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Original Contribution

High-flow nasal cannula improves pulmonary gas exchange during endoscopic retrograde cholangiopancreatography: A single-center randomized controlled trial

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HIGHLIGHTS

- In high-risk ERCP sedations, HFNC + did not prevent hypoxemia, but was associated to shorter and less severe events in post-hoc analyses.
- HFNC enhanced CO_2 clearance, decreasing both the incidence and severity of hypercapnia and respiratory acidosis.
- The benefits of HFNC extend beyond improved oxygenation, especially during prolonged procedures and in patients at high risk of hypercapnia.

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ABSTRACT

Background: Sedation during endoscopic retrograde cholangiopancreatography procedures (ERCP) increases the risk of hypoxemia and the need for respiratory support in high-risk patients. High flow nasal cannula (HFNC) provides humidified gas at high flow rates, improving alveolar ventilation. We aim to assess whether ventilatory support with HFNC improves gas exchange compared to standard low-flow nasal cannula (NC).

Methods: Single-center, randomized controlled trial, in adults undergoing ERCP. After providing informed consent, participants were randomized in a 1:1 ratio following obstructive sleep apnea (OSA) stratification to receive ventilatory support with HFNC (60 $L \cdot min^{-1}$, FiO_2 0.4) or NC (6 $L \cdot min^{-1}$). All procedures were performed under deep sedation. We collected clinical data, ECG, pulse oximetry (SpO2), blood pressure, Bispectral index, rescue airway maneuvers, and transcutaneous carbon dioxide ($PtCO_2$). The primary outcome was the incidence of hypoxemic events defined as $SpO_2 < 90\%$ lasting ≥ 15 s; the secondary outcome was $PtCO_2$, and the exploratory was need for airway rescue maneuvers. Post-hoc analyses explored the HFNC effect on the severity and duration of hypoxemia using the area under a threshold (AUC) for $SpO_2 < 90\%$.

Results: 191 patients were included (38% female, median age 67 years, 59% ASA III-IV, and 38% with OSA). A total of 92 patients were randomized to HFNC and 99 to NC. Sixteen (8%) patients presented hypoxemic events ($SpO_2 < 90\%$) and 64 (33%) needed airway rescue maneuvers. HFNC did not significantly reduce the incidence of hypoxemic events (3 vs. 13; $p = 0.05$). However, HFNC significantly reduced hypercapnia with lower $PtCO_2$ (HFNC, 51 [44–59] vs. NC, 56 [45–75] mmHg; $p < 0.005$), and the AUC for $SpO_2 < 90\%$ (HFNC, 175[167–226] vs. NC, 268[241–342] %·min; $p < 0.001$).

Conclusions: HFNC did not reduce the incidence of hypoxemic events. However, it resulted in a reduction of hypercapnic events.

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1. Introduction

Over 600,000 endoscopic retrograde cholangiopancreatography (ERCP) procedures are performed annually in the United States. [1] ERCP is a complex intervention used for the diagnosis and treatment of biliary and pancreatic diseases. The procedure is typically performed in the prone position. To ensure optimal conditions for therapeutic intervention as well as patient safety and comfort, either deep sedation or general anesthesia is required. [2] [3] Although, both anesthesia techniques are utilized during ERCP, current trends [2] [3] [4] and expert recommendations [5] favor the use of deep sedation. Nevertheless, respiratory depression remains the most frequent sedation-related adverse event during ERCP, particularly among sicker and those with obstructive sleep apnea (OSA). [6] Notably, despite the routine use of low-flow supplemental oxygen via nasal cannulas (NC), hypoxemia has been reported in up to 60% of ERCP procedures. [7] At the same time, hypercapnia often goes undetected, [8] though it may be common due to sedation-induced hypoventilation, which is further exacerbated by the continuous CO_2 insufflation required during ERCP. [9]

Ventilatory support using high-flow nasal cannula (HFNC) is widely used in critical care settings, as it reduces hypoxemia and hypercapnia in critically ill patients. [10] Compared to NC, HFNC allows the delivery of a higher and more consistent concentration of inspired oxygen. Additionally, it provides a degree of positive airway pressure, which can decrease the incidence of upper airway obstruction. As a result, HFNC has been increasingly adopted during procedural sedation outside of the operating room. [11–13] Previous studies suggest that employing HFNC during ERCP under sedation may lower the risk of hypoxemic events in low risk patients, though this benefit is not clear in elderly and high-risk patients. [14] Likewise, there is currently no evidence on the impact of HFNC on the occurrence of hypercapnia, nor on its potential benefits in specific patient populations—such as individuals with OSA—who are especially prone to ventilatory dysfunction during deep sedation. [15]

Therefore, we aimed to evaluate whether ventilatory support with HFNC improves gas exchange compared to NC. Specifically, we tested the hypothesis that, in adult patients undergoing ERCP under deep sedation, HFNC reduces the incidence of hypoxemic events compared to NC. Secondarily, we evaluated whether HFNC decreases the occurrence of hypercapnia. Finally, we also evaluated the need for airway rescue maneuvers.

2. Methods

2.1. Study design

This is a prospective, randomized controlled trial conducted at a single tertiary academic hospital (Hospital Clínic, Barcelona, Spain). The study protocol was approved by the Ethics Committee for Clinical Research of Hospital Clínic Barcelona (HCB/2019/0491) and registered at ClinicalTrials.gov (NCT04082208). The trial was designed in compliance with the fundamental principles established in the Declaration of Helsinki and the Convention of the European Council related to human rights and biomedicine and it follows the CONsolidated Standards of Reporting Trials (CONSORT). [16]

2.2. Study participants

We prospectively enrolled adult patients (over 18 years) scheduled to undergo ERCP under deep sedation in our endoscopy unit.

2.3. Randomization and masking

After participants received detailed study information and provided written informed consent, we assessed for obstructive sleep apnea (OSA) and use of continuous positive airway pressure (CPAP) therapy. For patients without a prior diagnosis of OSA, the STOP-BANG questionnaire was used for screening. [17] Randomization was then performed using a 1:1 allocation ratio, stratified by OSA status. The randomization sequence was generated by an independent investigator not involved in patient recruitment or data collection. Allocation concealment was maintained using sequentially numbered, opaque, sealed envelopes that were opened only after patient eligibility was confirmed. Due to study characteristics, anesthesiologists and patients were not blinded to intervention.

3. Study procedures

3.1. Monitoring

Prior to the procedure, patients' demographics, medical history, medication use, and fasting times were collected. Upon placement in the prone position, patients were continuously monitored using electrocardiography, non-invasive blood pressure, pulse oximetry (SpO_2), respiratory rate with impedance, bispectral index (BIS™, Medtronic), and transcutaneous carbon dioxide ($PtCO_2$) measured at the earlobe or face (SenTec®, Therwil, Switzerland).

3.2. Study protocol

Ventilatory support began prior to sedation in both groups. The HFNC group received humidified oxygen via the Optiflow THRIVE® system (Fisher & Paykel Healthcare, New Zealand) at 60 $L \cdot min^{-1}$ with an FiO_2 of 0.4. The control group received oxygen via standard nasal cannula at $6 \cdot L \cdot min^{-1}$, which yields a similar estimated 0.4 FiO_2 in the distal airway. [18]

3.3. Anesthesia management

Sedation was administered via a target-controlled infusion (TCI) system using propofol and remifentanil. Initial effect-site concentrations (Ce) were set at 1.5 μg/mL for propofol and 1.5 ng/mL for remifentanil. After allowing 3–5 min to reach Ce, adjustments in 0.3 unit increments were made to achieve a Ramsay Sedation Score of 4. [19] In cases of excessive sedation (Ramsay $\geq$5, respiratory rate $<$ 6 breaths/min, or signs of airway obstruction) Ce was reduced and/or airway rescue maneuvers were implemented.

3.4. Rescue maneuvers

In cases of hypoxemia (SpO_2 <90%), both groups received standard rescue airway interventions (jaw thrust, mouth opening, nasopharyngeal airway). If hypoxemia persisted, FiO_2 was increased to 1.0 for HFNC or oxygen flow to 10 $L \cdot min^{-1}$ for NC. In refractory cases, the procedure was paused and manual ventilation via face mask was used. After ERCP, patients were placed in the supine position and transferred to the post-anesthesia care unit once full consciousness, spontaneous breathing, and hemodynamic stability were confirmed.

3.5. Outcomes

The primary outcome was the incidence of hypoxemic events, defined as $SpO_2 < 90\%$ lasting $\geq$15 s, a threshold established to exclude artifacts, after clinical trial registration but before data analysis. The secondary outcome was transcutaneous CO_2 values, and the exploratory outcome was the need for airway rescue maneuvers (jaw thrust, mouth opening, nasopharyngeal cannula insertion).

3.6. Data collection and variables

Continuous monitoring data (heart rate, blood pressure, SpO_2, BIS values, and $PtCO_2$) as well as TCI infusion parameters were recorded using the Vital Recorder system (VitalDB, Seoul National University

Hospital, Republic of Korea). [20] Data were captured at a high resolution (1 Hz) and allowed for real-time manual annotation of clinical events. The number of desaturation episodes, procedure interruptions, and need for mask ventilation were documented. Additionally, venous blood samples were collected at the end of ERCP to measure oxygen (PvO_2), carbon dioxide ($PvCO_2$), and pH. We also registered adverse events defined as: hypotension, mean arterial pressure < 60 mmHg; bradycardia, heart rate below 50 b.p.m.; low BIS (BIS<50); severe hypercapnia ($PtCO_2 > 70$ mmHg); severe respiratory acidosis (pH < 7.25); and gag and movement response to endoscopy insertion.

3.7. Statistical analysis

Categorical variables are described as counts (percentages), while continuous variables are expressed as mean ± standard deviation (SD) for normally distributed data, and as median with interquartile range [IQR] for non-normally distributed data. For both the primary and secondary analyses, we compared the incidence of hypoxemic events, use of rescue maneuvers, and hypercapnia across groups using the Chi-squared test or Fisher's exact test, as appropriate. For continuous variables, comparisons were made using the independent samples t-test or the Mann–Whitney U test, depending on the distribution. We performed a pre-defined analysis stratified to the presence of OSA. We also conducted four post-hoc analyses: first, we tested the primary hypothesis on a sub-group of sicker patients (American society of Anesthesiology status (ASA) III-IV); second, we tested the effect of HFNC on the incidence of mild hypoxemic events, defined as $SpO_2 < 92\%$. Finally, we assessed the severity and duration of hypoxemic events using the area under a threshold (AUC) of SpO_2 <90% and SpO_2 <92%. [21] All statistical analyses were done according to an intention-to-treat approach and were conducted using R software (version 4.3.1), and a p-value <0.05 was considered statistically significant. The datasets generated and analyzed during the current study will be available from the corresponding author upon reasonable request. The prespecified statistical analysis plan is available in the study protocol included as Supplementary material.

3.8. Sample size calculation

The sample size was calculated to assess whether the incidence of hypoxemic events (defined as SpO_2 <90%) could be significantly reduced in HFNC group compared to the NC group. Based on prior literature, the expected incidence of hypoxemic events in the control group was estimated at 40%. A clinically relevant reduction was defined as a 50% decrease, corresponding to an incidence of 20% in the HFNC group.

Using a two-sided test with a significance level (α) of 0.05 and a statistical power (1–β) of 80%, the required sample size was calculated based on the comparison of two independent proportions. This resulted in a minimum of 162 patients (81 per group). To account for an anticipated 5% dropout rate, the total required sample size was adjusted to 172 patients. Ultimately, a total of 191 patients were enrolled, providing a higher than planned statistical power to detect the intervention effect.

4. Results

From November 2022 to October 2023, a total of 197 patients were screened for eligibility, of whom 191 met the inclusion criteria and were included in the study. After stratification for OSA, 73 patients with OSA and 118 without OSA were randomized to receive either HFNC or NC (Fig. 1). In total, 92 patients were assigned to the HFNC group and 99 to the NC group.

Of the 191 patients, 74 (38%) were female, median age was 67 [57–79] years, and the median body mass index was 25 [23–28] kg/m^2. Most patients were classified as ASA II ($n = 71$, 37%) or ASA III ($n = 109$, 57%). Demographic and clinical characteristics were balanced between groups, including the presence of OSA (Table 1).

Thirty-eight procedures (19%) were non-elective, with an overall median procedure duration of 30 [19–39] minutes. Mean effect-site concentrations of propofol and remifentanil ranged from 2.02 to 2.20 μg/mL and 1.02–1.40 ng/mL, respectively, to maintain a BIS near 60. There were no significant differences in anesthetic dosing between groups (Table 1).

Sixteen (8%) patients presented severe hypoxemic events (SpO_2 <90%) while mild hypoxemic events (SpO_2 <92%) occurred in 28 (15%) patients. Sixty-four (33%) patients required airway rescue maneuvers. HFNC did not significantly reduce the incidence of hypoxemic events (3 vs. 13; $p = 0.05$) or mild hypoxemic events (10 vs. 18; $p = 0.10$) compared to NC. Among patients who experienced hypoxemic events, the mean number of events per patient was similar between groups: 1.5 ± 0.7 in the HFNC group versus 1.6 ± 0.7 in the NC group.

In the post-hoc analysis, HFNC significantly reduced both the severity and duration of hypoxemia, as reflected by a lower median AUC for SpO_2 <90%: 175 [167–226] vs. 268 [241–342] %·min in the HFNC and NC groups, respectively ($p < 0.001$) (Table 2, Fig. 2).

HFNC patients also had lower maximum $PtCO_2$ values during the procedure (51 [44–59] vs. 56 [45–75] mmHg; $p < 0.005$) and a slower rate of $PtCO_2$ increase (0.15 vs. 0.19 mmHg·min^{-1}) mean difference − 0.04 mmHg·min^{-1} (95% CI: 0.03–0.06); p < 0.001) (Fig. 3). Venous blood gas analysis at the end of the procedure confirmed lower $PvCO_2$ levels in HFNC patients (51 [47–55] mmHg) compared to NC patients (58 [49–65] mmHg; p < 0.005) (Table 2). Finally, there was a trend toward a lower incidence of airway obstruction in the HFNC group (24 patients, 26%) compared to the NC group (40 patients, 40%) (Table 2).

4.1. Adverse events

The overall incidence of adverse events included: hypotension ($n = 40$, 20%), bradycardia ($n = 22$, 11%), low BIS ($n = 48$, 24%), severe hypercapnia ($PtCO_2$ >70 mmHg; n = 40, 20%), severe respiratory acidosis (pH <7.25; $n = 54$, 28%), gag response to endoscope insertion ($n = 15$, 7%), and movement in response to endoscope insertion ($n = 80$, 40%). No significant differences in overall adverse events were observed between groups, except for a significantly lower incidence of severe hypercapnia (9.9% vs. 30.3%) and reduced movement responses to endoscope insertion (30% vs. 51%) in the HFNC group ($p < 0.05$ for both) (Table 3). All procedures were completed without interruption, and no patient required manual ventilation or conversion to general anesthesia.

4.2. OSA sub-analysis

Of the 191 patients, 73 (38%) had OSA. The pre-defined subgroup analysis revealed no significant difference in the incidence of hypoxemic events among OSA patients treated with HFNC. However, among non-OSA patients, those treated with HFNC had lower incidence of hypoxemic events (2 vs. 11; $p < 0.01$) (**Supplemental Table 1**). HFNC also reduced the severity and duration of hypoxemia in both OSA and non-OSA patients with an AUC for SpO_2 <90% lower in HFNC patients (OSA: 204 [194–244] vs. 244 [206–289] %·min and non-OSA: 151 [128–218] vs. 291 [258–376] %·min ($p < 0.05$, each)). Finally, HFNC did not reduce the need for airway rescue maneuvers but was associated with significantly lower median $PtCO_2$ (OSA, 44 vs. 51 mmHg; $p = 0.04$; Non-OSA, 44 vs. 47 mmHg; $p = 0.02$) and median venous CO_2 (OSA, 51 vs. 57 mmHg; $p = 0.03$; Non-OSA, 51 vs. 55 mmHg; $p = 0.006$) in both groups.

4.3. ASA score III-IV sub-analysis

A post-hoc analysis of patients with higher comorbidity (ASA III–IV; $n = 112$) showed that HFNC did not significantly reduce the number of hypoxemic events (1.2 ± 0.4 vs. 1.4 ± 0.5), mild hypoxemic events (1.6

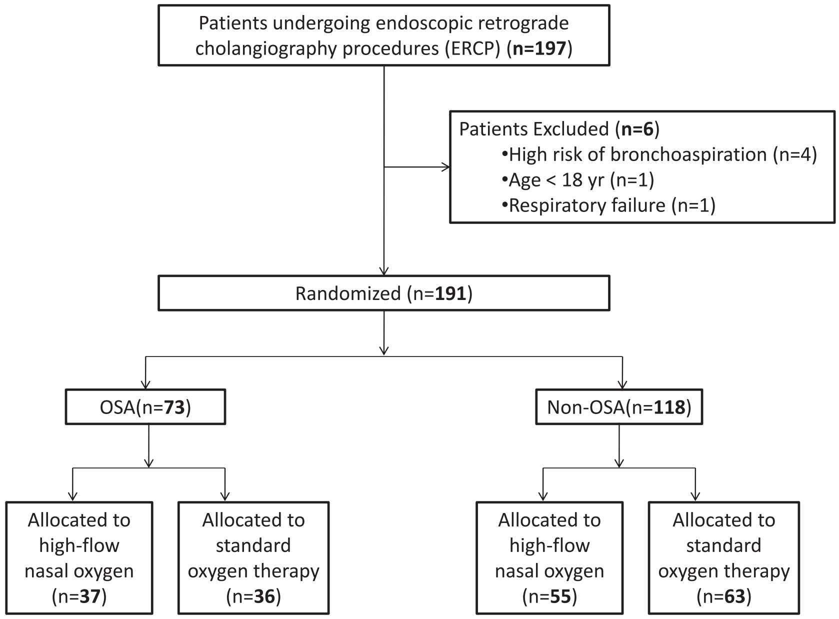

Fig. 1. Flow Chart.

Table 1
Patients and Procedure Characteristics.

	High-flow nasal cannula (n = 92)	Nasal cannula (n = 99)	*P value*
Patients Characteristics			
Age (years)	70 [57–79]	64 [54–76]	0.396
Sex, Male/Female, n	53 (58)/39 (42)	64 (65)/35 (35)	0.245
BMI (kg/m^2)	25 [23–29]	25 [23–27]	0.313
ASA-PS (I/II/III/IV),n	3(3)/33(36)/ 54(59)/2(2)	5(5)/38(38)/ 55(56)/1 (1)	0.816
OSA, n	37 (40)	36 (36)	0.965
Smoking, n	11 (12)	11 (11)	0.619
COPD, n	8 (9)	5 (6)	0.477
ICM, n	8 (9)	4 (4)	0.305
Hypertension, n	56 (61)	50 (51)	0.196
DM, n	35 (38)	22 (22)	**0.030**
ERCP Procedure Characteristics			
Duration (min)	28 [19–36]	33 [19–39]	0.874
Elective/Urgent procedures, n (%)	76 (87) /16 (17)	77 (78) /22 (22)	0.513
Ce Propofol (μg/ml)	2.22 [2.00–2.48]	2.20 [1.99–2.29]	0.205
Ce Remifentanil (ng/ml)	1.02 [1.01–1.32]	1.40 [1.40–1.50]	0.102
BIS	61 [49–67]	62 [55–70]	0.740

The qualitative data are presented as n (%), and the numerical data are presented as the median [Interquartile range (IQR)].
Abbreviations: BMI, body mass index; ASA-PS, American Society of Anesthesiologists physical status classification; OSA, obstructive sleep apnea; COPD, chronic obstructive pulmonary disease; ICM, ischemic cardiomyopathy; DM, diabetes mellitus; ERCP, endoscopic retrograde cholangiopancreatography; Ce, effect-site concentration; BIS, bispectral index.
The p values show significance at $p < 0.05$.

Table 2
Primary and Secondary outcomes.

	High-flow nasal cannula (n = 92)	Nasal cannula (n = 99)	*P value*
Hypoxemic events (SpO_2 < 90%), n	3 (3)	13 (13)	0.055
Episodes of SpO_2 < 90% per patient	1.5 ± 0.7	1.6 ± 0.7	0.714
Mild hypoxemic events (SpO_2 < 92%), n	10 (11)	18 (18)	0.100
Episodes of SpO_2 < 92% per patient	1.6 ± 1.0	1.7 ± 1.0	0.894
AUC of SpO_2 < 90%	175 [167–226]	268 [241–342]	**0.001**
AUC of SpO_2 < 92%	238 [220–265.9]	302 [278–382]	**0.001**
Airway rescue events, n	24 (26)	40 (40)	0.052
Transcutaneous Carbon dioxide monitoring			
$PtCO_2$ -mean, mmHg	44 [37–56]	48 [39–60]	**0.002**
$PtCO_2$-median, mmHg	45 [39–53]	48 [39–60]	**0.004**
$PtCO_2$-max, mmHg	51 [44–59]	56 [45–75]	**0.001**
Venous Blood Gasses			
$PvCO_2$, mmHg	51 [47–55]	58 [49–65]	**0.004**
PvO_2, mmHg	86 [64–108]	77[58–101]	**0.032**
pH	7.30 [7.26–7.32]	7.26 [7.21–7.30]	0.627

The qualitative data are presented as n (%), and the numerical data are presented as the average ± standard deviation or median [Interquartile range (IQR)]. Airway manipulation includes need to use an oral or nasal cannula or to do Esmarch.
Abbreviations: SpO_2, Pulse oximeter saturation; $PtCO_2$, transcutaneous carbon dioxide. $PvCO_2$, carbon dioxide pressure; PvO_2, Oxygen pressure.
The p values show significance at $p < 0.05$.

± 1.0 vs. 1.3 ± 0.5), or airway rescue maneuvers (17 vs. 47) compared to NC. However, HFNC significantly reduced hypercapnia, with median $PtCO_2$ levels of 42 [37–47] mmHg vs. 51 [39–58] mmHg in the NC group ($p < 0.005$).

5. Discussion

In this randomized controlled trial, we found that while HFNC did not significantly reduce the incidence of hypoxemic events, it substantially decreased their duration and severity. More notably, HFNC was associated with improved CO_2 clearance, evidenced by lower transcutaneous and venous CO_2 levels and reduced rates of severe hypercapnia and respiratory acidosis. These findings suggest a ventilatory advantage of HFNC that extends beyond its oxygenation benefits.

HFNC provides humidified gas at high flow rates, improving alveolar ventilation through anatomical dead space washout and generation of low-level positive airway pressure. [22] At flow rates ≥50–60 L·min^{-1},

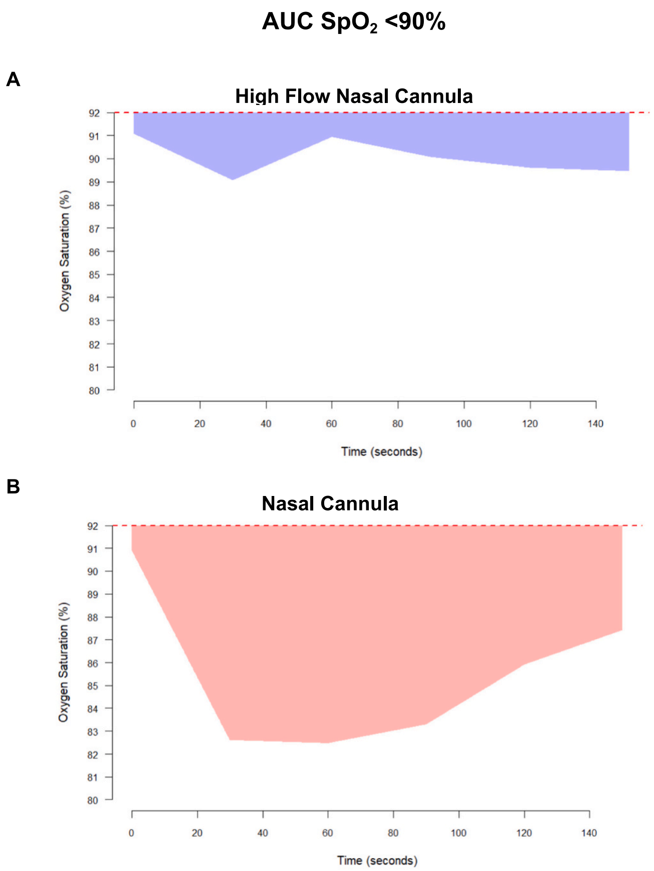

Fig. 2. Area under the curve for a value of SpO2 < 90% during ERCP procedures with sedation. **A** (upper panel), patients with ventilatory support with high-flow nasal cannula (HFNC at 60 L·min^{-1} with an FiO_2 of 0.4). **B** (bottom panel), patients with ventilatory support with standard nasal cannula at 6·L·min^{-1}, with an estimated 0.4 FiO_2.

this pressure can help maintain upper airway patency, increase functional residual capacity, and keep the alveoli open, reducing the cyclic collapse "de-recruitment". [23] These effects collectively support more effective gas exchange and may explain the reduced severity and duration of hypoxemic and hypercapnic events observed in our study.

In our cohort of high-risk patients (59% ASA III–IV, 38% with OSA), the incidence of hypoxemia was consistent with previously reported rates (8–21%). [24] [25] [26] HFNC did not significantly alter the incidence of hypoxemic episodes, but reduced their duration and severity, as measured by the area under the SpO_2 <90% threshold. Although this was found in a post-hoc analysis and should therefore be considered with caution, it is a common and logical method to consider hypoxemia burden, accounting not only for the number of events, but also their duration and severity. Previous randomized controlled trials and meta-analyses comparing HFNC and conventional low-flow nasal cannula oxygen therapy during ERCP showed a reduction in hypoxemic events during ERCP in patients with low risk for hypoxemia, [7] [27] but this benefit was not clear in high-risk patients, like our population. [15] [28] [29] [30,31] One factor that may explain this discrepancy is the difference in oxygen concentration used across studies: trials reporting stronger effects commonly delivered 100% oxygen, [29,30] while we selected a standardized FiO_2 of 0.4 in both groups. [29,32] This approach allowed us to isolate the physiological benefits of HFNC, such as positive airway pressure and dead-space washout—without confounding from varying oxygen levels. It also prioritized patient safety, particularly in our ASA III cohort with a high prevalence of OSA, in whom higher FiO_2 levels may exacerbate hypoventilation and promote absorption atelectasis. Although HFNC did not significantly reduce the need for airway rescue maneuvers, we observed a trend toward fewer interventions. This aligns with studies reporting limited benefit in high-risk populations but suggests a possible role in lower-risk or longer-duration procedures. [7].

Subgroup analysis revealed that HFNC significantly reduced hypoxemic events in non-OSA patients only. The modest airway pressure generated by HFNC may be insufficient to counter upper airway collapse in patients with OSA, particularly during mouth opening from bite blocks or endoscope insertion. [33]

Hypercapnia is an underrecognized complication during deep sedation, with potential neurological and cardiovascular consequences. [34] Our study showed that HFNC significantly reduced the incidence and magnitude of hypercapnia, as well as the rate of CO_2 accumulation. These findings support the hypothesis that HFNC enhances CO_2 clearance through reduced dead space and improved ventilation. Continuous $PtCO_2$ monitoring was instrumental in detecting these differences and may be preferable to end-tidal CO_2 in non-intubated patients. [35]

Previous findings on HFNC's effect on hypercapnia have been inconsistent, [15,28–30] and a recent metanalysis by *Wei* et al. [31] showed that although HFNC significantly reduced hypoxemia and the need for airway interventions, it did not lead to a significant reduction in hypercapnia levels. [31] Variability in sedation depth, procedure duration, HFNC flow, and CO_2 monitoring methods may explain the discrepancies. Our results support the utility of HFNC in managing ventilation, especially during high-risk or prolonged procedures.

5.1. Strengths and limitations

The strengths of this study include the use of a standardized sedation protocol based on target-controlled infusion (TCI) of propofol and remifentanil, continuous monitoring of sedation depth using both BIS and Ramsay scores, and automated physiological data capture through the Vital Recorder system. Additionally, all data were analyzed by an evaluator blinded to group assignment, ensuring objective assessment. Importantly, continuous and reliable $PtCO_2$ monitoring was performed alongside venous blood gas analysis. This comprehensive approach enabled a precise and high-resolution evaluation of both oxygenation and ventilation dynamics throughout the procedure.

There are several limitations. Its single-center nature may limit generalizability. The lack of intervention blinding could introduce performance bias, although objective outcomes (e.g., SpO_2, $PtCO_2$) were automatically recorded. The use of FiO_2 0.4 and the short procedure duration (~30 min) may have attenuated HFNC's oxygenation benefit. Hypoxemia was defined as SpO_2 <90% sustained for ≥15 s, a threshold established after clinical trial registration but before data analysis to exclude brief, artifactual signal drops detected in automated continuous recordings and to capture clinically significant desaturation events. The analyses of AUC, mild hypoxemia and ASA were post-hoc and potentially subject to bias. However, these variables were defined prior to performing any statistical analyses. Additionally, factors like mouth opening and endoscope interference may have reduced airway pressure delivery. The study did not assess post-procedural outcomes or endoscopist satisfaction. Finally, while transcutaneous CO_2 monitoring proved useful, its cost may limit widespread adoption.

6. Conclusion

HFNC did not reduce the incidence of hypoxemic events. However, it resulted in a reduction of hypercapnic events. HFNC could be advantageous in high-risk populations or procedures where hypercapnia is a concern.

CRediT authorship contribution statement

Julia Martínez-Ocón: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration,

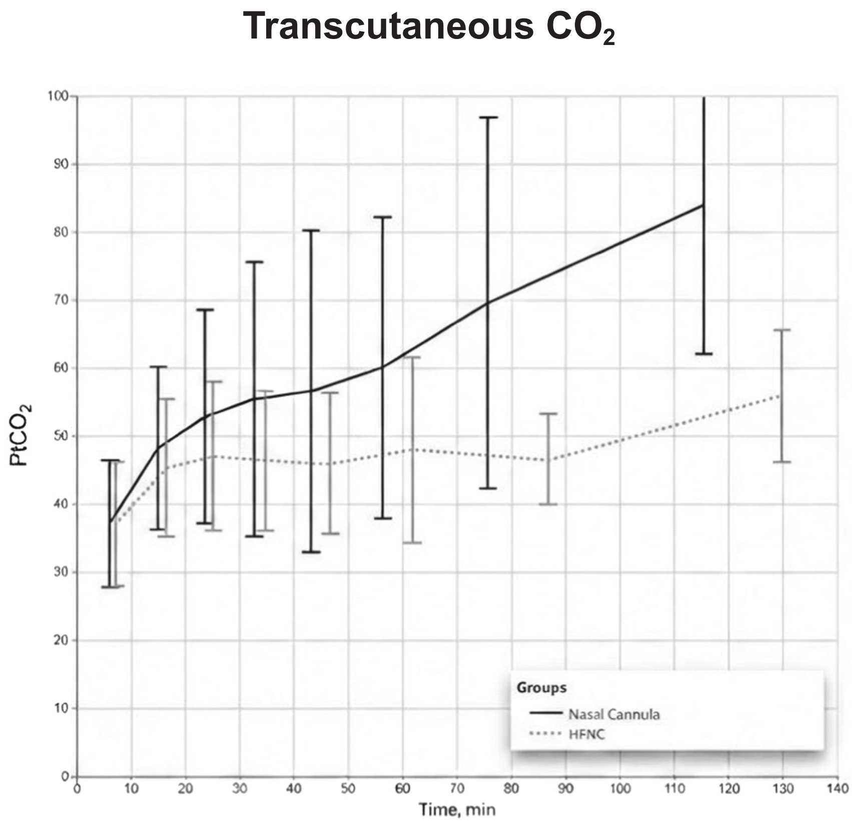

Fig. 3. Rate of transcutaneous CO_2 ($PtCO_2$) increase in patients during ERCP under sedation with ventilatory support with high-flow nasal cannula (HFNC) in **red color** and standard nasal cannula in **blue color**. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 3
Incidence Of Adverse Events.

	HFNC (n = 92)	NC (n = 99)	*P value*
Hypotension (MAP<60 mmH)*, n	16(17)	23 (24)	0.326
Bradycardia (Heart rate < 50 bpm)*, n	11 (12)	11 (11)	0.911
Low BIS (BIS<50), n	22 (25)	26 (26)	0.710
Hypercapnia ($PtCO_2$ > 70 mmHg)*, n	9 (10)	30 (30)	**0.001**
pH < 7.25, n	14 (15)	40 (40)	**0.003**
Gag response to endoscopy insertion, n	5 (6)	9 (9)	0.412
Movement response to endoscopy insertion, n	30 (30)	50 (51)	**0.023**

The adverse events data are presented as n (%).
MAP, mean arterial pressure; BIS, Bispectral index; $PtCO_2$, transcutaneous CO_2 values.
Statistical significance at P values <0.05.
* An adverse event was defined if the episode lasted for more than 2 min.

Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Maria Pérez:** Writing – review & editing, Writing – original draft, Software, Methodology, Formal analysis. **Andrea Calvo:** Writing – review & editing, Writing – original draft, Validation, Investigation, Data curation, Conceptualization. **Josep Sanahuja:** Writing – review & editing, Writing – original draft, Validation, Methodology, Data curation. **Marc Salazar:** Writing – review & editing, Writing – original draft, Software, Data curation. **Andrés Cárdenas:** Writing – review & editing, Writing – original draft, Visualization, Validation. **Pedro L. Gambús:** Writing – review & editing, Writing – original draft, Software, Methodology. **Carlos Ferrando:** Writing – review & editing, Writing – original draft, Validation, Supervision, Conceptualization. **Eva Rivas:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Graciela Martínez-Pallí:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Formal analysis, Conceptualization.

Ethical statement

The study received approval from Ethics Committee for Clinical Research of Hospital Clínic Barcelona (HCB/2019/0491).

The study was registered at ClinicalTrials.gov (NCT04082208).

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Fisher & Paykel (Fisher & Paykel Healthcare, New Zealand) provided the single-use HFNC equipment used in this study. The company had no involvement in the study design, data collection, analysis, interpretation, or manuscript preparation.

Declaration of competing interest

The authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinane.2026.112189.

Data availability

The datasets generated and analyzed during the current study will be available from the corresponding author upon reasonable request.

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