives. We found that adding 0.02 mg/kg of midazolam as premedication safely improves the propofol infusion-based sedation regimen, as shown by the increase in the proportion of patients willing to repeat the sedation method for future endoscopic procedures and no increase in respiratory/cardiovascular events or recovery time. Incorporating a small dose of midazolam as premedication to sedation protocols for GI endoscopy may be an effective method to increase patient comfort without affecting procedural performance or complications.

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**Compliance with ethical standards**

**Disclosures** Drs Seokyung Shin, Chan Hyuk Park, Hyun Ju Kim, Sang Hun Park, Sang Kil Lee and Young Chul Yoo have no conflicts of interest or financial ties to disclose.

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