

Meta-Analysis

The Usefulness of Nasal High Flow in Endoscopic Retrograde Cholangiopancreatography: A Systematic Review and Meta-Analysis

Shunzhe Song¹, Shen Zhang², Xu Wang^{3,*}

¹Digestive Endoscopy, First Affiliated Hospital of Dalian Medical University, Dalian, China.

²Department of Gastroenterology, The Fourth Affiliated Hospital of China Medical University, Shenyang, China.

³Department of Gastroenterology, The First Hospital of China Medical University, Shenyang, China.

*Corresponding Author: e-mail: wangxu_cmu@163.com

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Clinical Question Box

Is nasal high flow useful in the procedure of endoscopic retrograde cholangiopancreatography?

Compared to standard care, nasal high flow has shown to be more effective as the preferred method for oxygen delivery during endoscopic retrograde cholangiopancreatography. It reduces the incidence of hypoxemia and is associated with higher minimum percutaneous oxygen saturation and lower carbon dioxide partial pressure levels. However, extensive cost-effectiveness studies are lacking in supporting this conclusion fully.

Abstract

Introduction: Endoscopic Retrograde Cholangiopancreatography (ERCP) is a critical procedure in gastroenterology, typically performed under sedation with the administration of supplemental oxygen. Nasal High Flow (NHF) is a newer method of oxygen administration combined with sedation for oxygen delivery. This meta-analysis was designed to identify the effects of NHF during ERCP. **Method:** Three major online databases (PubMed, Web of Science, and Cochrane) were searched on July 30, 2024. The search was not limited by publication language and focused on randomized controlled trials that compared the use of NHF with usual care in patients undergoing ERCP. **Results:** A total of 198 studies were identified after searching the three databases. Finally, five studies, encompassing a total of 581 patients, were included in the meta-analysis. The pooled analysis showed that using NHF was associated with a significantly lower incidence of hypoxemia than usual care. The odds ratio was 0.29 (95% Confidence Interval [CI]: 0.14–0.60, $p < 0.001$, $I^2 = 21\%$). The NHF group showed a higher minimum SpO₂ value during the procedure, with a 2.55% increase in the mean difference (95% CI: 0.96, 4.13, $p = 0.002$; $I^2 = 57\%$). Compared to the usual care group, the NHF group demonstrated a reduction in CO₂ partial pressure level at the end of the procedure, with a mean difference of 1.83 mmHg (95% CI: –3.25, –0.42, $p = 0.01$; $I^2 = 0\%$). The duration of ERCP showed no statistically significant difference between the usual care group and the NHF group, with a mean difference of 0.7 min (95% CI: –0.14, 1.53, $p = 0.1$; $I^2 = 0\%$). **Conclusion:** NHF effectively reduces the incidence

of hypoxemia, supporting its consideration as the preferred method of oxygen delivery during ERCP, particularly for patients at higher risk of respiratory complications.

Keywords: Nasal High Flow, Endoscopic Retrograde Cholangiopancreatography, sedation, NHF, ERCP.

Introduction

Endoscopic Retrograde Cholangiopancreatography (ERCP) is a crucial procedure in gastroenterology, primarily used for the treatment of bile duct and pancreatic duct stones, as well as malignancies in these ducts.¹ Sedation and anesthesia are typically administered to alleviate patient discomfort and anxiety, improve the quality of the procedure, and reduce the patient's recollection of it.² However, ERCP carries significant risks, including pancreatitis, bleeding, perforation, cholangitis, and complications related to sedation, such as hypoxia.³ Hypoxemia occurs in 3–30% of gastrointestinal endoscopy cases,⁴ is the most frequent sedation-related issue and poses particular concerns for patients with pre-existing respiratory or cardiovascular conditions, as it may worsen these conditions, thereby increasing the risk of serious complications and mortality.⁵

Sedation during ERCP often involves using a low-flow nasal oxygen cannula or a mouthguard with an oxygen delivery port.⁶ When nasal oxygen is administered at flow rates between 2 L/min and 4 L/min, assuming nasal breathing only, the fraction of inspired oxygen (FiO₂) can reach 0.3–0.4.⁷ However, the actual FiO₂ may vary and decrease with mouth breathing due to its dependence on minute volume. Nasal High Flow (NHF) is a newer technique for enhancing oxygenation during sedation. It can deliver oxygen at rates of up to 70 L/min, offering an FiO₂ of up to 100% while also generating flow-dependent positive airway pressure, which can improve oxygenation.⁸ The use of NHF oxygen therapy has shown considerable progress in various medical settings, particularly in neonatal, pediatric, and adult critical care. Initially developed for neonatal and pediatric intensive care units to reduce intubation rates and improve respiratory outcomes, NHF has now been adopted in adult populations, especially during procedures requiring sedation.⁹ This therapy enhances oxygen delivery, assists in CO₂ clearance, reduces dead space ventilation, and provides some level of positive airway pressure.¹⁰

Nasal High-flow oxygen therapy has gained attention as a possible strategy to reduce the risks of hypoxemia and other respiratory complications during sedated procedures like ERCP.¹¹ Its mechanism involves delivering oxygen at high flow rates, thereby generating slight positive end-expiratory pressure, which enhances oxygen delivery efficiency.¹² The application of NHF in ERCP is a relatively new area of exploration. Emerging studies suggest that NHF may reduce the incidence of hypoxemia during ERCP by providing more stable oxygenation than traditional methods such as low-flow nasal cannula or simple face masks.^{13,14}

Despite the increasing evidence supporting NHF, its effectiveness in ERCP remains a subject of debate, especially due to the significant risks of hypoxemia associated with the procedure. This meta-analysis seeks to systematically review and consolidate the existing evidence on the effectiveness of NHF in ERCP, focusing on its impact on patient outcomes. The analysis will evaluate the incidence of hypoxemia, procedure duration, and other related complications to assess the overall effectiveness of NHF.

Methods

Study Overview

This systematic review and meta-analysis was structured according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.¹⁵ Due to the nature of this study, which reviewed published data, Institutional Review Board approval was waived.

Study Search

Three major online databases (PubMed, Web of Science, and Cochrane) were searched on July 30, 2024. The following search strategy was used for PubMed: patient: “endoscopic retrograde

cholangiopancreatography” or “ERCP”; intervention: “nasal high flow” or “high flow” or “NHF.” The search was not limited by publication language. It included randomized controlled trials (RCTs), observational studies, and cohort studies that compared the use of NHF with usual care in patients undergoing ERCP.

Data Extraction

Two authors (X.W. and S.S.) independently screened the study titles and abstracts and carefully evaluated the full text to select eligible articles; in cases of discrepancy, they reached a consensus through discussion. Review articles and the included original articles were manually searched by the authors (X.W. and S.S.) for additional research papers that met the inclusion criteria.

Inclusion and Exclusion Criteria

Studies were included if they: 1) involved adult patients (18+ years) undergoing ERCP, 2) compared nasal high-flow (NHF) oxygen therapy with standard care, and 3) the safety and efficiency were reported such as hypoxemia, procedure duration et.al. Studies were excluded if they: 1) lacked comparative data between NHF and standard care, 2) involved pediatric patients or non-ERCP procedures, or 3) were case reports, reviews, or opinion articles without original data.

Study Selection

Full articles, brief reports, and conference abstracts published in any language were included if they provided data on studies involving adult patients (18 years and older) undergoing ERCP and compared NHF oxygen therapy with standard care. Studies that reported the incidence of hypoxemia as a primary or secondary outcome, as well as those that offered sufficient data on patient characteristics, sedation practices, and procedural details, were included. Studies were excluded if they lacked comparative data between NHF and standard care, involved pediatric populations, or focused on non-ERCP procedures.

Outcomes

The primary outcome of interest was the incidence of hypoxemia during ERCP. Hypoxemia was defined as a drop in oxygen saturation below 90%. Secondary outcomes of interest included the lowest saturation of percutaneous oxygen (SpO₂) during the procedure, the partial pressure level of carbon dioxide (CO₂) at the end of the procedure, and the duration of the procedure.

Statistics

Data were presented with means and standard deviations. This meta-analysis used a random-effects model to account for potential heterogeneity between the studies. The odds ratio (OR) was calculated for dichotomous outcomes, and the mean difference was calculated for continuous outcomes. The threshold for significance was set at 0.05. Heterogeneity, evaluated using I^2 statistics, was interpreted as follows: when $I^2 = 0\%$, there is no heterogeneity; when $I^2 > 0\%$ but $<25\%$, there is minimal heterogeneity; when $I^2 \geq 25\%$ but $<50\%$, there is mild heterogeneity; when $I^2 \geq 50\%$ but $<75\%$, there is moderate heterogeneity; and when $I^2 \geq 75\%$, there is strong heterogeneity.¹⁶ All analyses were performed using Review Manager version 5.3 (Cochrane Collaboration, Oxford, UK).

Results

Characteristics of Included Studies

A total of 198 studies were identified after searching the three databases. Forty-three duplicate records were removed. After the first and second screenings, 142 and seven studies were excluded, respectively. Finally, five studies met the inclusion criteria and were included in the meta-analysis (Fig. S1). These studies were conducted in various countries, including Australia, China, Japan, and Korea, and represented a total of 581 patients (314 males and 267 females; see Table 1).^{17–21} Key demographic and clinical variables such as age, sex, BMI, the American Society of Anesthesiologists (ASA) grade, and

Table 1. Characteristics of reviewed studies

Authors	Country	NHF	Usual	M/F	Age (years)	BMI (kg/m ²)	Sedation	Usual (L/min)	NHF (L/min)
Chen 2023	China	58	58	64/52	80.6 (6.6)	25.0 (1.9)	Propofol plus fentanyl	3–5	30–40
Kim 2021	Korea	36	36	47/25	66.3 (13.8)	22.6 (3.8)	Propofol plus fentanyl	5	50
Lee 2022	Korea	95	92	102/85	78.5 (7.0)	23.2 (4.8)	Propofol	5	50 ^a
Sawase 2023	Japan	37	38	46/29	64.6 (7.6)	23.3 (3.1)	Midazolam plus pethidine	1–2	40–60 ^b
Thiruvengkatarajan 2022	Australia	65	66	55/76	67.3 (18.3)	29.1 (7.1)	Fentanyl	4	60

Note: ^a: fraction of inspiratory oxygen: 0.5; ^b: room air; NHF: nasal high flow; M: male; F: female; BMI: body mass index.

procedure duration were reported in all studies (Table S1). The patient populations across the studies were similar in age, with mean ages ranging from 64.6 to 80.6 years. In the usual care group, oxygen was administered at rates of 1 L/min to 5 L/min, while in the NHF group, flow rates ranged from 30 L/min to 60 L/min. Three of the studies used 100% oxygen, while the other two used 50% oxygen and room air. Sedation practices varied; most of the studies used propofol-based sedation, while the rest used combinations of midazolam, fentanyl, and pethidine.

Efficacy of NHF in ERCP

The primary outcome of hypoxemia was consistently reported across all the studies. The pooled analysis showed that using NHF was associated with a significantly lower incidence of hypoxemia than usual care. The OR for hypoxemia in the NHF group was 0.29 (95% Confidence Interval [CI]: 0.14–0.60, $p < 0.001$, $I^2 = 21\%$), indicating a 71% reduction in the OR of hypoxemia compared to usual care (Fig. 1).

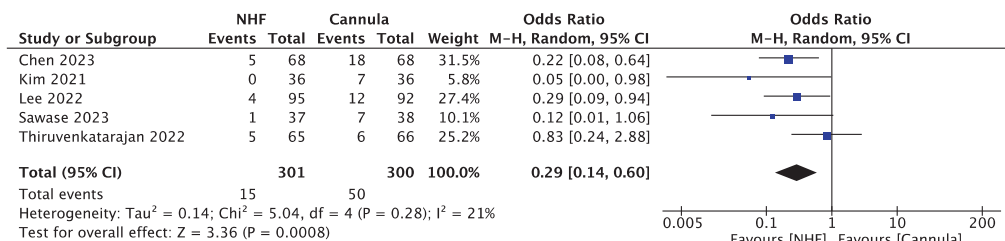


Figure 1. Comparison of the odds ratio of hypoxemia between the usual care and NHF groups. NHF: nasal high flow; CI: confidence interval.

The NHF group showed a higher minimum SpO₂ value during the procedure (Fig. 2). The pooled data analysis revealed a 2.55% increase in the mean difference (95% CI: 0.96, 4.13, $p = 0.002$; $I^2 = 57\%$). The CO₂ partial pressure level at the end of the procedure is shown in Fig. 3. Compared to the usual care group, the NHF group demonstrated a reduction in CO₂ with a mean difference of 1.83 mmHg (95% CI: -3.25, -0.42, $p = 0.01$; $I^2 = 0\%$).

Four of the five studies reported the duration of the ERCP procedure (Fig. 4). The pooled data showed no statistically significant difference between the usual care group and the NHF group, with a mean difference of 0.7 minutes (95% CI: -0.14, 1.53, $p = 0.1$; $I^2 = 0\%$).

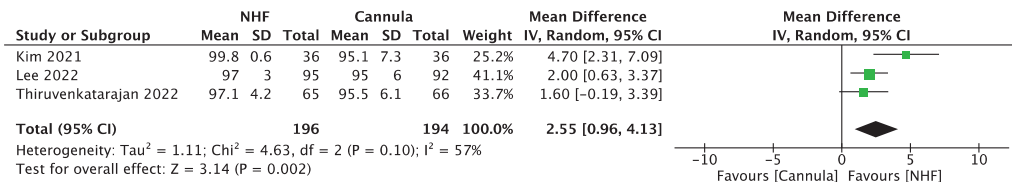


Figure 2. Comparison of the lowest SpO₂ between the usual care and NHF groups. NHF: nasal high flow; SD: standard deviation; IV: inverse variance; CI: confidence interval.

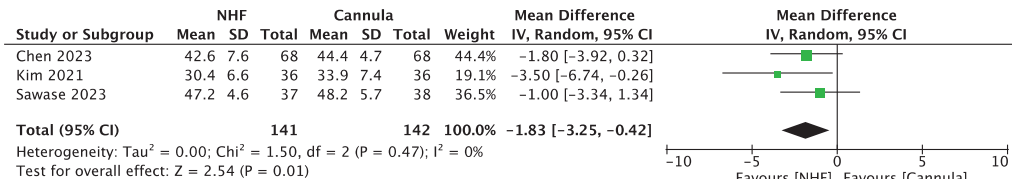


Figure 3. The CO₂ partial pressure level at the end of the procedure. NHF: nasal high flow; SD: standard deviation; IV: inverse variance; CI: confidence interval.

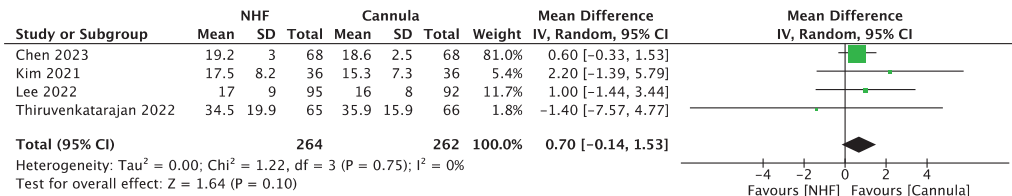


Figure 4. Comparison of duration of ERCP procedure between the usual care and NHF groups. ERCP: endoscopic retrograde cholangiopancreatography; NHF: nasal high flow; SD: standard deviation; IV: inverse variance; CI: confidence interval.

Risk of Bias

We included only RCTs in the meta-analysis and evaluated their quality using the Cochrane Risk of Bias Tool. Due to the unique characteristics of NHF therapy, adequate blinding of participants and personnel was impossible in any of the included studies, resulting in a high risk of bias in this domain. Detailed information on the risk of bias assessment is provided in Figs. S2 and S3. However, the compared outcomes showed no obvious publication bias (Figs. S4–S7).

Discussion

The findings of this meta-analysis highlight the potential benefits of NHF oxygen therapy during ERCP, particularly in reducing the incidence of hypoxemia. The higher number of lowest SpO₂ values observed in the NHF group further support the effectiveness of NHF in maintaining better oxygenation throughout the procedure. Given the risks associated with hypoxemia during sedated procedures, particularly in elderly patients or those with underlying respiratory or cardiovascular conditions, this finding is consistent with that of previous research.²² Additionally, the reduction in CO₂ partial pressure levels in the NHF group indicates improved ventilation and gas exchange, likely due to the positive airway pressure generated by high-flow oxygen therapy. This suggests that NHF can reduce the risk of hypercapnia, which is particularly relevant for patients with COPD, among whom hypercapnia is a significant concern. The meta-analysis did not find a significant difference in the duration of the ERCP procedure between the NHF and usual care groups, suggesting that while NHF improves oxygenation and ventilation, it does not necessarily impact procedural efficiency or duration, which is mainly determined by the complexity of ERCP itself.

While there were some differences in patient backgrounds across studies, randomization ensured that the experimental and control groups were comparable within each study. The pooled analysis revealed an I^2 score of 21%, suggesting low heterogeneity and supporting the reliability of the overall conclusions drawn regarding the respiratory effects of ERCP under varying patient conditions. The consistency of the findings across different countries and patient populations suggests that the benefits of NHF are likely generalizable to a wide range of clinical settings. This is particularly important as ERCP is performed worldwide, often in settings with varying levels of resources and expertise. The effectiveness of NHF has been demonstrated across various patient populations, including those at higher risk, such as individuals with obesity, obstructive sleep apnea, or COPD.^{23–25} Given the significant reduction in hypoxemia incidence, NHF therapy should be considered a standard oxygenation strategy during ERCP, particularly for patients with respiratory or cardiovascular comorbidities.

Besides its clinical benefits, the adoption of NHF during ERCP could influence sedation practices. The ability of NHF to maintain higher oxygen levels and reduce CO₂ retention might allow for deeper sedation levels without increasing the risk of respiratory complications.²⁶ This could lead to better patient comfort, reduced movement during the procedure, and lower doses of sedative medications, thereby decreasing the risk of sedation-related side effects such as hypotension or prolonged recovery times.²⁷ Furthermore, in high-risk patient populations, such as those with obstructive sleep apnea or severe COPD, the use of NHF could be particularly beneficial in preventing peri-procedural respiratory decompensation.²⁸ This concern often limits the depth of sedation that can be safely administered.

The significant reduction in hypoxemia observed in the NHF group highlights its potential to address one of the most common complications associated with sedated endoscopic procedures. However, NHF systems are more complex and expensive than traditional oxygen delivery methods, and their routine use during ERCP could increase the overall cost of the procedure. Therefore, studies examining cost-effectiveness are essential to determine whether the benefits of NHF justify the additional expense, particularly in resource-limited settings where healthcare budgets are constrained. Studies have shown that long-term domiciliary HFNC treatment is likely to be a cost-effective addition to usual care for COPD and infants.^{29,30} However, while this meta-analysis strongly supports the use of NHF, the need for more comparative data on the cost-effectiveness of usual care and NHF treatment during ERCP remains, leading to a gap in evidence in this area.

It is important to recognize the limitations of this meta-analysis. First, the studies included in the analysis exhibited a high risk of performance and detection bias, primarily due to differences in the oxygen delivery methods between the NHF and usual care groups. Second, the heterogeneity observed in some outcomes, such as the lowest SpO₂, indicates variability in the effectiveness of NHF across different patient populations and settings. Third, the research was conducted in only four countries, with a relatively small sample size. Larger studies with more homogeneous populations and standardized protocols are needed to confirm these findings and explore the potential benefits of NHF in specific patient subgroups, particularly those with a higher baseline risk for hypoxemia. Another limitation of this meta-analysis was the absence of data on long-term outcomes, including post-ERCP complications, in the included studies. None of the RCTs investigated the effect of NHF therapy on post-ERCP complications, such as pancreatitis, bleeding, or infections. The focus of the available studies was limited to short-term respiratory outcomes. Future research should aim to address these longer-term effects to provide a more comprehensive evaluation of NHF in the context of ERCP.

Conclusion

This meta-analysis provides evidence that NHF effectively reduces the incidence of hypoxemia. These findings support the consideration of NHF as a preferred method of oxygen delivery during ERCP, particularly for patients at higher risk of respiratory complications.

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Author Contributions

X.W. contributed to the study search, quality check, data extraction, and drafting. As principal investigators, X.W. and S.S. worked on the study search, quality check, data extraction, and analysis. X.W., S.S., and S.Z. worked on the interpretation of data and the revision process. All authors have read the manuscript and agree with the content and data.

Data Availability

The data supporting this study's findings are available from the corresponding author upon reasonable request.

Ethical Statement

Institutional Review Board approval was waived due to the nature of the meta-analysis.

Conflict of Interest

The authors declare no conflict of interest related to this study.

Supplemental Information

Supplemental information for this article can be found online at <https://sup.jclinque.com/api/articles/47/download-suppl>.

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