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ORIGINAL ARTICLE

Comparison of high-flow nasal cannula and conventional nasal cannula during deep sedation for endoscopic submucosal dissection: a randomized controlled trial

Seungwon Lee[1] · Ji Won Choi[1] · In Sun Chung[1] · Tae Jun Kim[2] · Woo Seog Sim[1] · Seojin Park[1] · Hyun Joo Ahn[1]

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Abstract

Purpose Adequate oxygenation and airway management during deep sedation can be challenging. We investigated the effect of high-flow nasal cannula (group HF) and conventional nasal cannula (group CO) during sedation for endoscopic submucosal dissection (ESD).

Methods Patients undergoing ESD with deep sedation were enrolled. The primary outcome was difference in lowest oxygen saturation (SpO_2) between the groups. Incidence of hypoxia ($SpO_2 < 90\%$), patients with $SpO_2 < 95\%$, hypercapnia, and airway interventions; operator satisfaction; and adverse events were recorded.

Results Thirty-two patients in each group completed the study. The mean of minimum SpO_2 values was significantly higher in group HF than in group CO (96.8% ± 4.2% vs. 93.3% ± 5.3%, $p = 0.005$). The incidence of hypoxia was comparable between the groups (4 [12.5%] vs. 6 [18.8%], $p = 0.491$); however, patients with $SpO_2 < 95\%$ were significantly less in group HF (5 [15.6%] vs. 18 [56.3%], $p = 0.003$). Incidence of hypercapnia was higher in group HF than in group CO (14 [46.7%] vs. 5 [16.7%], $p = 0.013$). Airway rescue interventions were significantly less common in group HF. Satisfaction of operators and post-procedural complications were comparable between the two groups. In multivariable analysis, group CO and higher body mass index were risk factors for airway managements (odds ratio [95% confidence interval]: 6.204 [1.784–21.575], $p = 0.004$; 1.337 [1.043–1.715], $p = 0.022$, respectively).

Conclusions Compared to conventional nasal cannula, high-flow nasal cannula maintained higher minimum SpO_2 value during deep sedation with propofol–remifentanil for ESD.

Trial registration Clinical Trial Registry of the Republic of Korea (KCT0006618, https://cris.nih.go.kr; registered September 29, 2021; principal investigator: Ji Won Choi).

Keywords Airway management · Deep sedation · Endoscopic submucosal dissection · High-flow nasal oxygenation · Hypoxia

Introduction

Endoscopic submucosal dissection (ESD) is a less-invasive treatment widely performed at a high rate for complete resection of early gastric cancer [1]. However, ESD requires highly skilled endoscopic techniques, because it carries the risk of perforation or bleeding that may result from a difficult tumor location or patient body movements. Therefore, generally, deep sedation and analgesic management are necessary during the procedure. During deep sedation, patients are more likely to be exposed to the risk of hypoxia because of airway obstruction, respiratory depression, or decreased chest wall compliance and require intermittent airway management to prevent hypoxia [2].

✉ Ji Won Choi
jiwon0715.choi@samsung.com

[1] Department of Anesthesiology and Pain Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-Ro, Gangnam-Gu, Seoul 06351, Korea

[2] Division of Gastroenterology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

In most centers, oxygen is provided using a nasal cannula (NC) during sedation for ESD. However, when using NCs, a high-concentration oxygen supply is not possible because of oxygen dilution in hypoxic conditions, and FiO_2 according to change in oxygen flow varies unpredictably [3, 4]. Moreover, in addition to placing limitations on the efficient supply of oxygen during ESD, it is difficult to measure reliable end-tidal CO_2 ($EtCO_2$) values due to the nature of the endoscopic procedure. Therefore, maintaining adequate oxygenation and ventilation in patients undergoing ESD with deep sedation is a challenge for anesthesiologists.

A high-flow NC (HFNC) system provides humidified, heated, high-flow oxygen (30–70 L/min) and maintains stable FiO_2 values, which can be increased to 1.0. Several studies have demonstrated the superiority of HFNC compared to conventional NC in the prevention of hypoxia during gastrointestinal endoscopic procedures [5–8]. The authors in these studies suggested that HFNC could be an alternative approach in sedated patients at risk of hypoxia during endoscopic procedures. However, conflicting results on oxygenation between HFNC and conventional oxygenation, or serious adverse events related to HFNC, such as pneumothorax and pneumomediastinum, especially in patients with respiratory disease, have been reported [9–14].

Therefore, in this prospective randomized controlled trial, we investigated the effects related to oxygenation via HFNC (group HF) and conventional NC (group CO) during ESD with deep sedation. We conducted this study with the hypothesis that HFNC would result in an improvement of the lowest SpO_2 during deep sedation for ESD compared to conventional NC.

Materials and methods

This prospective, randomized, single-blind study was conducted at a Tertiary Academic Hospital in Seoul, Korea. The study protocol was approved by the Institutional Review Board of Samsung Medical Center (approval no.: SMC 2021-07-195; approval date: August 24, 2021) and registered with the Korean Clinical Research Information Service (registration no.: KCT0006618; principal investigator: Ji Won Choi; registration date: September 29, 2021; http://cris.nih.go.kr). This study was performed in accordance with the ethical principles of the 1964 Declaration of Helsinki and its later amendments. The trial was conducted following the original protocol and CONSORT guideline [15].

Study population

Adult patients scheduled to undergo elective ESD under deep sedation by an anesthesiologist and with an American Society of Anesthesiologists physical status (ASA-PS) of I–III were included. Patients were excluded from the study if they met any of the following criteria: age < 18 years, requirement for oxygen therapy, inability to breathe through the nose, severely impaired coagulation profile, nasal bleeding, development or worsening of congestive heart failure within the last 6 months, increased intracranial pressure, ASA-PS ≥ IV, unstable hemodynamics, history of pneumothorax, oral or nasal infection, pregnancy or lactation, lack of understanding of the study or refusal to participate, and history of serious psychological disease.

Randomization and blinding method

A randomization table was established using computer-generated block randomization (with a fixed block size of 4) in a 1:1 ratio to select patients to undergo HFNC or CO therapy by the statistical team of our institution who did not participate in the study. A study group member (I.S.C.) checked the randomization table the day before the procedure, and the patient was allocated to group CO or group HF. Because the two oxygen delivery devices had different shapes, the physician (endoscopists), attending anesthesiologist, and patient were not blinded to group allocation. However, the outcome investigators and data analysts were blinded to group assignment, and they were not involved in the sedation procedure.

Sedation procedure

Upon arrival in the endoscopy room, patients were monitored for pulse oximetry, non-invasive blood pressure, and electrocardiography in the supine position. Carbon dioxide (CO_2) was measured percutaneously ($PtCO_2$) in the patient's earlobe (Sentec®; SenTec AG, Therwil, Switzerland). After standard ASA monitoring, the patient moved into the left lateral decubitus position. In the conventional NC (group CO) group, 100% oxygen was administered at 6 L/min via an NC throughout the procedure. In the HFNC (group HF) group, referring to previous studies [16], 100% oxygen was administered at 30 L/min via an HFNC system (OptiFlow THRIVE; Fisher and Paykel Healthcare, Panmure, Auckland, New Zealand) throughout the procedure. A bolus of 1.5 mg midazolam (1 mg if age > 70 years or body weight < 50 kg) was delivered, followed by continuous infusion of propofol and remifentanil using a target-controlled infusion (TCI) pump. The targeted level of sedation was equivalent to a Modified Observer's Assessment of Alertness/Sedation (MOAA/S) Scale score < 2 points [17]. If sedation or analgesia was insufficient, midazolam 0.5 mg was additionally administered or the propofol/remifentanil concentration was adjusted. If desaturation or apnea occurred, different interventions, including jaw thrust, patient stimulation, drug adjustment (reduction or discontinuation of propofol/remifentanil), oxygen flow

increase (50–60 L/min), and nasal airway insertion, were performed at the attending anesthesiologist's discretion. If the patient did not recover from desaturation or apnea despite these interventions, the procedure was stopped, and manual ventilation with an Ambu bag or laryngeal mask airway or conversion to mechanical ventilation was performed. After endoscopic hemostasis, the concentration of drugs was reduced; the drugs were discontinued immediately after the procedure.

ESD procedure and post-procedure process

The type of lesion was previously determined as A, B, or C by the endoscopist in the order of difficulty according to location, size, and degree of fibrosis through gastroscopy prior to ESD.

Three gastroenterologists performed all gastric ESD procedures using standard techniques. First, a circumferential mark was made around the lesion using a needle knife or a dual knife. Thereafter, fluid (normal saline [100 mL], epinephrine [1 mL], and 0.8% indigo carmine [0.1 mL]) was injected into the submucosal layer. A circumferential mucosal precut was made, and the submucosal layer was dissected using various types of knives. Endoscopic hemostasis was simultaneously performed whenever bleeding was observed.

After the procedure, the patient was moved into the supine position and awakened. Then, the patient was monitored for vital signs and adverse events in the recovery room. After staying in the recovery room for about 30 min, the patients underwent chest X-ray examination to identify complications, such as pneumoperitoneum. Post-procedure atelectasis or aspiration was diagnosed by radiological examination after ESD; to make such a diagnosis, the chest radiographs from before and after ESD were reviewed by two radiologists who were blinded to the endoscopic procedure. After examination of their chest radiographs, patients were discharged to the ward. If room air SpO_2 of the patients was < 95%, patients were discharged with oxygen supplementation. In the ward, SpO_2 of the patients was monitored on the day of their procedure.

Outcome measurement

The primary endpoint was the lowest SpO_2, i.e., the minimum SpO_2 value measured via pulse oximetry during the procedure (when the SpO_2 was continuously changed, the value maintained for > 10 s was recorded). The secondary endpoints were incidence of hypoxia (SpO_2 < 90%), incidence of patients with SpO_2 < 95%, incidence of hypercapnia ($PtCO_2$ > 60 mmHg), and interventions related to desaturation or apnea during the procedure. Drug dosages (midazolam, propofol, remifentanil); SpO_2 in the recovery room after stopping oxygen; first SpO_2 in the ward after the procedure; satisfaction of operators; findings of chest X-ray; and adverse events (e.g., xeromycteria, rhinalgia, early procedure termination related to sedation, emergency surgery in relation to the procedure) were also recorded.

Sample size calculations and data analysis

The sample size was calculated based on the primary objective using PASS 2021 (version 21.0.1; NCSS, Kaysville, UT, USA). Based on a previous study [8], the population mean difference was 4.7 with standard deviations (SDs) of 0.6 and 7.3. As a result of the calculation, 28 patients per group were estimated to achieve a significance (alpha) level of 5% and a power of 90% using a two-sided, two-sample unequal-variance *t* test. Assuming a dropout rate of 10%, we aimed to enroll 32 patients per group.

Continuous variables were reported as mean (SD) or median (interquartile range [IQR]), and categorical variables were presented as number (%). The normality of the data distribution was assessed with the Shapiro–Wilk test. For continuous variables, comparisons were performed using either a *t* test or the Wilcoxon rank-sum test. Categorical variables were compared using the Chi-square test or Fisher's exact test. Logistic regression was used to assess protective factors for airway interventions. Variables with $p < 0.2$ in the univariable analysis were included in the multivariable analysis [18]. All outcomes were analyzed using a two-sided test, and a $p < 0.05$ was considered statistically significant. Data analysis was performed using SAS software (version 9.4; SAS Institute, Cary, NC, USA) and SPSS (version 29.0; IBM Corporation, Armonk, NY, USA).

Results

Study participants

A flow diagram of the study is shown in Fig. 1. From September 30, 2021, to November 25, 2021, 72 patients were assessed for eligibility and contacted by the primary investigators to obtain written informed consent 1 day before the procedure. Among 72 patients, 8 who did not meet the inclusion criteria ($n = 3$, received general anesthesia) or who had their procedures canceled ($n = 5$) were excluded. The remaining 64 patients were randomized into two groups (1:1 allocation), with 32 patients in group CO and 32 patients in group HF. A total of 64 patients completed the study. The baseline characteristics of the participants and perioperative outcomes between the groups are presented in Table 1. There was no difference in the baseline SpO_2 before preoxygenation between the two groups.

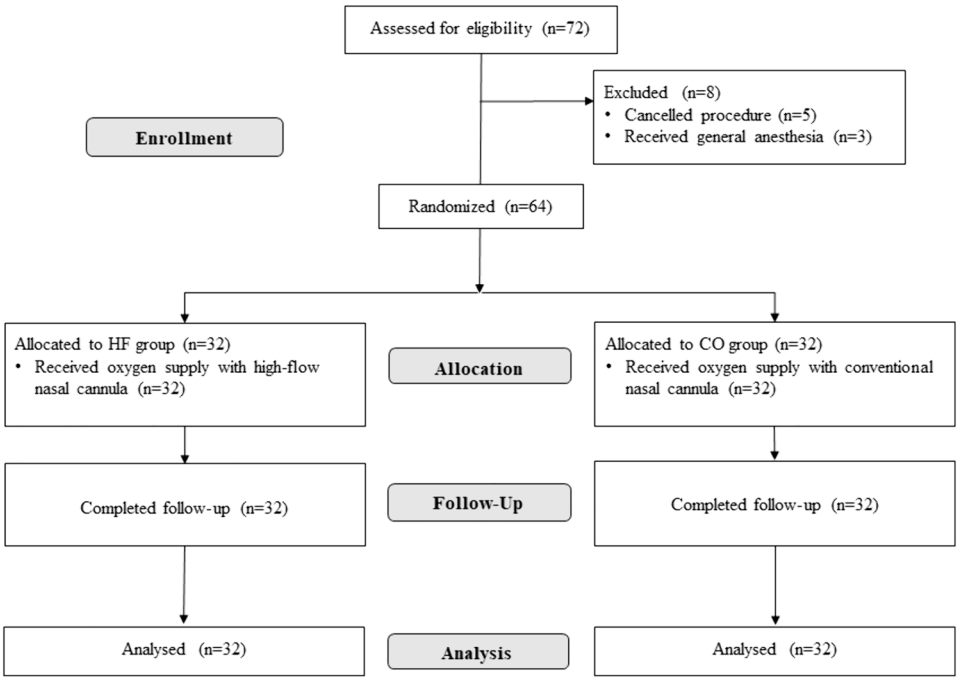

Fig. 1 CONSORT flow diagram of participants in the study. *HF group* high-flow nasal cannula group, *CO group* conventional nasal cannula group

Lowest oxygen saturation (SpO_2) during procedure

The mean of minimum SpO_2 values during ESD, a primary outcome, was significantly higher in the group HF than in the group CO (96.8% ± 4.2% vs. 93.3% ± 5.3%; mean difference, 3.4%; 95% confidence interval, 1.1–5.8%; $p = 0.005$). However, the mean of minimum SpO_2 values during the sedation was lower than the baseline SpO_2 in both groups.

Hypoxia incidence and other secondary outcomes

The incidence of hypoxia ($SpO_2 < 90\%$) was comparable between the groups (4 [12.5%] vs. 6 [18.8%], $p = 0.491$). The incidence of patients with $SpO_2 < 95\%$ was significantly lower in group HF (5 [15.6%] vs. 18 [56.3%], $p = 0.003$). Meanwhile, the incidence of hypercapnia ($PtCO_2 > 60$ mmHg) was significantly greater in group HF than in group CO (14 [46.7%] vs. 5 [16.7%], $p = 0.013$).

Airway rescue interventions, including jaw thrust, drug adjustment, and oxygen flow increase, were significantly less common in group HF (Table 2). Patients with $SpO_2 < 95\%$ had higher body mass index (BMI), and lower baseline SpO_2 in room air and SpO_2 in the recovery room after stopping oxygen compared to patients with $SpO_2 \geq 95\%$ during the procedure (Table 3). Satisfaction of operators, post-procedural atelectasis on chest X-ray, and other complications (rhinalgia, 1/32 [3.1%] vs. 0/32 [0%]; nausea or vomiting, 3/32 [9.4%] vs. 1/32 [3.1%]) were comparable between the two groups. Two hypoxia patients were discharged from the recovery room with oxygen supplementation; however, they recovered soon in the wards without any sequelae. No serious adverse events occurred in either group during the hospital stay.

In multivariable analysis, group CO and higher BMI were risk factors for airway intervention during sedation (odds ratio [95% confidence interval]: 6.204 [1.784–21.575], $p = 0.004$ and 1.337 [1.043–1.715], $p = 0.022$, respectively, Table 4).

Discussion

In this randomized controlled study, the mean of lowest SpO_2 between the HF group and the CO group was different during deep sedation with propofol–remifentanil for ESD. Application of HFNC maintained higher minimum SpO_2 values compared to application of conventional NC. It reduced the incidence of both patients with $SpO_2 < 95\%$ and airway rescue interventions, however, group HF showed a higher incidence of hypercapnia as secondary outcomes. In multivariable analysis, group CO and higher BMI were risk factors for airway rescue intervention during sedation.

Our findings are consistent with other previous studies and meta-analyses demonstrating the superiority of HFNC over conventional methods for oxygenation and prevention of hypoxia during sedation in gastrointestinal endoscopic procedures [5, 6, 8, 16, 19]. It seems clear that the use of HFNC carries an advantage in effective oxygenation during sedation of various endoscopic procedures compared to conventional NC. HFNC enables the administration of FiO_2 up to 100% at a maximum flow rate of 70 L/min via soft NC [16]. Physiologically, HFNC contributes to a washout of

Table 1 Baseline patient characteristics and data from the endoscopic procedure

	High-flow nasal cannula ($n=32$)	Conventional nasal cannula ($n=32$)	p value
Age (years)	64.1 (±11.0)	67.0 (±10.1)	0.276*
Sex, male/female	25/7 (78.1/21.9)	21/11 (65.6/34.4)	0.266†
BMI (kg/m^2)	24.5 (±3.2)	25.3 (±3.1)	0.290*
Smoking	7 (21.9)	7 (21.9)	>0.99†
Snoring mentioned by family	14 (43.8)	17 (53.1)	0.453†
Obstructive sleep apnea	0	0	N/A
Operator (1/2/3)	14/13/5	11/17/4	0.696‡
Type (A/B/C)	12/15/4§	14/12/6	0.647†
Baseline SpO_2 in room air (%)	97.9 (±1.3)	97.2 (±1.6)	0.066*
Duration (min)	31 (24, 50.5)	25.5 (19, 40.5)	0.046**
Dose of propofol (mg)	124.1 (99.6, 154.5)	103.9 (90.1, 139.2)	0.034**
Dose of remifentanil (μg)	159.4 (132.0, 248.2)	150 (110.5, 195.4)	0.197**
Dose of midazolam (mg)	2.5 (2, 3.75)	3 (2.5, 3.5)	0.418**
Hypoxia ($SpO_2<90\%$)	4 (12.5)	6 (18.8)	0.491†
$SpO_2<95\%$¥	5 (15.6)	18 (56.3)	0.003†
Hypercapnia ($PtCO_2>60$ mmHg)§	14 (46.7)	5 (16.7)	0.013†
Satisfaction of operators (1–5)	5 (4, 5)	4 (3, 5)	0.312
SpO_2 in PACU (after stopping oxygen)	99.2 (±1.4)	99.0 (±1.7)	0.629*
First SpO_2 in ward (after procedure)	97.3 (±1.8)	97.2 (±1.4)	0.901*

The qualitative data are presented as no. (%), while the numerical data are presented as mean (±SD) or median [interquartile range]

BMI body mass index, *PACU* post-anesthetic care unit, *$PtCO_2$* percutaneous carbon dioxide, *SD* standard deviation, *SpO_2* oxygen saturation

¥ Patients whose SpO_2 fell below 95% at least once during the procedure

*p value was calculated using the t test

**p value was calculated using the Wilcoxon rank-sum test

†p value was calculated using Pearson's Chi-square test

‡p value was calculated using Fisher's exact test

§One patient's data were missing for type in group HF; four patients' data were missing for hypercapnia (two per group)

Satisfaction was evaluated on a 5-point scale score (1: worst, 5: best)

the pharyngeal dead space, reducing the work of breathing, generating a positive end-expiratory pressure, and improving mucociliary clearance [20]. These effects could explain the advantages of HFNC for improving oxygenation during the sedation. However, in most previous studies, the depth of sedation was moderate, and the duration of included procedures (procedure time) was usually < 20 min. In this study, the depth of sedation was maintained deep (MOAA/S Scale score 0 or 1), and the procedure time was relatively long.

There have also been studies reporting conflicting results on oxygenation. One study determined that there was no statistical difference in the incidence of hypoxia between the HFNC and conventional NC during colonoscopy in morbidly obese patients with propofol sedation and similar FiO_2 levels [9]. The authors suggested an inaccuracy in FiO_2 delivery to obese patients, with varying degrees of hypoventilation under deep sedation and without consistently noting the patients' mouth positions during the procedure as potential causes of the lack of difference between the two groups. Another study [10] revealed no differences between two groups in the incidence of hypoxia and lowest SpO_2 during ERCP with propofol and fentanyl sedation in high-risk patients (ASA physical status ≥ 3, BMI > 30 kg/m^2 or with OSA). They had added mouthguard oxygen insufflation in addition to low-flow nasal oxygen and used a TCI propofol regimen that included titrated opioid administration. In this study, although not a study of high-risk patients, the minimum SpO_2 values were higher in group HF, and the incidence of hypoxia was comparable between the groups. We also used the TCI protocol for maintaining deep sedation, and the patient's mouth was open during the procedure. As mentioned in previous studies, it is thought that different results for HFNC were obtained under various conditions during endoscopic procedures or patient's characteristics.

In this study, although it was not a primary outcome, the incidence of patients with $SpO_2<95\%$ was significantly

Table 2 Airway rescue interventions during sedation, adverse events, and chest X-ray findings after procedure

	High-flow nasal Cannula ($n=32$)	Conventional nasal cannula ($n=32$)	p value
Airway rescue interventions, *n* (%)			
Jaw thrust	5 (15.6)	15 (46.9)	0.007
Patient stimulation	2 (6.3)	1 (3.1)	> 0.99
Drug adjustment	5 (15.6)	16 (50)	0.003
O_2 flow increase	3 (9.4)	12 (37.5)	0.008
Nasal airway insertion	2 (6.3)	3 (9.4)	> 0.99
Ambu bagging	0 (0.0)	0 (0.0)	N/A
LMA insertion	0 (0.0)	0 (0.0)	N/A
Adverse events, *n* (%)			0.355
Rhinalgia	1 (3.1)	0	
Nausea or vomiting	3 (9.4)	1 (3.1)	
Chest X-ray, *n* (%)			0.537
Normal	24 (75)	27 (84.4)	
Atelectasis	6 (18.8)	2 (6.3)	
Otherwise[a]	2 (6.3)	3 (9.4)	

The qualitative data are presented as no. (%)

LMA laryngeal mask airway

[a]Otherwise included pneumoperitoneum, pneumomediastinum, and presumed pulmonary edema

lower in group HF (5 [15.6%] vs. 18 [56.3%]). This was thought to be a result of aggressive airway rescue interventions for recovery of apnea or prevention of hypoxia by a study protocol. Ten of 23 patients (4/5 patients in the HFNC group and 6/18 patients in the CO group) progressed to hypoxia despite rescue interventions. Considering the high risk of hypoxia in deep sedation and the "steep" area of the oxygen–hemoglobin dissociation curve, early interventions for airway management in desaturation may be important.

Since hypoxia developed in only 10 patients, we compared the patients of $SpO_2 \geq 95\%$ with the patients of $SpO_2 < 95\%$ during the procedure. Compared to the patients of $SpO_2 \geq 95\%$, patients with $SpO_2 < 95\%$ had higher BMI and lower baseline SpO_2 in room air and SpO_2 in the recovery room after stopping oxygen. Most of them were discharged from the recovery room without adverse events. However, 2 patients in group CO required oxygen supply on discharge from the recovery room because their SpO_2 level was < 95% (in 1 patient, it was only 92%) despite administering O_2 via an NC at a rate of 4 L/min. Both patients had BMIs > 28 kg/m^2, SpO_2 level ≤ 95% before sedation, a history of snoring, and the use of ≥ 3.5 mg of midazolam. In a retrospective study of EGD with a moderate level of sedation ($n=4065$) [21], more than half of hypoxemia occurred during the recovery period (46/84 cases). Another study in ERCP ($n=30$) with midazolam sedation showed that the patients were most hypoxic in the first 30 min after the procedure [22]. Since it was difficult to predict the timing (or onset) of hypoxemia from the patient's baseline characteristics, the authors emphasized the importance of monitoring by pulse oximetry during the recovery period [21, 22].

According to the study protocol, patients with $SpO_2 < 95\%$ were nearly matched to those requiring airway intervention ($n=23$ vs. $n=26$, respectively). And, in the current data, higher BMI was a risk factor for airway intervention. As we already know, obesity, especially a BMI > 30 kg/m^2, has been suggested as a contributing factor for hypoxia during sedation in many studies [23–26]. In one meta-analysis, the authors inferred that HFNC may prolong the safe apnea time and elevate the minimum peri-intubation SpO_2 of obese patients compared to those in the control group [16]. They also reported that the use of HFNC decreased the requirement of airway interventions except for jaw thrust [16]. In this study, the incidence of jaw thrust, drug adjustments, and increase in O_2 flow was reduced in group HF. This may have resulted from differences in timing of airway intervention or sedation protocols between several studies.

Current guidelines on procedural sedation recommend monitoring with capnography (to avoid severe hypercapnia), especially in high-risk patients or advanced endoscopic procedures [27, 28]. However, in endoscopic procedures during deep sedation, detection of end-tidal CO_2 via capnography is sometimes unable because of shallow breathing and mouth opening [8, 9]. In general, HFNC has been reported to improve CO_2 washout from the nasopharyngeal dead space, thus, prevent hypercapnia during sedation [8, 20]. Nevertheless, some studies have shown that the incidence of hypercapnia was not reduced with the use of HFNC [7, 10, 16,

Table 3 Comparision of the patients with $SpO_2 < 95\%$¥ and the patients with $SpO_2 \geq 95\%$¥¥ during the procedure

	$SpO_2 < 95\%$ ($n = 23$)	$SpO_2 \geq 95\%$ ($n = 41$)	*p* value
Age (years)	66.3 (± 9.6)	65.2 (± 11.2)	0.685*
Sex, male/female	16/7 (69.6/30.4)	30/11 (73.2/26.8)	0.758†
BMI (kg/m^2)	26.5 (± 2.9)	24.0 (± 2.9)	0.001*
Snoring mentioned by family	13 (56.5)	18 (43.9)	0.332†
Operator (1/2/3)	8/11/4	17/19/5	0.795†
Type (A/B/C)	6/13/3§	20/14/7	0.150†
Baseline SpO_2 in room air (%)	96.9 (± 1.8)	97.9 (± 1.2)	0.020*
Duration (min)	29 (19, 63)	29 (23, 42)	0.911**
Dose of propofol (mg/kg/h)	3.2 (2.7, 4.3)	3.8 (3.2, 4.7)	0.200**
Dose of remifentanil (mcg/kg/h)	4.3 (4.0, 5.7)	5.0 (4.2, 5.5)	0.429**
Dose of midazolam (mcg/kg)	47.9 (36.5, 54.9)	38.3 (31.0, 53.2)	0.294**
Lowest SpO_2 (%)	89.3 (± 3.9)	98.3 (± 1.3)	< 0.001*
Group (HF/CO)	5/18	27/14	< 0.001†
Hypercapnia ($PtCO_2 > 60$)§	8 (38.1)	11 (28.2)	0.432†
$PtCO_2$ at procedure end	50.2 (46.5, 57.2)	52.5 (50.2, 57.1)	0.535**
SpO_2 in PACU (after stopping oxygen)	99 (96, 100)	100 (99, 100)	0.008**
First SpO_2 in ward (after procedure)	97 (96, 98)	97 (96, 99)	0.705**

The qualitative data are presented as no. (%), while the numerical data are presented as mean (± SD) or median [interquartile range]

BMI body mass index, *CO* conventional nasal cannula group, *HF* high-flow nasal cannula group, *PACU* post-anesthetic care unit, *$PtCO_2$* percutaneous carbon dioxide

¥ Patients whose SpO_2 fell below 95% at least once during the procedure

¥¥ Patients whose SpO_2 remained above 95% throughout the procedure

**P* value was calculated using the *t* test

***P* value was calculated using the Wilcoxon rank-sum test

†P value was calculated using Pearson's Chi-square test

‡P value was calculated using Fisher's exact test

§One patient's data were missing for type in the hypoxia group; four patients' data were missing for hypercapnia (two per group)

29]. Authors in those studies [7, 10] reported that increased FiO_2 via HFNC is unlikely to improve hypoxia developing from pharmacologically induced hypoventilation, and demonstrated that patients with chronic lung disease who applied HFNC had higher incidence of hypercapnia during sedation of anesthetized depth. Thus, other evidence suggested that the use of HFNC may increase the arterial partial pressure of CO_2 in obese patients with hypoventilation syndrome [30]. The present study did not include the patients with pulmonary comorbidities or severe obesity; therefore, further studies on hypercapnia in healthy patients using HFNC during deep or anesthetized sedation are necessary.

This study has several limitations. First, this was a single-center study. Therefore, the findings of this study may not be generalized for routine ESD procedures in other situations. Second, due to the nature of the intervention and the different appearances of two devices, patients and practitioners were not blinded. To minimize bias, we adhered to a standardized sedation protocol and the outcome investigators and data analysts were not involved in the sedation procedure. Third, we could not monitor parameters of the objective sedation depth, such as the bispectral index, between the groups. Furthermore, propofol has a narrow therapeutic window [31], and the depth of sedation could rapidly change, potentially leading to unexpected respiratory suppression. Fourth, since we calculated the sample size based on the difference in minimum SpO_2 values between the two groups, it would have been underpowered to detect the incidence of hypoxia or hypercapnia, which are more clinically significant than the lowest oxygen saturation, between the two groups.

In conclusion, this randomized controlled trial showed that the high-flow nasal cannula maintained higher minimum oxygen saturation value without any serious complications during deep sedation with propofol–remifentanil for ESD compared to conventional nasal cannula. It may offer an enhancement on oxygenation for patient safety in these procedures and further studies are needed on other outcomes, such as hypercapnia.

Table 4 Logistic regression analysis of risk factors associated with airway intervention

	Univariable analysis*		Multivariable analysis*	
	Odds ratio (95% CI)†	*p* value	Odds ratio (95% CI)†	*p* value
Group CO	5.952 (1.977–17.920)	0.002	6.204 (1.784–21.575)	0.004‡
Female sex	0.643 (0.215–1.926)	0.430		
Age	1.002 (0.956–1.050)	0.935		
BMI	1.336 ((1.092–1.635)	0.005	1.337 (1.043–1.715)	0.022‡
ASA-PS (I§)		0.518		
II	1.653 (0.373–7.322)	0.508		
III	2.722 (0.479–15.468)	0.259		
Snoring Hx	0.610 (0.224–1.656)	0.332		
Operator (I§)		0.289		
II	1.185 (0.396–3.545)	0.761		
III	3.556 (0.712–17.763)	0.122		
Type (C§)				
A&B	1.524 (0.393–5.915)	0.543		
Baseline SpO_2	0.644 (0.445–0.934)	0.020	0.872 (0.564–1.348)	0.538
Duration of procedure	1.005 (0.989–1.022)	0.538		
Dose of propofol (mg/kg/h)	0.859 (0.609–1.213)	0.387		
Dose of remifentanil (mcg/kg/h)	1.008 (0.973–1.045)	0.651		
Dose of midazolam (mg/kg)	8.028 (0.000–6.712*E^{14})	0.899		

ASA-PS American Society of Anesthesiologists physical status classification, *BMI* body mass index, *HF* high-flow nasal cannula

*Variables with $p < 0.2$ in the univariable analysis were included in the multivariable analysis

†Odds ratios increased for continuous variables (age; BMI; baseline SpO_2; duration of procedure; and doses of propofol, remifentanil, and/or midazolam at enrollment)

‡Risk factors with significant odds ratios in the multivariable analysis

§Reference

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Author contributions Conceptualization: Seungwon Lee, Ji Won Choi, Woo Seog Sim, Hyun Joo Ahn; Data curation: Seungwon Lee, Ji Won Choi, In Sun Chung, Tae Jun Kim, Seo Jin Park; methodology: Seungwon Lee, Ji Won Choi, In Sun Chung, Woo Seog Sim, Tae Jun Kim, Seojin Park; formal analysis and investigation: Seungwon Lee, Ji Won Choi, In Sun Chung; writing—original draft preparation: Seungwon Lee, Ji Won Choi; writing—review and editing: In Sun Chung, Tae Jun Kim, Woo Seog Sim, Seojin Park, Hyun Joo Ahn; funding acquisition: Ji Won Choi; Resources: Seungwon Lee, Ji Won Choi, In Sun Chung, Tae Jun Kim; Supervision: Ji Won Choi, Woo Seog Sim, Hyun Joo Ahn; all authors read and approved the final manuscript.

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Declarations

Conflict of interest The authors declare no conflicts of interest.

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