ORIGINAL ARTICLE - ENDOSCOPY

# Comparison of three sedation models for same-day painless bidirectional endoscopy: A multicenter randomized controlled trial

Yue Sui,* [iD] Xing Chen,*,† Ting Ma,* Junhui Lu,* Tao Xiao,‡ Zhenzhen Wang,§ Qing Wen,§ Guanfeng Wang,§ Hui Jia,¶ Fengzhen Cao,¶ Xiaopeng Wu,** Yiping Zhang,†† Junlian Hao‡‡ and Naping Wang§§

*Shanxi Medical University, †The First Hospital of Shanxi Medical University, ‡Shanxi Cancer Hospital, Taiyuan, §The Second People's Hospital of Datong, ††Datong Shoujia Digestive Disease Hospital, Datong, ¶Erdos Kangning Physical Examination Center, Erdos, **Lvliang Traditional Chinese Medicine Hospital, Lvliang, ‡‡Xiaoyi Traditional Chinese Medicine Hospital, Xiaoyi, §§The First Hospital of Shanxi Medical University, Yuncheng, China

## Abstract

**Background and Aim:** We investigated the most beneficial propofol sedation model for same-day painless bidirectional endoscopy (BDE).
**Methods:** Asymptomatic participants scheduled for same-day painless BDE examination from October 2020 to September 2021 were randomized to three groups: sedated esophagogastroduodenoscopy followed by unsedated colonoscopy (Group A); sedated esophagogastroduodenoscopy followed by sedated colonoscopy (Group B); and sedated esophagogastroduodenoscopy followed by sedated insertion colonoscopy (Group C). Patient discomfort, colonoscopy performance, doses of propofol, cardiovascular stress, anesthesia resuscitation, and sedation-related adverse events were evaluated.
**Results:** A total of 3200 participants were analyzed. Baseline demographics, patient discomfort, cecal intubation rate, adenoma detection rate and sedation-related adverse events were similar in the three groups. Propofol dose was the lowest in Group A $(137.65 \pm 36.865 \text{ mg})$ compared with Group B $(177.71 \pm 40.112 \text{ mg}, P < 0.05)$ and Group C $(161.63 \pm 31.789 \text{ mg}, P < 0.05)$. Decline in vital signs was most obvious in Group B during the procedure $(P < 0.05)$. Recovery time was the shortest in Group A $(5.01 \pm 1.404 \text{ min})$ compared with Group B $(9.51 \pm 2.870 \text{ min}, P < 0.05)$ and Group C $(5.83 \pm 2.594 \text{ min}, P < 0.05)$; discharge time was the shortest in Group A $(3.53 \pm 1.685 \text{ min})$ compared with Group B $(11.29 \pm 5.172 \text{ min}, P < 0.05)$ and Group C $(6.47 \pm 2.338 \text{ min}, P < 0.05)$. Adenomas per positive patient of Group A $(2.29 \pm 1.055)$ and Group C $(2.28 \pm 0.931)$ were more than that in Group B $(2.11 \pm 0.946, P < 0.05)$.
**Conclusions:** Sedated esophagogastroduodenoscopy followed by unsedated colonoscopy is the superior model for same-day painless BDE with the benefits of satisfactory patient comfort, reduced sedation dose, less cardiovascular stress, faster recovery, shorter discharge time and high colonoscopy quality.

## Introduction

The combination of esophagogastroduodenoscopy (EGD) and colonoscopy, which is termed bidirectional endoscopy (BDE), is commonly administered for physical check-ups in China. The benefits of same-day BDE include a shorter hospital stay, reduced medical costs, a reduction of sedation doses and the convenience for patients.[1-6] A national survey showed that the sedation rate for gastrointestinal endoscopy in China was ~50%, and the predicted number of gastroenterological endoscopies in China could reach 51 million by 2030.[7]The dramatic increase in sedated gastroenterological endoscopy is challenging with the shortage of anesthesiologists and anesthesia nurses, and sedation is supposed to

bring patient adequate comfort during the examination as well as rapid recovery and discharge, especially in the COVID-19 era; thus, a safe sedation model with a rapid turnover and discharge time is essential for this high-volume practice to remain efficient.

Propofol is an ideal drug for use in the vast majority of patients who require deep sedation for endoscopic examinations,[8,9] because its unique pharmacokinetic properties make endoscopy almost painless, with a very predictable and rapid recovery process. Propofol has a narrow therapeutic window and no antidote, and higher doses are associated with increased risks of respiratory and circulatory inhibitions, which may lead to adverse events that require cardiopulmonary support.[10,11] Given the

possibility of propofol-induced adverse events, it needs to be clear why we use it and, when doing so, to give no more than necessary. The present study aimed to compare the efficacy, safety and colonoscopy performance of different propofol administration methods to determine the superior model for same-day painless BDE.

## Methods

***Study design.*** This multicenter prospective randomized controlled study was conducted between October 2020 and September 2021 at the following seven hospitals in China: Shanxi Tumor Hospital; The Second People's Hospital of Datong; Datong Shoujia Digestive Disease Hospital; Xiaoyi Traditional Chinese Medicine Hospital; Lvliang Traditional Chinese Medicine Hospital; Erdos Kangning Physical Examination Center and The First Hospital of Shanxi Medical University, Yanhu District Branch. The study was approved by the Chinese Ethics Committee of Registering Clinical Trials (IRB number ChiECRCT20210642) and was registered in the Chinese Clinical Trial Registry (ChiCTR2200056917).

Asymptomatic population aged 35–60 years who were scheduled for same-day painless BDE as part of routine physical examination were included. Written informed consent was obtained from all individuals prior to their inclusion in the study. Eligible participants were randomized to the following three groups with allocation ratio of 1:1:1 using the random number table algorithm made by a third-party statistician with the SPSS software (version 24.0, Inc., Chicago, IL, USA): sedated EGD followed by unsedated colonoscopy (Group A); sedated EGD followed by sedated colonoscopy (Group B); and sedated EGD followed by sedated insertion colonoscopy (Group C). The engaged endoscopists and anesthesiologists were told the allocation results at the beginning of the BDE procedure by assistant nurses. The exclusion criteria were as follows: patients with an American Society of Anesthesiologists (ASA) classification of $\geq 4$; patients with an allergy to propofol; patients without companion; patients with polyposis syndrome; patients with colorectal cancer; patients with poor bowel preparation (Boston Bowel Preparation Scale, BBPS score < 6 points or any segmental score < 2 points); failure to reach the cecum due to bowel obstruction; colonoscope withdrawal time less than 6 min; and patients who refused to participate in the study. Demographic data, including age, sex, height, weight and history of abdominal, or pelvic surgery were recorded. The examinations were performed by experienced endoscopists with an average colonoscope insertion time less than 5 min, and ADR > 40% in the past 3 years. Propofol (AstraZeneca Italy, Caponago, Italy) sedation was administered by experienced anesthesiologists.

***Study procedure.*** Each participant underwent bowel preparation in accordance with the local practices of the hospitals. Dyclonine hydrochloride mucilage (Yangtze River Pharmaceutical Group Co., Ltd. 0.1 g/10 mL) was given 15 min before gastroscopy for oropharyngeal topical anesthesia. No antispasmodic medication was administered before or during the procedure. Before starting the procedure, nasal oxygen was given at a flow rate of 3 L/min. Vital signs were monitored throughout the procedure using standard monitors. All procedures began with the

participants in the left lateral position. Examinations were performed with gastroscopes (GIF-HQ290, GIF-H290Z, GIF-H260; Olympus Co. Ltd, Tokyo, Japan; BL-7000, Fujifilm, Japan) and colonoscopes (CF-HQ290I, CF-H260AI, Olympus, Japan; BL-7000, Fujifilm, Japan). Room air was used for insufflation. All examinations followed the EGD-colonoscopy sequence. Once the EGD was finished, the subsequent colonoscopy was carried out immediately. For induction, a standard premedication of 2 mg/kg of propofol was given. Additional doses of propofol (0.5 mg/kg) were administered as per the requirement according to the changes in vital signs such as deeper in breath, increase of heart rate or even body movement. In Group A, propofol was not administered any more after the EGD examination finished; in Group B, propofol was administered until the whole procedure finished; and in Group C, propofol was not administered any more after colonoscope inserted into the cecum. Cecal intubation was confirmed by the observation of cecal landmarks. Individuals in Group A and Group C underwent dynamic position changes during colonoscope withdrawal as follows: the supine position for the cecum, ascending colon, hepatic flexure (left lateral position when necessary) and transverse colon, the right lateral position (or 30 degrees to the right) for the splenic flexure and descending colon, and the left lateral position for the sigmoid colon and rectum.[12] Individuals in Group B were kept in the left lateral position throughout the procedure. The bowel preparation quality was rated by the endoscopist according to the BBPS. The location, size, and morphology of any polyp found during the procedure were recorded. When a polyp was detected, a biopsy was taken or the polyp was removed and placed in a separate bottle and sent for histopathological examination. No complicated therapy was carried out in outpatient service, such as complex polypectomy for polyps larger than 5 mm in diameter and endoscopic submucosal dissection. The procedure time for EGD and colonoscopy were measured with a stopwatch. During the procedure, blood pressure, heart rate and $SpO_2$ were recorded at three periods: before propofol administration; when the vital sign reached the lowest value; and when the whole examination finished. Individuals were monitored in the recovery unit after the examination and were not discharged until their Aldrete score were 9 or higher.[13] The total dose of propofol, Modified Gloucester Comfort Scale (MGCS) score, recovery time, discharge time and sedation-related adverse events were recorded.

***Definition.*** The MGCS score, as observed by the assistant, was assessed with discomfort scored on a scale of 1–5 (1, no discomfort; 5, extreme discomfort). Scores of 1–3 were considered to indicate comfort, and scores of 4 and 5 were considered to indicate significant discomfort.[14] Adenoma detection rate (ADR) was defined as the proportion of patients with at least one adenoma detected. Adenomas per positive patient (APP) was defined as the average number of adenomas detected in positive patient. Recovery time was defined as the interval between the last time when propofol was administered and the first response after being woken up. Discharge time was defined as the interval between the end of the whole endoscopy procedure and Aldrete score reached 9 or higher.[13]

***Study outcomes.*** The primary outcome was patient comfort. The secondary outcomes were colonoscopy performance,

including the cecal intubation rate (CIR), ADR and APP, total doses of propofol, changes in vital signs, recovery time, discharge time, and sedation-related adverse events.

***Statistical analysis.*** SPSS version 24.0 (SPSS Inc., Chicago, IL, USA) was used for the data analysis. Based on clinical experience, we assume that the patient comfort rate (the proportion of patients with MGCS score of 1–3) in sedated EGD followed by sedated colonoscopy could be 99%, and the rate may be 90% in sedated EGD followed by unsedated colonoscopy. With alpha risk set at 2.5%, a statistical power of 80%, noninferiority margin set at −0.01 and 20% exclusion rate after randomization, 98 subjects in each group are needed, 294 in total.

Exploratory data analysis and Shapiro–Wilk tests were performed to determine the normality of the data distribution. Normally distributed continuous data are expressed as the mean ± standard deviation (SD). Categorical variables are presented as counts and percentages. Continuous variables were compared using Student's $t$ test between groups and by one-way analysis of variance among multiple groups. Comparisons between time-based measurements within each group were performed with repeated-measures analysis of variance. Categorical variables were compared using the Pearson $\chi^2$ test. A probability $P$ value of < 0.05 was considered statistically significant, and all tests were two-sided.

## Results

***Baseline demographic and clinical characteristics.*** A total of 3200 eligible individuals (1067 in Group A, 1067 in Group B and 1066 in Group C) were finally analyzed (Fig. 1). The participants in the three groups were comparable in terms of their demographic and clinical data. As shown in Table 1, there was no significant difference among the three groups in terms of age, sex, body mass index, history of abdominal or pelvic

surgery, EGD examination time, colonoscope insertion time, and colonoscope withdrawal time ($P > 0.05$).

***Patient discomfort.*** The MGCS scores of the three groups are presented in Table 2. In Group A, 944 participants (88.5%) were scored 1 point (no discomfort), 85 participants (8.0%) were scored 2 points (minimal discomfort), and 38 participants (3.5%) scored 3 points (mild discomfort). In Group B and Group C, all participants were scored 1 point. The MGCS of the three groups were all rated as comfortable (scale 1–3). Mild discomfort rarely caused involuntary movements, and abdominal press by an assistant was taken in time when necessary.

***Colonoscopy performance.*** The CIR was 100% in each group. As shown in Table 3, the ADRs of Group A, Group B, and Group C were 46.9% (500/1067), 42.6% (455/1067), and 45.0% (480/1066), respectively. There was no significant difference between the three groups ($\chi^2 = 3.858$, $P > 0.05$). The APPs of Group A, Group B, and Group C were 2.29 ± 1.055, 2.11 ± 0.946, and 2.28 ± 0.931, respectively. The APP of Group B was significantly lower than those of Group A and Group C ($P < 0.05$), and there was no significant difference between Group A and Group C ($P > 0.05$).

***Sedation-related indicators.*** As shown in Table 4, there was no significant difference in systolic blood pressure, diastolic blood pressure, heart rate or SpO$_2$ between the three groups before propofol administration (T$_0$) ($P > 0.05$). The vital signs declined to different degrees during the procedure (T$_1$) in all groups, and the decline was most obvious in Group B ($P < 0.05$). These change episodes were transient, and the patients recovered soon afterward.

As shown in Table 5, the total doses of propofol in Group A, Group B and Group C were 137.65 ± 36.865 mg, 177.71 ± 40.112 mg, and 161.63 ± 31.789 mg, respectively. The
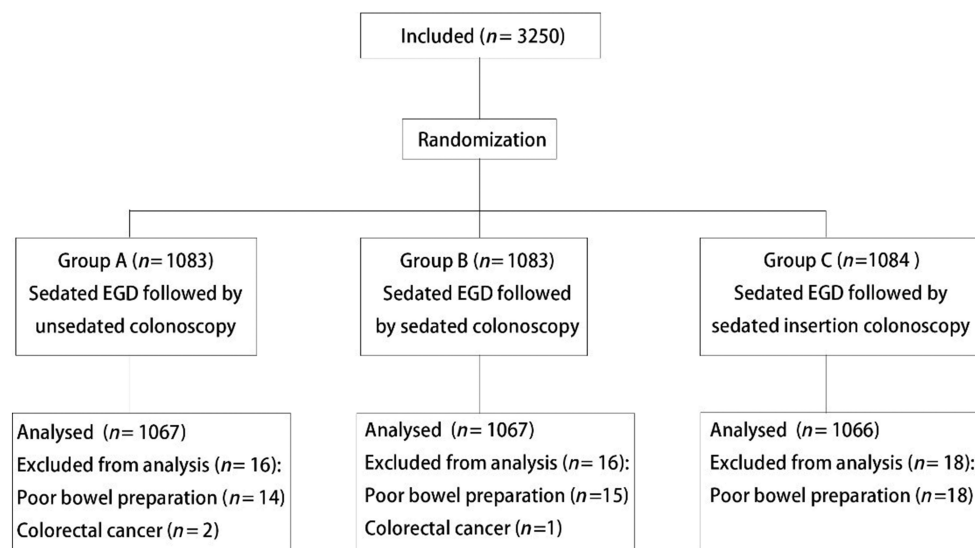


**Figure 1** Flow diagram illustrating the selection of study subjects.

**Table 1** Demographic and clinical data of the three groups

|  | Group A (*n* = 1067) | Group B (*n* = 1067) | Group C (*n* = 1066) | $F/\chi^2$ | *P* |
|---|---|---|---|---|---|
| Male/female | 521/546 | 550/517 | 544/522 | 1.779 | 0.411 |
| Age (years) | 47.49 ± 7.416 | 47.70 ± 7.542 | 47.17 ± 7.376 | 1.343 | 0.261 |
| Body mass index (kg/m$^2$) | 26.43 ± 5.467 | 26.81 ± 5.661 | 26.89 ± 5.971 | 2.006 | 0.135 |
| History of abdominal or pelvic surgery, *n* (%) | 141(13.2) | 135(12.7) | 138(12.9) | 0.150 | 0.928 |
| EGD examination time (s) | 269.33 ± 17.50 | 270.01 ± 17.69 | 269.53 ± 17.48 | 0.423 | 0.655 |
| Colonoscope insertion time (s) | 150.66 ± 17.53 | 151.17 ± 17.44 | 149.98 ± 17.58 | 1.251 | 0.286 |
| Colonoscope withdrawal time (s) | 425.01 ± 52.22 | 425.95 ± 53.67 | 424.67 ± 52.12 | 0.169 | 0.844 |

EGD, esophagogastroduodenoscopy.

**Table 2** Comparison among patient discomfort in the three groups during the examination

|  | Group A (*n* = 1067) | Group B (*n* = 1067) | Group C (*n* = 1066) |
|---|---|---|---|
| MGCS, *n* (%) | | | |
| 1 | 944 (88.5) | 1067 (100) | 1066 (100) |
| 2 | 85 (8.0) | - | - |
| 3 | 38 (3.5) | - | - |
| 4 | - | - | - |
| 5 | - | - | - |

MGCS, Modified Gloucester Comfort Scale; 1, no discomfort; 2, minimal discomfort; 3, mild discomfort; 4, obvious discomfort; 5, extreme discomfort.

**Table 3** Comparison of ADR and APP between three groups

|  | Group A (*n* = 1067) | Group B (*n* = 1067) | Group C (*n* = 1066) | $\chi^2/F$ | *P* |
|---|---|---|---|---|---|
| ADR | 46.9% | 42.6% | 45.0% | 3.858 | 0.145 |
| APP | 2.29 ± 1.055 | 2.11 ± 0.946[a] | 2.28 ± 0.931[b] | 5.059 | 0.006 |

[a]Compared with Group A, $P < 0.05$.
[b]Compared with Group B, $P < 0.05$.
ADR, adenoma detection rate; APP, adenomas per positive patient.

total doses of propofol in Group A was significantly lower than those in Group B and Group C ($P < 0.001$). The recovery time in Group A, Group B, and Group C were 5.01 ± 1.404 min, 9.51 ± 2.870 min, and 5.83 ± 2.594 min, respectively. The recovery time in Group A was significantly shorter than those in Group B and Group C ($P < 0.001$). The discharge time in Group A, Group B, and Group C were 3.53 ± 1.685 min, 11.29 ± 5.172 min, and 6.47 ± 2.338 min, respectively. The discharge time in Group A was significantly shorter than those in Group B and Group C ($P < 0.001$).

As shown in Table 6, sedation-related adverse events were observed in 316 individuals, such as transient apnea (lack of respiratory activity for < 15 s), coughing, and hiccup. The patients recovered soon after instant intervention such as patient stimulation, chin lift, and increasing oxygen supplementation. None of them experienced any severe adverse events such as emergent intubation, unanticipated hospitalization or death. There was no significant difference in the incidence of sedation-related adverse events between the three groups (9.3% *vs* 10.3% *vs* 10.0%, $P > 0.05$).

## Discussion

The benefits of sedatives in transoral endoscopy have been relatively well described in previous studies, such as improving patient receptivity, satisfaction, and examination performance, and it is suggested that upper gastrointestinal endoscopy should be performed under sedation.[11,15,16] Thus, we performed sedated EGD

for all participants in this study. EGD followed by colonoscopy is believed to be the most beneficial sequence for same-day painless BDE as a result of lower sedative doses, less cardiovascular stress, faster recovery, and less discomfort.[1,3,6] The onset of the effect of propofol is 0.5–1 min, the peak effect is 2 min after intravenous injection, and the duration of the effect is 4–8 min.[11,17] Discomfort during colonoscopy varies during the procedure, most often occurring during insertion. In the EGD-colonoscopy sequence with propofol sedation, patients are still under the influence of the initial bolus of propofol at the completion of EGD,[18] which may alleviate the discomfort during colonoscope insertion. Consequently, a smaller or even no additional dose of propofol was needed to relieve the pain during colonoscopy. As shown in the present study, the discomfort scores in the three groups were all classified at the scale of comfortable according to the MGCS.

Besides the quality of the patient experience during and after sedation, the medical costs and recovery unit turnover should also be considered. In the present study, the recovery time and discharge time were both the shortest in the sedated EGD followed by unsedated colonoscopy group, which had the lowest propofol dose. In addition to general flow of an endoscopy unit, rapid recovery has a major impact on patient satisfaction and postprocedure education.

Changing position during colonoscopy is one of the easiest ways to improve colonoscopy quality,[19] which removes the liquid from the area to be observed, places the bowel segment at the highest location in the abdominal cavity, opens the sharp angle at the folds, and improves the luminal distention with a small amount of air insufflation.[20] However, deep-sedated colonoscopy is conducted entirely in the left lateral position because it is difficult to move a deep-sedated patient to change their position, and the supine position during deep sedation may increase respiratory movements, choking rates, and other respiratory problems.[21] Several

**Table 4** Comparison among vital signs in the three groups throughout the examination

| | | $T_0$ | $T_1$ | $T_2$ | F | P |
|---|---|---|---|---|---|---|
| SBP (mmHg) | Group A | 117.12 ± 26.186 | 109.86 ± 21.269 | 120.49 ± 18.881 | 66.202 | < 0.001 |
| | Group B | 115.62 ± 19.9 | 96.81 ± 13.81[a] | 104.52 ± 14.14[a] | 365.314 | < 0.001 |
| | Group C | 117.13 ± 27.915 | 102.94 ± 23.11[ab] | 102.08 ± 24.031[ab] | 125.839 | < 0.001 |
| | F | 1.297 | 115.938 | 282.182 | | |
| | P | 0.274 | < 0.001 | < 0.001 | | |
| DBP (mmHg) | Group A | 69.53 ± 20.592 | 64.98 ± 19.537 | 68.67 ± 16.24 | 17.501 | < 0.001 |
| | Group B | 70.88 ± 13.702 | 54.03 ± 14.354[a] | 66.39 ± 10.516[a] | 507.286 | < 0.001 |
| | Group C | 70.02 ± 17.225 | 60.27 ± 15.676[ab] | 69.67 ± 11.437[b] | 151.654 | < 0.001 |
| | F | 1.631 | 115.872 | 17.864 | | |
| | P | 0.196 | < 0.001 | < 0.001 | | |
| HR (n/min) | Group A | 78.69 ± 13.059 | 72.7 ± 10.119 | 74.7 ± 12.293 | 71.934 | < 0.001 |
| | Group B | 79.26 ± 9.578 | 67.98 ± 9.678[a] | 75.75 ± 9.022[a] | 388.831 | < 0.001 |
| | Group C | 78.68 ± 11.957 | 69.86 ± 12.831[ab] | 76.75 ± 12.335[ab] | 152.847 | < 0.001 |
| | F | 0.874 | 50.015 | 8.712 | | |
| | P | 0.417 | < 0.001 | < 0.001 | | |
| SpO$_2$(%) | Group A | 97.13 ± 2.065 | 93.01 ± 5.747 | 97.6 ± 1.725 | 530.750 | < 0.001 |
| | Group B | 97.14 ± 1.802 | 88.53 ± 6.032[a] | 98.05 ± 1.401[a] | 2133.726 | < 0.001 |
| | Group C | 97.04 ± 2.398 | 91.46 ± 3.999[ab] | 97.55 ± 1.752[b] | 1483.080 | < 0.001 |
| | F | 0.705 | 194.159 | 30.336 | | |
| | P | 0.494 | < 0.001 | < 0.001 | | |

[a]Compared with Group A, $P < 0.05$.
[b]Compared with Group B, $P < 0.05$.
Continuous variables were compared using one-way analysis of variance among multiple groups. Comparisons between time-based measurements within each group were performed with repeated-measures analysis of variance.
SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate. $T_0$, before propofol administration; $T_1$, when the vital sign reached the lowest value; $T_2$, when the whole examination finished.

**Table 5** Comparison of propofol doses, recovery time, and discharge time between the three groups

| | Group A ($n = 1067$) | Group B ($n = 1067$) | Group C ($n = 1066$) | F | P |
|---|---|---|---|---|---|
| Doses of propofol (mg) | 137.65 ± 36.865 | 177.71 ± 40.112[a] | 161.63 ± 31.789[ab] | 326.964 | 0.000 |
| Recovery time (min) | 5.01 ± 1.404 | 9.51 ± 2.870[a] | 5.83 ± 2.594[ab] | 1085.622 | 0.000 |
| Discharge time (min) | 3.53 ± 1.685 | 11.29 ± 5.172[a] | 6.47 ± 2.338[ab] | 1400.152 | 0.000 |

[a]Compared with Group A, $P < 0.05$.
[b]Compared with Group B, $P < 0.05$.

**Table 6** Comparison of sedation-related adverse events between the three groups

| | Group A ($n = 1067$) | Group B ($n = 1067$) | Group C ($n = 1066$) | $\chi^2$ | P |
|---|---|---|---|---|---|
| Total, *n* (%) | 99 (9.3) | 110 (10.3) | 107 (10.0) | 0.685 | 0.710 |
| Transient apnea | 24 (2.2) | 36 (3.4) | 31 (2.9) | 2.466 | 0.291 |
| Coughing | 33 (3.1) | 42 (3.9) | 38 (3.6) | 1.119 | 0.571 |
| Hiccup | 42 (3.9) | 32 (3.0) | 38 (3.6) | 1.407 | 0.495 |

studies demonstrated that the use of sedation during colonoscopy increased the ADR comparing with unsedated colonoscopy, but they did not mention whether dynamic position changes were performed in unsedated colonoscopy,[22–26] which may underestimate the quality of unsedated colonoscopy. As shown in the present study, the ADRs in all three groups were high and did not differ significantly from each other. Our result is in accordance with one research that showed unsedated colonoscopy had a high lesion

detection rate, and the ADR was no lower than that of sedated colonoscopy.[27] However, the ADR only ascertains whether at least one adenoma is identified, while more detected adenomas lead to higher risk stratification and shorter surveillance intervals. Dynamic position change is believed to be associated with more adenomas detected per patient,[20,28–31] which was also verified in our results of APP. The APPs were higher in groups with position changes during withdrawal ($P < 0.05$).

A nationwide population-based study showed that sedation during endoscopy was significantly associated with minor, but not major, cardiocerebrovascular disease adverse events,[32] and no severe adverse events were reported in our study. The major adverse effects of propofol are respiratory depression and hypotension.[17] Intraoperative and postoperative hypotension commonly occur and are associated with organ injury and poor outcomes.[33] The risk factors for anesthesia-related adverse events during endoscopy procedures remain uncertain. Geng *et al*.[34] found that hypoxemia had no relationship with the total dosage of propofol during routine sedation for gastrointestinal endoscopy. A retrospective cohort study showed that higher propofol doses were associated with a higher incidence of arterial hypotension events.[10] Similarly, an exploratory analysis found that longer periods of propofol sedation and larger propofol doses were associated with longer-lasting and more-profound hypotension.[33] In the present study, blood pressure, heart rate, and $SpO_2$ in the majority of the subjects declined to different degrees during the procedure; the decline became obvious with time and an increase in total propofol doses. Individuals undergoing deep-sedated EGD followed by deep-sedated colonoscopy (Group B) received the highest dose of propofol and experienced a greater drop in vital signs than the other two groups ($P < 0.05$). Previous studies demonstrated that hypoxemia is not uncommon (6.8% to 32%) with propofol sedation in gastrointestinal endoscopy examinations.[35–43] The mean $SaO_2$ dropped to $88.53 \pm 6.032\%$ in Group B in the present study, but previous studies mainly focused on the incidence of hypoxemia without reporting the mean value of $SaO_2$ with propofol mono-sedation. Similar with the result in a study conducted by Gustavo Andrade de Paulo *et al*.[41], the mean lowest $SaO_2$ in monitored anesthesia care group was $90.03 \pm 7.37\%$, but fentanyl was used besides propofol on a case-by-case basis. As there is no universally recognized definition of hypoxemia which varied in literature with differences in duration of oxygen desaturation (for $\geq 15$ s; for $> 30$ s; for $\geq 5$ min; for any duration during the endoscopy procedure; duration not mentioned), and oxygen saturation ($< 90\%$; $< 85\%$; $< 92\%$),[35–43] the results of hypoxemia rate were uncomparable.

This is the first multicenter prospective study investigating the optimal model for same-day painless BDE under propofol sedation. Our study was designed with high-quality control by only including the following: experienced endoscopists; high-definition colonoscopes; patients with high bowel preparation quality; endoscopists with a colonoscopy withdrawal time no less than 6 min; and adapted dynamic position changes during withdrawal in unsedated colonoscopy, which are unique in eliminating many of the confounding variables found in prior studies. However, there were also several limitations. First, although the study intended to distinguish tiny difference which could be exaggerated in large outpatient volume between different sedation models and demonstrate a convincing conclusion with large sample size, it might create an exaggerated tendency to reject null hypotheses with clinically negligible differences. Second, the use of dynamic position changes in two of the three study groups might introduced unknown bias. However, position changes were regularly taken in routine colonoscopy without deep sedation and the use of dynamic position change reflects the real-world condition. Third, the endoscopists and patients were not absolutely blinded to the sedation model, which was inevitable considering the study design. Fourth, the procedures were performed by experienced endoscopists, so such a conclusion cannot be applied to trainee endoscopists. But this suggests that endoscopists should improve their insertion skills rather than depend on sedation. Fifth, propofol was used for sedation in this study, and other sedative agents warrant further investigation.

In conclusion, for same-day painless BDE, deep-sedated esophagogastroduodenoscopy followed by unsedated colonoscopy appears to be an effective sedative strategy with the benefits of satisfactory patient comfort, reduced sedation dose, less cardiovascular stress, faster recovery, shorter discharge time and high colonoscopy quality. Tailoring sedation use to achieve comfortable procedures, enhance examination performance, and speed up patient turnover while lowering risks and costs, remains an important area for future research.

## Acknowledgments

## References

1 Cao Y, Yang J, Li J *et al*. Comparison of procedural sequences in same-day painless bidirectional endoscopy: Single-center, prospective, randomized study. *Dig. Endosc.* 2017; **29**: 330–7.

2 Laoveeravat P, Thavaraputta S, Suchartlikitwong S *et al*. Optimal sequences of same-visit bidirectional endoscopy: Systematic review and meta-analysis. *Dig. Endosc.* 2020; **32**: 706–14.

3 Cho JH, Kim JH, Lee YC, Song SY, Lee SK. Comparison of procedural sequences in same-day bidirectional endoscopy without benzodiazepine and propofol sedation: starting at the bottom or the top. *J. Gastroenterol. Hepatol.* 2010; **25**: 899–904.

4 Chen SW, Cheng CL, Liu NJ *et al*. Optimal procedural sequence for same-day bidirectional endoscopy with moderate sedation: A prospective randomized study. *J. Gastroenterol. Hepatol.* 2018; **33**: 689–95.

5 Choi GJ, Oh HC, Seong HK, Kim JW, Ko JS, Kang H. Comparison of procedural sequence in same-day bidirectional endoscopy: a systematic review and meta-analysis. *Korean J. Intern. Med.* 2019; **35**: 331–41.

6 Choi GJ, Oh HC, Seong HK, Kim JW, Ko JS, Kang H. Comparison of procedural sequence in same-day bidirectional endoscopy: a systematic review and meta-analysis. *Korean J. Intern. Med.* 2020; **35**: 331–41.

7 Zhou SJ, Zhu ZY, Dai WB *et al*. National survey on sedation for gastrointestinal endoscopy in 2758 Chinese hospitals. *Br. J. Anaesth.* 2021. https://doi.org/10.1016/j.bja.2021.01.028

8 Dossa F, Megetto O, Yakubu M, Zhang DDQ, Baxter NN. Sedation practices for routine gastrointestinal endoscopy: a systematic review of recommendation. *BMC Gastroenterol.* 2021; **21**: 22.

9  Basavana G. Big Sleep: Beyond Propofol Sedation During GI Endoscopy. *Dig. Dis. Sci.* 2019; **64**: 1–3.

10 Guzzo MEG, Fernandez MS, Novas DS *et al*. Deep sedation using propofol targetcontrolled infusion for gastrointestinal endoscopic procedures: a retrospective cohort study. *BMC Anesthesiol.* 2020; **20**: 195.

11 Liu FK, Wan L, Shao LJZ, Zou Y, Liu SH, Xue FS. Estimation of effective dose of propofol mono-sedation for successful insertion of upper gastrointestinal endoscope in healthy, non-obese Chinese adults. *J Clin Pharm The* 2020; **00**: 1–8.

12 Chen X. *The Importance of Position Change during Withdrawal. In: One Man Method and the Technique for Colonoscope*. Shanghai: Shanghai Science and Technology Press, 2005; 103–5.

13 Robert C, Soulier A, Sciard D *et al*. Cognitive status of patients judged fit for discharge from the post-anaesthesia care unit after general anaesthesia: a randomized comparison between desflurane and propofol. *BMC Anesthesiol.* 2021; **21**: 76.

14 Ball AJ, Rees CJ, Corfe BM, Riley SA. Sedation practice and comfort during colonoscopy: lessons learnt from a national screening programme. *Eur. J. Gastroenterol. Hepatol.* 2015; **27**: 741–6.

15 Gotoda T, Akamatsu T, Abe S *et al. Guidelines for sedation in gastroenterological endoscopy*, second edn. *Dig. Endosc.* 2021; **33**: 21–53. https://doi.org/10.1111/den.13882

16 Chen MJ, Wu W, Pan S, Lin CJ. Sedated gastroscopy improves detection of gastric polyps. *Exp. Ther. Med.* 2018; **16**: 3116–20.

17 Wadhwa V, Issa D, Garg S, Lopez R, Sanaka MR, Vargo JJ. Similar risk of cardiopulmonary adverse events between propofol and traditional anesthesia for gastrointestinal endoscopy: a systematic review and meta-analysis. *Clin Gastroenterol H* 2016. https://doi.org/10.1016/j.cgh.2016.07.013

18 Hsieh YH, Lin HJ, Tseng KC. Which should go first during same-day bidirectional endosocopy with propofol sedation? *J. Gastroenterol. Hepatol.* 2011; **26**: 1559–64.

19 Zhao SB, Wan H, Fu HY *et al*. Quantitative assessment of the effect of position changes during colonoscopy withdrawal. *J. Dig. Dis.* 2016; **17**: 357–65.

20 East JE, Bassett P, Arebi N, Thomas-Gibson S, Guenther T, Saunders BP. Dynamic patient position changes during colonoscope withdrawal increase adenoma detection: a randomized, crossover trial. *Gastrointest. Endosc.* 2011; **73**: 456–63.

21 Allescher HD, Weingart V. Optimizing Screening Colonoscopy: Strategies and Alternatives. *Visc Med* 2019; **35**: 215–25.

22 Tinmouth J, Kennedy EB, Baron D *et al*. colonoscopy quality assurance in ontario: systematic review and clinical practice guideline. *Can. J. Gastroenterol. Hepatol.* 2014; **28**: 251–74.

23 Zhao S, Deng XL, Wang L *et al*. The impact of sedation on quality metrics of colonoscopy: a single-center experience of 48,838 procedures. *Int. J. Colorectal Dis.* 2020; **35**: 1155–61.

24 Khan F, Hur C, Lebwohl B, Krigel A. Unsedated Colonoscopy: Impact on Quality Indicators. *Dig. Dis. Sci.* 2020; **65**: 3116–22.

25 Chen CW, Chiu CT, Su MY *et al*. Factors associated with polyp detection during colonoscopy: A retrospective observational study. *Kaohsiung J. Med. Sci.* 2019; **35**: 572–7.

26 Triantafyllou K, Sioulas AD, Kalli T *et al*. Optimized sedation improves colonoscopy quality long-term. *Gastroenterol. Res. Pract.* 2015. https://doi.org/10.1155/2015/195093

27 Lee T, Rees C, Blanks R *et al*. Colonoscopic factors associated with adenoma detection in a national colorectal cancer screening program. *Endoscopy* 2014; **46**: 203–11.

28 Brand EC, Wallace MB. Strategies to Increase Adenoma Detection Rates. *Curr Treat Options Gastroenterol* 2017; **15**: 184–212.

29 Atkin WS, Valori R, Kuipers EJ *et al*. European guidelines for quality assurance in colorectal cancer screening and diagnosis. First Edition--Colonoscopic surveillance following adenoma removal. *Endoscopy* 2012; **44**: SE151–63.

30 Lee SW, Chang JH, Ji JS *et al*. Effect of Dynamic Position Changes on Adenoma Detection During Colonoscope Withdrawal: A Randomized Controlled Multicenter Trial. *Am. J. Gastroenterol.* 2016; **111**: 63–9.

31 Li P, Ma B, Gong S, Zhang X, Li W. Effect of dynamic position changes during colonoscope withdrawal: a meta-analysis of randomized controlled trials. *Surg. Endosc.* 2020. https://doi.org/10.1007/s00464-020-07483-x

32 Kim SY, Moon CM, Kim MH *et al*. Impacts of age and sedation on cardiocerebrovascular adverse events after diagnostic GI endoscopy: a nationwide population-based study. *Gastrointest. Endosc.* 2020; **92**: 591–602.

33 Sneyd JR, Absalom AR, Barends CRM, Jones JB. Hypotension during propofol sedation for colonoscopy: an exploratory analysis. *Br. J. Anaesth.* 2021. https://doi.org/10.1016/j.bja.2021.10.044

34 Geng WJ, Jia DY, Wang YC *et al*. A prediction model for hypoxemia during routine sedation for gastrointestinal endoscopy. *Clinics* 2018. https://doi.org/10.6061/clinics/2018/e513

35 Cristina LM, Andrés SY, José CCS, Lapuerta JAR, Suárez ABM. Quality of sedation with propofol administered by non-anesthetists in a digestive endoscopy unit the results of a one year experience. *Rev. Esp. Enferm. Dig.* 2018; **110**: 231–6.

36 Beitz A, Riphaus A, Meining A *et al*. Capnographic Monitoring Reduces the Incidence of Arterial Oxygen Desaturation and Hypoxemia During Propofol Sedation for Colonoscopy A Randomized, Controlled Study (ColoCap Study). *Am. J. Gastroenterol.* 2012; **107**: 1205–12.

37 Dhariwal A, Plevris JN, Lo NTC, Finlayson NDC, Heading RC, Hayes PC. Age, anemia, and obesity-associated oxygen desaturation during upper gastrointestinal endoscopy. *Gastrointest. Endosc.* 1992; **38**: 684–8.

38 Friedrich-Rust M, Welte M, Welte C *et al*. Capnographic monitoring of propofol-based sedation during colonoscopy. *Endoscopy* 2014; **46**: 236–44.

39 Riphaus A, Geist C, Schrader K, Martchenko K, Wehrmann T. Intermittent manually controlled versus continuous infusion of propofol for deep sedation during interventional endoscopy: A prospective randomized trial. *Scand. J. Gastroenterol.* 2012; **47**: 1078–85.

40 Klare P, Huth R, Haller B *et al*. Patient position and hypoxemia during propofol sedation for colonoscopy: a randomized trial. *Endoscopy* 2015; **47**: 1159–66.

41 Paulo GA, Martins FPB, Macedo EP *et al*. Sedation in gastrointestinal endoscopy a prospective study comparing nonanesthesiologist-administered propofol and monitored anesthesia care. *Endoscopy International Open* 2015; **3**: E7–13.

42 Vaessen H, Bruens E, Knape J. Clinical analysis of moderate-to-deep-sedation by nonmedical sedation practitioners in 597 patients undergoing gastrointestinal endoscopy a retrospective study. *Endoscopy International Open* 2016; **4**: E564–71.

43 Sieg A, Beck S, Scholl SG *et al*. Safety analysis of endoscopist-directed propofol sedation A prospective, national multicenter study of 24 441 patients in German outpatient practices. *J. Gastroenterol. Hepatol.* 2014; **29**: 517–23.