High-Flow Nasal Cannula Oxygen in Patients Having Anesthesia for Advanced Esophagogastroduodenoscopy: HIFLOW-ENDO, a Randomized Clinical Trial

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BACKGROUND: Over 6 million esophagogastroduodenoscopy (EGD) procedures are performed in the United States each year. Patients having anesthesia for advanced EGD procedures, such as interventional procedures, are at high risk for hypoxemia.

METHODS: Our primary study aim was to evaluate whether high-flow nasal cannula (HFNC) oxygen reduces the incidence of hypoxemia during anesthesia for advanced EGD. Secondarily, we studied whether HFNC oxygen reduces hypercarbia or hypotension. After obtaining written informed consent, adults having anesthesia for advanced EGD, expected to last longer than 15 minutes, were randomly assigned to receive HFNC oxygen or standard nasal cannula (SNC) oxygen. The primary outcome was occurrence of one or more hypoxemia events during anesthesia, defined by arterial oxygen saturation <92% for at least 15 consecutive seconds. Secondary outcomes were occurrence of one or more hypercarbia or hypotension events. A hypercarbia event was defined by a transcutaneous CO_2 measurement 20 mm Hg or more above baseline, and a hypotension event was defined by a mean arterial blood pressure measurement 25% or more below baseline.

RESULTS: Two hundred seventy-one adult patients were enrolled and randomized, and 262 patients completed study procedures. Eight randomized patients did not complete study procedures due to changes in their anesthesia or endoscopy plan. One patient was excluded from analysis because their procedure was aborted after 1 minute. Patients who received HFNC oxygen (N = 132) had a significantly lower incidence of hypoxemia than those who received SNC oxygen (N = 130; 21.2% vs 33.1%; hazard ratio [HR] = 0.59 [95% confidence interval {CI}, 0.36–0.95]; *P* = .03). There was no difference in the incidence of hypercarbia or hypotension between the groups. The HR for hypercarbia with HFNC oxygen was 1.29 (95% CI, 0.89–1.88; *P* = .17), and the HR for hypotension was 1.25 (95% CI, 0.86–1.82; *P* = .25).

CONCLUSIONS: HFNC oxygen reduces the incidence of hypoxemia during anesthesia for advanced EGD and may offer an opportunity to enhance patient safety during these procedures. (Anesth Analg 2021;132:743–51)

KEY POINTS

- **Question:** Does high-flow nasal cannula (HFNC) oxygen reduce the risk of hypoxemia during anesthesia for advanced esophagogastroduodenoscopy?
- **Findings:** In a randomized controlled trial that included 262 adult patients having anesthesia for advanced esophagogastroduodenoscopy, we found that HFNC oxygen significantly reduced the incidence of one or more hypoxemia events from 33.1% to 21.2% (hazard ratio [HR] = 0.59 [95% confidence interval {CI}, 0.36–0.95]; *P* = .03).
- **Meaning:** Administration of HFNC oxygen may enhance patient safety during anesthesia for advanced esophagogastroduodenoscopy by reducing the incidence of hypoxemia.

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GLOSSARY

APC = argon plasma coagulation; **ASA** = American Society of Anesthesiologists; **BMI** = body mass index; **CI** = confidence interval; **CONSORT** = Consolidated Standards of Reporting Trials; **COPD** = chronic obstructive pulmonary disease; **EGD** = esophagogastroduodenoscopy; **ERCP** = endoscopic retrograde cholangiopancreatography; **EUS** = endoscopic ultrasound; **HFNC** = high-flow nasal cannula; **HR** = hazard ratio; **P_tCO_2** = transcutaneous blood carbon dioxide; **RFA** = radiofrequency ablation; **SD** = standard deviation; **SNC** = standard nasal cannula; **Spo_2** = arterial oxygen saturation

Over 6 million esophagogastroduodenoscopy (EGD) procedures are performed in the United States each year.[1] EGD is commonly performed under general anesthesia to provide amnesia, comfort, and optimal procedural conditions. Anesthetic drugs depress normal ventilation and predispose patients to upper airway obstruction, which can cause hypoxemia, hypercarbia, respiratory acidosis, hypotension, and, in rare cases, brain injury or death.[2–5] Advanced EGDs, including interventional and combined procedures, appear to increase the risk for hypoxemia, and novel strategies may be needed to enhance patient safety during these procedures.[6,7]

The current standard of care for most patients receiving general anesthesia for an advanced EGD procedure is to administer supplementary oxygen via standard nasal cannula (SNC).[8] SNC provides oxygen flows up to 15 L/min and an inspired oxygen concentration in the distal airways between 30% and 40%.[9] Higher inspired oxygen concentrations are not possible with SNC because of air mixing and dilution with carbon dioxide from dead space.[9,10] High-flow nasal cannula (HFNC) delivers higher inspired oxygen concentrations to the distal airways, because HFNC flows exceed peak inspiratory flows during respiration.[11,12] HFNC oxygen also increases distending pressure in the upper airway, reducing airway obstruction.[13] Currently available HFNC systems are capable of delivering oxygen flows of up to 60 L/min.[9]

Randomized controlled trials have shown that HFNC oxygen reduces hypoxemia in critically ill patients with acute respiratory failure.[14,15] However, few studies have evaluated HFNC oxygen in patients undergoing anesthesia. The primary aim of our study was to determine whether HFNC oxygen reduces the incidence of hypoxemia during anesthesia for advanced EGD. Secondarily, we sought to understand whether HFNC oxygen affects the incidence of hypercarbia or hypotension during anesthesia for advanced EGD.

To evaluate our primary aim, we tested the hypothesis that HFNC oxygen reduces the incidence of one or more hypoxemia events, defined by an arterial oxygen saturation (Spo_2) <92% for 15 consecutive seconds, during anesthesia for advanced EGD. To evaluate our secondary aims, we tested the hypothesis that HFNC oxygen affects the incidence of one or more hypercarbia or hypotension events during anesthesia for advanced EGD.

METHODS

Patients

The institutional review board at the University of Maryland, Baltimore, approved the study (HP-0071111), and it was registered with clinicaltrials.gov (NCT03028688, principal investigator: Michael Mazzeffi, date of registration: January 23, 2017) before patient enrollment. Patient enrollment occurred between June 21, 2017 and May 9, 2019. Written informed consent was obtained from all participants.

Adults (>17 years of age) having anesthesia for advanced EGD with an anticipated duration >15 minutes were eligible for study participation. Simple procedures lasting <15 minutes were excluded because they have a lower risk for hypoxemia.[6,7] Common advanced EGD procedures meeting eligibility criteria included EGDs with radiofrequency ablation for Barrett esophagus, endoscopic ultrasound procedures, and endoscopic retrograde cholangiopancreatography (ERCP) procedures. Patients having procedures with argon plasma coagulation (APC) were excluded because of the potential risk for fire with high oxygen concentrations in the upper airway or esophagus. Pregnant patients and patients having procedures with planned endotracheal intubation were also excluded. For all patients, baseline demographic data and pertinent medical histories were collected from electronic medical records, the gastroenterologist's history and physical, and the preoperative anesthesiology evaluation.

Study Procedures and Treatment

The original study protocol is included as a Supplemental Digital Content 1, Document, http://links.lww.com/AA/D75. The study was designed as a randomized controlled trial performed in a single tertiary care academic medical center. Study investigators and a study coordinator enrolled all patients. Patients were assigned in a 1:1 ratio in randomly permuted blocks of random size (4, 6, and 8 subjects) to receive either SNC oxygen given at 6 L/min during anesthesia or HFNC oxygen given at 20 L/min using Vapotherm Precision Flow (Vapotherm Inc, Stevensville, MD; Supplemental Digital Content 2,

Figure 1, http://links.lww.com/AA/D76). An oxygen flow rate of 20 L/min was selected for the study, because during study planning the investigators observed difficulty with consistent end-tidal carbon dioxide monitoring at higher oxygen flows. The study statistician sealed all group assignments in sequentially numbered opaque envelopes before study commencement. Subjects were randomly assigned to a group immediately after enrollment by the study coordinator. Physicians and nurses caring for patients were not blinded to study interventions.

Oxygen flows were not titrated unless the anesthesia provider deemed titration necessary for patient safety. Anesthetic drugs were limited to propofol, fentanyl, and midazolam, except in the case of emergent endotracheal intubation, where providers could use neuromuscular-blocking drugs. Anesthesia providers selected drug doses without a prespecified protocol and in accordance with their "usual" practice. Patient monitoring was performed in accordance with the American Society of Anesthesiologists (ASA) recommendations for monitoring during general anesthesia.[16] The target depth of anesthesia was general anesthesia, as defined by the ASA.[17] An independent data safety monitoring board performed a safety review every 6 months during the study.

Study Outcomes

The study's primary outcome was occurrence of one or more hypoxemia events during anesthesia. A hypoxemia event was defined as Spo_2 <92% for at least 15 consecutive seconds. Once Spo_2 increased above this threshold, the desaturation event was considered ended, and the patient was eligible for further desaturation events. Since there is no standardized definition for hypoxemia in the anesthesiology literature, we based our definition on prior studies, which used a similar definition.[4–6,18] Spo_2 was measured continuously in all patients using a pulse oximeter (MAXA Oximax, Covidien, Minneapolis, MN), and all hypoxemia events were recorded in real time by a trained research coordinator who did not provide clinical care for the patient. The lowest Spo_2 during anesthesia was also recorded in real time for each patient. All hypoxemia events were confirmed post hoc using electronic anesthesia records (Metavision, iMDsoft, Tel Aviv-Jaffa, Jaffa, Israel).

Secondary outcomes included one or more hypercarbia or hypotension events during anesthesia. Blood carbon dioxide levels were measured with a transcutaneous blood carbon dioxide (P_tCO_2) measuring device (Radiometer TCM CombiM, Radiometer Inc, Brea, CA), of which the accuracy had been confirmed in a prior study.[19] The P_tCO_2 device has a small transcutaneous probe, which is placed approximately 1–2 inches below the midclavicle and provides a continuous measurement of P_tCO_2. Clinicians were blinded to all P_tCO_2 measurements during the case. A hypercarbia event was defined as a P_tCO_2 measurement >20 mm Hg above the baseline measurement.

Blood pressure measurements were taken using an oscillometric blood pressure cuff. A hypotension event was defined as a mean arterial blood pressure 25% or more below the baseline measurement. Both hypercarbia and hypotension events were recorded in real time by a trained research coordinator. Hypertension was not studied as a study outcome.

Statistical Analysis

Statistical analysis was performed using SAS 9.4 (SAS Corporation, Cary, NC). Sample size calculation was performed a priori. Sample size was based on a review of 500 prior advanced EGDs (duration >15 minutes) in our institution, where the rate of one or more hypoxemia events (Spo_2 <92% for at least 15 consecutive seconds) was 18%. With this hypoxemia event rate, an α of .05 and 80% power, we calculated that 262 patients would allow for detection of a 12% absolute reduction in hypoxemia incidence with HFNC oxygen, which was deemed to be clinically significant. The study protocol, study outcomes, and group comparisons were agreed upon and published on clinicaltrials.gov before beginning the study. Before data review and analysis, the investigators agreed upon the final statistical plan (Supplemental Digital Content 2, Statistical Analysis Plan, http://links.lww.com/AA/D76), and its details were posted on clinicaltrials.gov.

Data analysis was performed using a modified intention-to-treat approach. Patient characteristics and anesthetic details were summarized as the mean value ± standard deviation or number and percentage of patients. Anesthetic and procedure details were compared between groups using either the Student t test or the χ^2 test. Study outcomes were analyzed using time-to-event (Kaplan–Meier) analysis to account for the fact that patients were under anesthesia for different lengths of time and thus had different risk intervals for hypoxemia. Cox proportional hazards models were fit, and hazard ratios (HRs) with 95% confidence intervals (CIs) were reported for study outcomes. Appropriate model diagnostics were performed, including testing of the proportional hazards assumption.

Two variables were explored post hoc for possible effect modification, obesity (body mass index [BMI] ≥30), and chronic lung disease, defined as chronic obstructive pulmonary disease (COPD), asthma, or interstitial lung disease. A diagnosis of chronic lung disease was based on prior documented medical history in the electronic medical record (Epic Corporation, Verona, WI), gastroenterologist's history

and physical, or preoperative anesthesiology evaluation. To test whether obesity was an effect modifier, an interaction term was entered into a Cox proportional hazards model with the study intervention and obesity modeled as independent variables. A similar analysis was performed to test whether chronic lung disease was an effect modifier. All statistical tests were 2 sided, and a *P* value <.05 was considered statistically significant.

RESULTS

Study screening and enrollment details are shown in the Consolidated Standards of Reporting Trials (CONSORT) diagram in Figure 1. A total of 658 patients were screened for the study, 271 patients were enrolled and randomized, and 262 patients completed study procedures and were analyzed. Eight patients did not complete study procedures because of changes to their anesthetic plan or EGD plan after randomization (eg, use of APC during the procedure or plan for elective intubation). There was no reason to believe that group assignment impacted the decision to change the endoscopy or anesthesia plan in the 8 patients who did not complete study procedures. Decisions to alter the plan were determined by patient- and disease-specific factors. One additional patient was excluded from final analysis because their EGD procedure was aborted after 1 minute. Of the 262 patients who completed study procedures, 130 received SNC oxygen and 132 received HFNC oxygen.

Protocol deviations occurred in both groups. Three patients in the HFNC oxygen group had their oxygen flows titrated up to between 30 and 40 L/min during a hypoxemia event, while 7 patients in the SNC group had their oxygen flows titrated up to between 8 and 10 L/min during a hypoxemia event. One patient in the SNC group briefly required mask ventilation without intubation. Two patients in the HFNC oxygen group required mask ventilation and intubation, and 1 patient in the SNC oxygen group required mask ventilation and intubation. Fourteen patients in the SNC group had nasal cannula oxygen flows between 2 and 4 L/min, which was below the 6 L/min required by the study protocol.

Table 1 shows demographics and comorbidities for patients who completed study procedures. Randomization produced similar groups. Supplemental Digital Content 2, Table 1, http://links.lww.com/AA/D76, shows demographics and comorbidities for 9 patients who were randomized but did not complete study procedures and were not analyzed. Table 2 shows procedure type, patient position, anesthetic drug doses, endoscopy time, and anesthesia time. There were no significant differences in procedure type, patient position, or mean anesthetic drug doses between the groups. Mean anesthesia time was 57.3 ± 23.4 minutes, mean endoscopy time was 31.1 ± 19.6 minutes for the cohort, and there were no significant differences in anesthesia time or endoscopy time between groups.

Table 3 shows study outcomes. Twenty-eight patients (21.2%) in the HFNC oxygen group had one or more hypoxemia events compared to 43 patients (33.1%) in the SNC group. The absolute risk reduction with HFNC oxygen was 11.9%, corresponding to a number needed to treat of 8.4. Figure 2 shows results of the Kaplan–Meier analysis for the primary study outcome. Patients who received HFNC oxygen had a significantly lower incidence of hypoxemia during anesthesia, with the Kaplan–Meier curves separating in the first 10–15 minutes of anesthesia. The HR for hypoxemia with HFNC oxygen was 0.59 (95% CI, 0.36–0.95; *P* = .03). Figure 3 shows the total number of hypoxemia events for patients in the HFNC and SNC groups. There were 14 patients in the HFNC group who had multiple hypoxemia events and 21 patients in the SNC group who had multiple hypoxemia events. Supplemental Digital Content 2, Figure 2, http://links.lww.com/AA/D76, shows the lowest Spo_2 for patients who had one or more hypoxemia events in both groups. There were 5 patients in the HFNC group and 7 patients in the SNC group who had Spo_2 <80% during anesthesia. Two patients in the SNC group had Spo_2 <60% during anesthesia. Of the 14 patients in the SNC group whose oxygen flows were <6 L/min during anesthesia, 4 (28.6%) had one or more hypoxemia events.

There were no differences in the incidence of hypercarbia or hypotension between the 2 groups (Table 3). Mean baseline P_tCO_2 in the SNC oxygen group was 32.4 ± 5.6 mm Hg and in the HFNC oxygen group was 33.3 ± 5.3 mm Hg (*P* = .17). Mean maximum P_tCO_2 was 51.5 ± 11.3 in the SNC oxygen group and 54.3 ± 11.2 in the HFNC oxygen group (*P* = .04). Seven patients (2.7%) had missing P_tCO_2 data due to machine malfunction during their procedure. Three of these patients were in the SNC oxygen group and 4 were in the HFNC oxygen group.

Post hoc analysis demonstrated that obesity was not an effect modifier for the relationship between HFNC oxygen and hypoxemia (*P* value interaction term = .72). Similarly, chronic lung disease was not an effect modifier for the relationship between HFNC oxygen and hypoxemia (interaction term *P* = .27). Obesity and chronic lung disease were not effect modifiers for the relationship between HFNC oxygen and hypotension (interaction term *P* = .33 and .57, respectively), and obesity was not an effect modifier for the relationship between HFNC oxygen and hypercarbia (interaction term *P* = .77). Chronic lung disease was an effect modifier for the

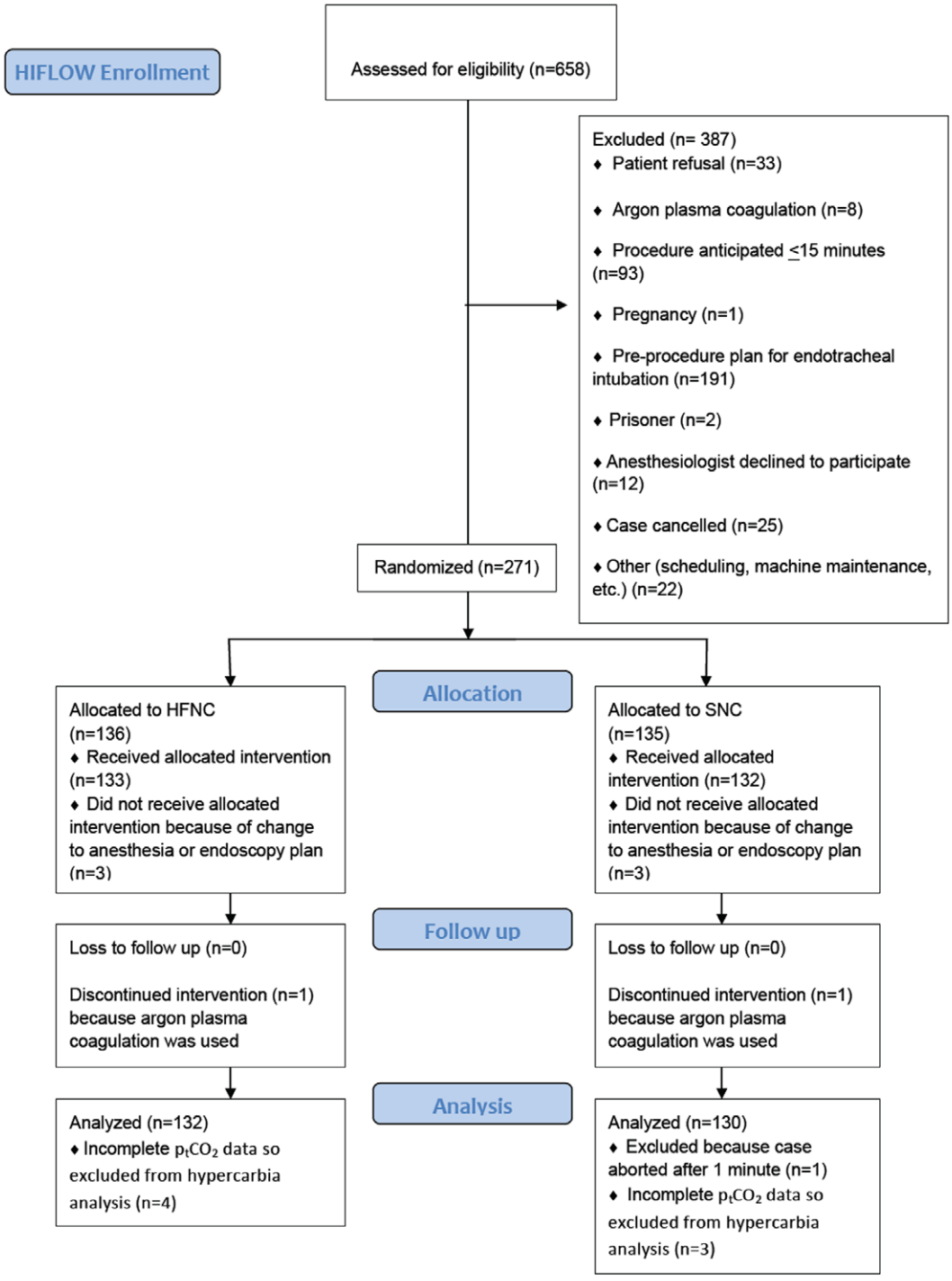

Figure 1. CONSORT diagram showing patients screened, enrolled, randomized, and analyzed. CONSORT indicates Consolidated Standards of Reporting Trials; HFNC, high-flow nasal cannula; P_tCO_2, transcutaneous blood carbon dioxide; SNC, standard nasal cannula.

relationship between HFNC oxygen and hypercarbia (interaction term $P = .03$). The HR for one or more hypercarbia events was 5.89 (95% CI, 1.33–26.11) in patients with chronic lung disease who received HFNC oxygen and was 1.10 (95% CI, 0.74–1.63) in patients who did not have chronic lung disease who received HFNC oxygen.

DISCUSSION

In a randomized controlled trial that compared HFNC oxygen with SNC oxygen in patients having anesthesia for advanced EGD, we found that HFNC oxygen significantly reduced the incidence of hypoxemia from 33.1% to 21.2%. This represents an absolute risk reduction of 11.9% or relative risk reduction

Table 1. Study Patient Characteristics

Variable	Standard Nasal Cannula Oxygen N = 130	High-Flow Nasal Cannula Oxygen N = 132
Age, mean (SD), y	62 (15)	62 (13)
Sex, n (%), male	71 (54.6)	87 (65.9)
Body mass index, mean (SD), kg/m^2	28.2 (6.2)	28.3 (6.5)
Hypertension, n (%)	74 (56.9)	92 (69.7)
Diabetes mellitus, n (%)	32 (24.6)	34 (25.8)
Prior cerebral vascular accident, n (%)	11 (8.5)	9 (6.8)
Peripheral vascular disease, n (%)	2 (1.5)	1 (0.8)
Congestive heart failure, n (%)	3 (2.3)	3 (2.3)
Coronary artery disease, n (%)	15 (11.5)	23 (17.4)
Cancer, n (%)	36 (27.7)	46 (34.8)
Obstructive sleep apnea, n (%)	16 (12.3)	16 (12.1)
COPD, n (%)	6 (4.6)	14 (10.6)
Asthma, n (%)	11 (8.5)	12 (9.1)
Interstitial lung disease, n (%)	2 (1.5)	0 (0)
Current or prior tobacco use, n (%)	67 (51.5)	77 (58.3)
Baseline Spo_2, mean (SD), % saturation	97 (2)	97 (3)
Baseline mean arterial pressure, mean (SD), mm Hg	99 (13)	101 (14)

Abbreviations: COPD, chronic obstructive pulmonary disease; SD, standard deviation; Spo_2, arterial oxygen saturation.

Table 2. Anesthetic and Esophagogastroduodenoscopy Details

Variable	Standard Nasal Cannula Oxygen N = 130	High-Flow Nasal Cannula Oxygen N = 132	*P*
Procedure type, n (%)			.95
ERCP	27 (20.8)	31 (23.5)	
EGD with EUS	68 (52.3)	65 (49.2)	
EGD with RFA or cryoablation	19 (14.6)	20 (15.2)	
Other EGD	16 (12.3)	16 (12.1)	
Patient position, n (%)			.65
Supine	1 (0.8)	2 (1.5)	
Lateral	89 (68.5)	95 (72.0)	
Prone	40 (30.7)	35 (26.5)	
Fentanyl dose, mean (SD), μg	26.8 (40.5)	29.0 (44.5)	.32
Midazolam dose, mean (SD), mg	0.1 (0.4)	0.1 (0.4)	.91
Propofol dose, mean (SD), mg	403.2 (221.8)	436.8 (231.5)	.23
Endoscopy time, mean (SD), min	30.2 (20.6)	32.0 (18.6)	.47
Anesthesia time, mean (SD), min	55.9 (24.8)	58.7 (21.9)	.33

Abbreviations: EGD, esophagogastroduodenoscopy; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; RFA, radiofrequency ablation; SD, standard deviation.

of 36.0%. In our study, 7 patients in the SNC group and 5 patients in the HFNC group had a desaturation below 80%. Two patients in the SNC group and no patient in the HFNC group had a desaturation below 60%. These findings are important because they suggest that HFNC oxygen may enhance patient safety during general anesthesia for advanced endoscopy procedures by reducing the incidence of hypoxemia.

Serious anesthesia-related events such as prolonged hypoxemia or bradycardia occur at a rate of approximately 7 in every 1000 endoscopies.[20] Hypoxemia is more common in advanced endoscopic procedures, which require a longer duration of anesthesia.[6,7] Cardiac arrest occurs at a rate of 4 in every 10,000 endoscopies, but it can result in death and it may be preventable.[21] According to the ASA closed claims registry, the majority of patients who had cardiac arrest from anesthetic overdose received propofol without endotracheal intubation.[2]

Since there are over 6 million EGDs performed each year in the United States and most are with general anesthesia without an endotracheal tube, there is good reason to seek strategies to enhance patient safety.[1] One strategy to reduce hypoxemia is to administer HFNC oxygen, which improves oxygenation by delivering higher inspired oxygen concentrations to the distal airways. Prior studies have shown that HFNC oxygen administration reduces hypoxemia during anesthesia for endoscopy. In 1 quasi-experimental study, the incidence of hypoxemia was reduced during endoscopic ultrasound and ERCP after introduction of HFNC oxygen into standard practice.[22] In a recently published multicenter randomized controlled trial, Lin et al[23] compared HFNC oxygen (60 L/min) with SNC oxygen in almost 2000 outpatients having gastroscopy with propofol sedation. In that study, HFNC oxygen reduced the incidence of a hypoxemia event to 0%.[23] Our study differs from the Lin et al[23] study in that we excluded patients having EGDs that were expected to last <15 minutes. In our study, mean endoscopy time was approximately 30 minutes, compared to 5 minutes in the Lin et al[23] study. Other important differences are that mean BMI was 28 kg/m^2 in our study compared to 22 kg/m^2 in the Lin et al[23] study, and approximately 12% of patients in our study had obstructive sleep apnea compared to 1% in the Lin et al[23] study. These differences could have reduced the incidence of hypoxemia in the Lin et al[23] study compared to ours.

Multiple mechanisms account for the therapeutic effects of HFNC oxygen, including a reduction in dead space, increased positive end-expiratory pressure, increased functional residual capacity, and delivery of higher inspired oxygen concentrations to the distal airways.[24] Oxygen humidification, which some HFNC systems provide, reduces airway constriction and work of breathing.[24] Several HFNC systems are commercially available in the United States, and these systems differ in how many liters of oxygen flow they can provide (40–60 L/min) and whether they add humidification. They also differ in cost. To our knowledge, no HFNC system has been demonstrated to be superior over another in terms of reducing hypoxemia in a randomized controlled trial.

In our study, HFNC oxygen administration reduced the incidence of hypoxemia, but this does not mean

Table 3. Study Outcomes

Variable	Standard Nasal Cannula Oxygen N = 130	High-Flow Nasal Cannula Oxygen N = 132	HR With 95% CI[a]	*P*
Hypoxemia event, n (%)	43 (33.1)	28 (21.2)	0.59 (0.36–0.95)	.03
Hypercarbia event, n (%)[b]	50 (39.4)	63 (49.2)	1.29 (0.89–1.88)	.17
Hypotension event, n (%)	49 (37.7)	60 (45.5)	1.25 (0.86–1.82)	.25

Abbreviations: CI, confidence interval; HR, hazard ratio.

[a]HRs represent the HR for the outcome with high-flow nasal cannula oxygen.

[b]Three patients in the standard nasal cannula oxygen group and 4 patients in the high-flow nasal cannula oxygen group missing hypercarbia data.

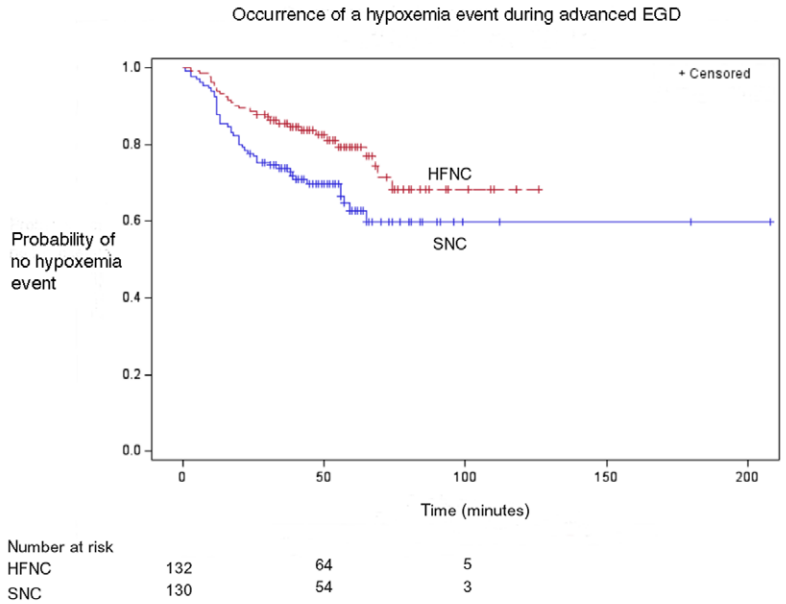

Figure 2. Time-to-event analysis showing freedom from one or more hypoxemia events in HFNC oxygen patients and SNC oxygen patients. Vertical marks on the survival curves represent censoring. EGD indicates esophagogastroduodenoscopy; HFNC, high-flow nasal cannula; SNC, standard nasal cannula.

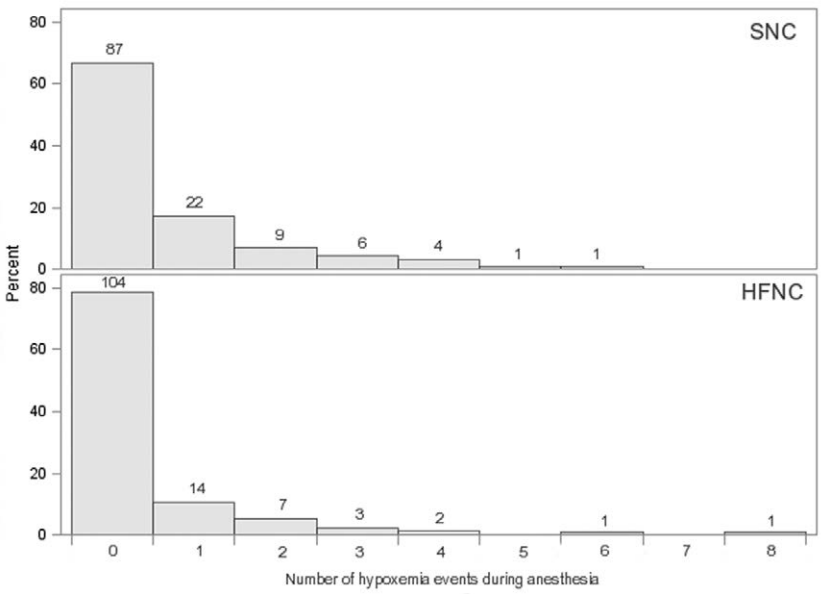

Figure 3. Number of hypoxemia events for each patient in the SNC oxygen and HFNC oxygen groups. The number of patients in each category is listed above each bar. HFNC indicates high-flow nasal cannula; SNC, standard nasal cannula.

that all patients having anesthesia for EGD will benefit from HFNC oxygen administration. The number needed to treat to prevent a hypoxemia event is close to 9 based on our study results. Although this number is relatively low, it is unclear how many patients would need to be treated to prevent a more serious event, such as cardiac arrest or anoxic brain injury. Future studies with many more patients would be necessary to evaluate whether HFNC oxygen administration reduces the incidence of these serious events.

Cost is also an important consideration before implementing HFNC oxygen administration into routine anesthesia practice. The disposable HFNC oxygen circuits used in our study cost approximately $80 per unit compared to $5 for an SNC. Further, an upfront investment was required to purchase the delivery system, which costs approximately $3500.

Our post hoc analyses did not show that obesity or chronic lung disease were effect modifiers for the relationship between HFNC oxygen and hypoxemia; however, they suggested that chronic lung disease was an effect modifier for the relationship between HFNC oxygen and hypercarbia. Patients with chronic lung disease who received HFNC oxygen had a significantly higher incidence of hypercarbia. This finding was not anticipated, as several previous studies have reported improved ventilation and carbon dioxide clearance with HFNC oxygen.[25,26] Our study population differs in that patients were anesthetized, and approximately one-third of patients were hypoventilating based on transcutaneous carbon dioxide measurements. High levels of supplementary oxygen can worsen hypercarbia in COPD patients because of changes in hypoxic pulmonary vasoconstriction and physiologic dead space.[27] They can also reduce hypoxemic respiratory drive and increase blood carbon dioxide levels because of the Haldane effect.[28] Since HFNC oxygen administration worsened hypercarbia in patients with chronic lung disease in our study, caution should be exercised when using HFNC to reduce hypoxemia during anesthesia in this patient population.

Our study has important limitations. First, although HFNC oxygen reduced the incidence of hypoxemia in our study, clinical definitions for hypoxemia vary and there is ambiguity about what constitutes a clinically "significant" hypoxemia event. Second, our study may have been underpowered to detect a significant difference in the incidence of hypercarbia or hypotension between groups. Third, it is unclear whether higher oxygen flows (eg, 40–60 L/min) could have reduced the risk of hypoxemia further. At higher flows, end-tidal carbon dioxide monitoring becomes inconsistent in our experience, but future studies are needed to confirm this. Fourth, our study findings may not be generalizable to routine EGD procedures of shorter duration. Fifth, there were several protocol deviations in the SNC group, with some patients having their oxygen flows below 6 L/min during anesthesia. Finally, our study did not evaluate the duration of a hypoxemia event.

In summary, in a randomized controlled trial that compared HFNC oxygen and SNC oxygen in patients having anesthesia for advanced EGD, we demonstrated that HFNC oxygen significantly reduced the incidence of having one or more hypoxemia events from 33.1% to 21.2%. Based on these findings, HFNC oxygen may offer an opportunity to enhance patient safety during anesthesia for advanced EGD. ■

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DISCLOSURES

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