





High-Flow Nasal Cannula Oxygen Therapy in Perioperative Respiratory Care: Application and Prospects

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Abstract: High-flow nasal cannula (HFNC) oxygen therapy is an oxygen delivery technique that provides warmed and humidified high-flow oxygen through a non-sealing nasal cannula. With multiple physiological advantages, HFNC had been increasingly used in perioperative respiratory management. Evidence indicates that HFNC significantly reduces the incidence of hypoxemia and decreases procedural interruptions during procedural sedation. As an updated HFNC technique, transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) had been proved to extend the safe apneic time and promote safety during laryngoscopic examination and endotracheal intubation. In tubeless pharyngeal surgery, it effectively balances the dilemma between a clear surgical field and adequate intraoperative oxygenation. In the postoperative recovery period, HFNC helps to reduce the incidence of postoperative hypoxemia and other postoperative pulmonary complications, and decreases the need for reintubation. HFNC demonstrates broad potential in perioperative respiratory care. However, current evidence is limited by the heterogeneity of oxygen protocols and inconsistent results among studies, especially for high-risk patients. The efficacy of HFNC is difficult to predict, which may lead to intubation delay and limits the application of HFNC. Future research should focus on optimizing clinical application strategies for HFNC, developing reliable efficacy prediction models, and validating these findings through large-sample, multicenter randomized controlled trials to advance perioperative respiratory management toward greater effectiveness and safety.

Keywords: oxygen therapy, hypoxemia, airway management, intubation, anesthesia

Introduction

High-flow nasal cannula (HFNC) oxygen therapy is a non-invasive respiratory support method which continuously supplies warmed and humidified oxygen at high flow via a non-sealing nasal cannula.¹ Before delivery, the gas is conditioned to ensure a constant inspired oxygen concentration (FiO₂) (21–100%), stable temperature (31–37°C), near-saturated humidity (approximately 100% relative humidity), and high flow rates (up to 80 L/min or higher). HFNC was initially used as an adjunctive oxygen therapy for patients with respiratory failure² or bronchitis,³ and subsequently applied to patients with mechanical ventilation, demonstrating effective oxygenation support during endotracheal intubation¹ and post-extubation sequential treatment.⁴

In perioperative respiratory management, however, there remains an unmet need for a technique that provides reliable oxygenation without compromising procedures or patient comfort. Standard nasal cannulas, which are frequently employed during procedural sedation and postoperative recovery, are often constrained by their upper limits of oxygen fraction and flow, posing risks of hypoxemia and other complications for patients.⁵ While facemasks or non-invasive ventilation (NIV) can achieve better oxygenation, they are often unsuitable for concurrent use during gastroscopic laryngoscopy or tracheal intubation. In addition, tight facemasks bring issues such as poor patient tolerance, skin injury, impaired communication, and hindered airway secretion clearance.⁶ HFNC could overcome these limitations and provide



effective oxygenation at the same time. Besides, its unique capacity for effective apneic oxygenation allows its application during laryngoscopy, tracheal intubation, and even brief tubeless laryngopharyngeal surgery, ensuring effective oxygenation without interrupting the procedure.^{7,8} HFNC has thus emerged as a promising solution for perioperative respiratory management.

Recently, the applications of HFNC have rapidly expanded into various perioperative scenarios. Moreover, recent high-quality multicenter trials have further elucidated its efficacy in these settings.^{9–11} This ongoing expansion, coupled with the publication of new evidence^{9,12} and evolving indications, necessitates an updated synthesis of current knowledge to guide clinical practice. Therefore, this study aims to summarize the current evidence regarding the perioperative clinical applications of HFNC technology, providing a reference for decision making regarding oxygen therapy strategies.

Physiological Advantages of HFNC

The physiological benefits of HFNC are primarily mediated by two core mechanisms: the continuous flushing effect of high-flow gas and the generation of positive end-expiratory pressure (PEEP) (Figure 1). The high-flow gas delivered by HFNC continuously flushes the nasopharyngeal space, reducing the rebreathing of exhaled gas, stabilizing the FiO_2 , and diminishing anatomical dead space.¹³ This flushing action exhibits flow-dependent efficacy, with airway dead space clearance increasing by approximately 1.8 mL/s for every 1 L/min rise in flow rate.¹⁴ The reduction in anatomical dead space enhances alveolar effective ventilation, improves ventilation–perfusion matching, and increases respiratory efficiency. Furthermore, the flushing effect of high-flow gas reduces airway resistance, enhances lung dynamic compliance, and decreases the breathing work.^{13,15} In patients with acute hypoxic respiratory failure, those treated with HFNC exhibited a lower respiratory rate compared with mask oxygen therapy, at equivalent levels of arterial carbon dioxide pressure (PaCO_2) and pH.¹⁵

The constant high-flow gas delivered by HFNC generates PEEP, which attenuates the pressure gradient between capillary hydrostatic pressure and alveolar pressure,^{16,17} thereby promoting alveolar recruitment, increasing end-expiratory lung volume, and mitigating atelectasis and hypoxemia.¹³ The magnitude of PEEP produced by HFNC is influenced by several factors, including the patients' age and gender, and the mouth being closed or open during therapy.¹⁷ Measurements in healthy volunteers indicated that for every 10 L/min increase in flow rate, the generated PEEP rose by approximately 1.16 cmH_2O .¹⁶ However, some studies have noted that while PEEP increased in a flow-dependent manner, this relationship was not strictly linear, with higher flow rates producing disproportionately greater increases in airway pressure.¹⁷

Moreover, the adequately warmed and humidified oxygen supplied by HFNC enhances mucociliary clearance function, and facilitates the removal of respiratory secretions.¹⁸ At the same time, it helps to improve patient comfort and decrease airway resistance.

Application of HFNC During Procedural Sedation

In recent years, more than 50% of gastrointestinal endoscopic procedures have been performed under sedation.¹⁹ Sedatives are administered to alleviate patient discomfort and intolerance, improving patients' satisfaction and facilitating operational conditions. However, these agents carry risks of respiratory depression and subsequent hypoxemia,²⁰ which represent the most frequent adverse events during procedural sedation, with reported incidence rates ranging from 1.8% to 69%.^{20–22} Severe hypoxemia may lead to arrhythmias, myocardial ischemia,²¹ permanent neurological injury, and death.²³ Therefore, hypoxemia during procedural sedation often requires immediate airway interventions, including mask ventilation, jaw thrust, and endotracheal intubation, which often interrupt the procedure. Conventional oxygen therapy (COT) employed during gastrointestinal endoscopy uses standard nasal cannulas, which are limited by poor sealing and low maximum flow rates, resulting in entrainment of room air and reduced inspiratory oxygen fraction. HFNC overcomes these limitations and provides gas with a constant oxygen fraction, which helps to maintain pulse oximetry during gastrointestinal endoscopy (Table 1). Clinical studies have demonstrated that compared with COT, the application of HFNC significantly reduces the overall incidence of hypoxemia and the need for airway interventions during gastroscopy under sedation.^{9,10,24} This efficacy had also been validated in obese patients, with HFNC markedly reducing the incidence of hypoxia, subclinical respiratory depression, and severe hypoxemia, thereby minimizing procedural

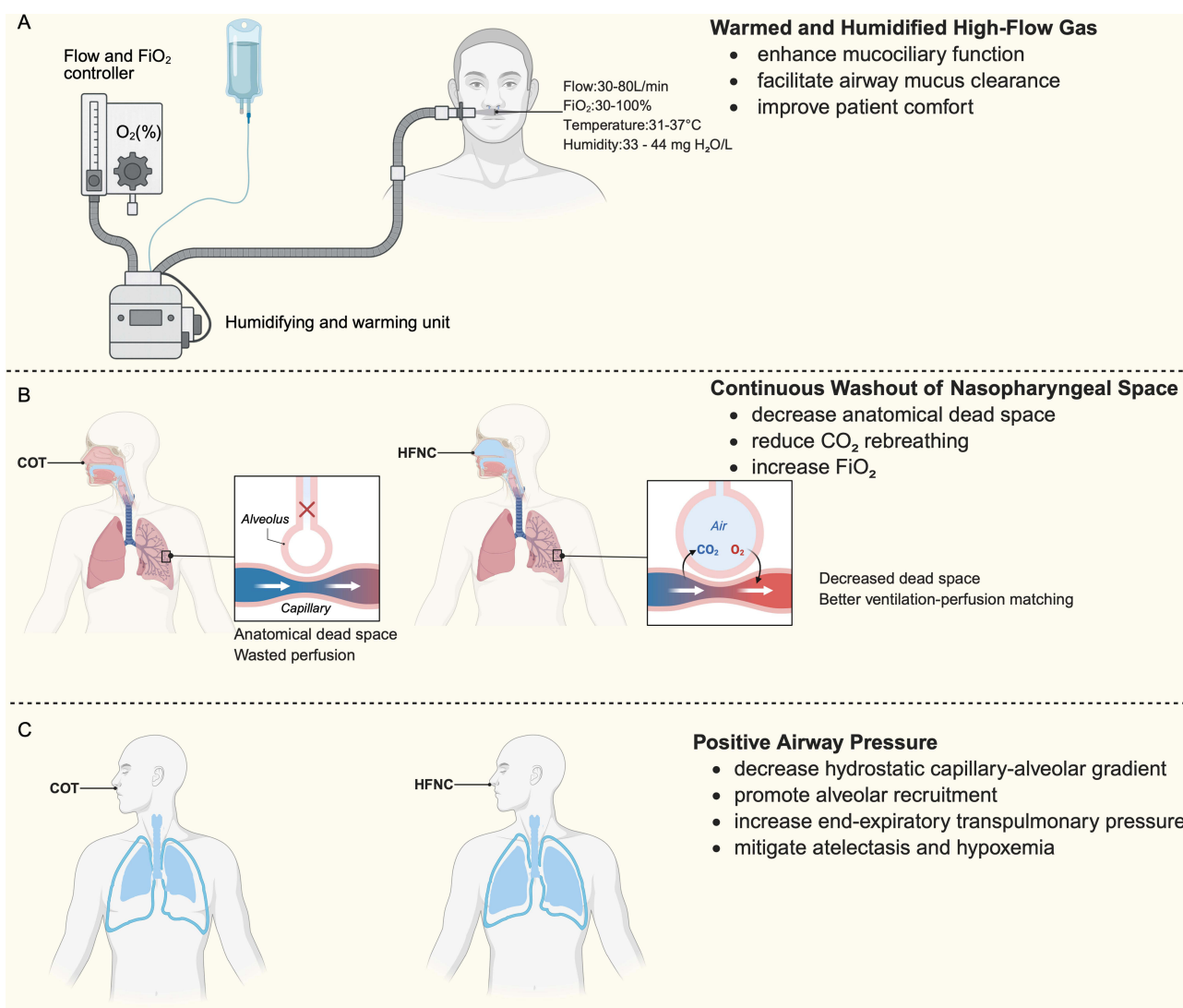


Figure 1 Physiological benefits of high-flow nasal cannula oxygen therapy. **(A)** Warmed and humidified gas enhances mucociliary clearance, facilitates the removal of respiratory secretions, and improves patient comfort. **(B)** Reduction of anatomical dead space and increase of inspired oxygen fraction through continuous flushing of the nasopharyngeal space. **(C)** Generation of positive end-expiratory pressure by constant high-flow gas. In **(B)**, the box outlines the alveolar region. The black arrows indicate the direction of gas exchange (oxygen, carbon dioxide). White arrows represent the direction of blood flow. Capillary color denotes blood oxygen content (dark blue: low; red: high). Blue areas in the alveoli and upper airway represent alveolar air and the fresh gas delivered by HFNC, respectively. The blue-covered area in the upper airway indicates regions of CO₂ washout by HFNC fresh gas.

Abbreviations: COT, conventional oxygen therapy; HFNC, high-flow nasal cannula.

interruptions and airway interventions.⁹ The beneficial effects of HFNC during procedural sedation can be primarily attributed to the high-flow gas, which facilitates continuous flushing of dead space and generates PEEP, improving oxygenation efficiency. A multicenter randomized controlled trial (RCT) confirmed that, even at comparable FiO₂, HFNC during procedural sedation for gastroscopy significantly reduced episodes of desaturation by 20% compared with standard oxygen therapy.¹⁰ Nevertheless, it is appropriate to moderately increase the FiO₂ for high-risk populations. A small-sample trial applied HFNC with FiO₂ of 36–40% in morbidly obese patients and observed no differences in desaturation compared with the COT group.²⁵ During esophagogastroduodenoscopy, mouth opening was often required. Studies indicated that nasal breathing decreased to approximately 47%, and patients would switch to oral breathing during gastrointestinal endoscopy.²⁶ This may lead to leakage of high-flow gas, potentially attenuating the oxygenation efficacy of HFNC. Nevertheless, subgroup analyses from current RCTs have not identified a statistically significant influence of endoscopic type on the overall effectiveness of HFNC oxygen therapy.¹⁰

Table 1 Summary of Current Trials Evaluating HFNC in Procedural Sedation

Application	Design	Population (n)	Comparison	Results	Reference
Gastrointestinal endoscopy	RCT	Adults with BMI ≥ 28 kg/m ² (n=984)	HFNC (60 L/min, FiO ₂ =100%) vs COT (6 L/min)	Lower incidence of hypoxia (75% \leq SpO ₂ <90% for <60 s) in HFNC group (2.0%) than in COT group (21.2%)	[9]
Gastrointestinal endoscopy	RCT	Adults with risks of hypoxemia (n=379)	HFNC (70 L/min, FiO ₂ =50%) vs COT (6 L/min)	Lower incidence of SpO ₂ \leq 92% in HFNC group (9.4%) than in COT group (33.5%)	[10]
Gastrointestinal endoscopy	RCT	Adults, ASA I–II (n=1994)	HFNC (30–60 L/min, FiO ₂ =100%) vs COT (2 L/min)	Lower incidence of hypoxia (75% \leq SpO ₂ <90% for <60 s) in HFNC group (0%) than in COT group (8.4%)	[11]
Gastrointestinal endoscopy	RCT	Adults, BMI >40 kg/m ² (n=59)	HFNC (60 L/min, FiO ₂ =36–40%) vs COT (4 L/min)	No difference in the incidence of SpO ₂ \leq 90% in HFNC group (39.3%) and COT group (45.2%)	[25]
Gastrointestinal endoscopy	RCT	Children, 6–18 years old (n=50)	HFNC (2 L/kg/min) vs COT	No differences in the number of respiratory events	[27]
Bronchoscopy	RCT	Adults (n=60)	HFNC (30–70 L/min, FiO ₂ =100%) vs COT (10 L/min)	Lower incidence of SpO ₂ <90% in HFNC group (4/30) than in COT group (10/30)	[28]
Bronchoscopy	RCT	Adults (n=40)	HFNC (30–70 L/min, FiO ₂ =100%) vs COT (2 L/min)	Smaller drop in SpO ₂ was observed in HFNC group	[29]
Bronchoscopy	RCT	Post-lung-transplant patients (n=76)	HFNC (30–50 L/min) vs COT (4–10 L/min)	Fewer patients experienced SpO ₂ <94% with HFNC (43.2%) than with COT (89.7%)	[30]
Bronchoscopy	RCT	Adults (n=36)	HFNC (60 L/min) vs COT	Higher PaO ₂ with HFNC than with COT	[31]
CT-guided hepatic tumor radiofrequency ablation	RCT	Adults, >20 years old (n=59)	HFNC (10 L/min before sedation and 50 L/min during the procedure) vs COT (10 L/min)	Less postprocedural atelectasis with HFNC than with COT	[32]
Operative hysteroscopy	RCT	Adults, ASA I–II (n=180)	HFNC (30 L/min before sedation and 70 L/min during the procedure, FiO ₂ =100%) vs mechanical ventilation	No difference in intraoperative respiratory support success rate (99% in both groups)	[33]
Awake craniotomy	RCT	Patients 14–70 years old (n=65)	HFNC (40 L/min, FiO ₂ =60%), HFNC (60 L/min, FiO ₂ =60%) vs NPA (6 L/min, FiO ₂ =60%)	Higher PaO ₂ /FiO ₂ was achieved with HFNC than with NPA	[34]

Abbreviations: ASA, American Society of Anesthesiologists physical status classification; BMI, body mass index; COT, conventional oxygen therapy; CT, computed tomography; FiO₂, inspired oxygen concentration; HFNC, high-flow nasal cannula; NPA, nasopharynx airway; PaO₂, partial pressure of oxygen in artery; RCT, randomized controlled trial; SpO₂, peripheral capillary oxygen saturation.

Owing to the characteristic of “shared airway”, airway management in fiberoptic bronchoscopy or endobronchial ultrasound is very difficult. Hypoxemia is a common complication during fiberoptic bronchoscopy examination.³⁵ If desaturation occurs, immediate airway interventions are necessary, which often involve interruption of the procedure and rescue ventilation. Prospective observational studies indicate that HFNC is an effective and safe therapy that can perform effective oxygenation during bronchoscopy.³⁶ Multiple RCTs have demonstrated that HFNC can reduce the incidence of desaturation and hypoxemia,^{28–30} decrease the need for airway interventions,²⁹ improve post-oxygenation saturation levels, and elevate the minimum intraoperative peripheral oxygen saturation (SpO₂).²⁸

HFNC technology can mitigate the loss of end-expiratory lung volume and improve the oxygenation effect.³¹ Compared with standard nasal cannula oxygen therapy, it has demonstrated better oxygenation effects in other clinical scenarios of procedural sedation, such as computed tomography-guided hepatic tumor radiofrequency ablation,³² operative hysteroscopy,³³ and awake craniotomy.³⁴ A meta-analysis summarized the practical data from both pediatric and adult patients across various clinical settings (such as digestive endoscopy, fiberoptic bronchoscopy, cardiovascular intervention surgery, and dentistry). It was concluded that HFNC consistently reduced the risk of hypoxemia, irrespective of the oxygen fraction, propofol administration, or baseline hypoxemia risk.⁵ Compared with COT, HFNC use was associated with fewer hypoxemic events, higher minimum SpO₂, and less requirement for airway maneuvers and procedural interruptions.⁵ Therefore, for patients with high risks for intraoperative hypoxemia (such as those with comorbidities, obesity, or obstructive sleep apnea) or complex procedures, HFNC should be considered as a suitable oxygenation technique.

Applications of HFNC During Anesthesia Induction

Preoxygenation is often performed during anesthesia induction to improve patients’ oxygen reserves and prevent desaturation and hypoxemia during tracheal intubation. A conventional oxygen delivery device cannot ventilate during laryngoscopy and endotracheal intubation, which poses risks of desaturation, especially in patients with difficult airways. Transnasal humidified rapid-insufflation ventilatory exchange (THRIVE), proposed by Patel and Nouraei in 2015, is an upgraded technique of HFNC,³⁷ which aims to facilitate apneic oxygenation through high flow and high FiO₂. Figure 2 illustrates the mechanism of apneic oxygenation during THRIVE therapy. Patel and Nouraei conducted preoxygenation using THRIVE with a flow rate of 70 L/min, in the position of 40-degree head-up tilt angle, and observed an average safe

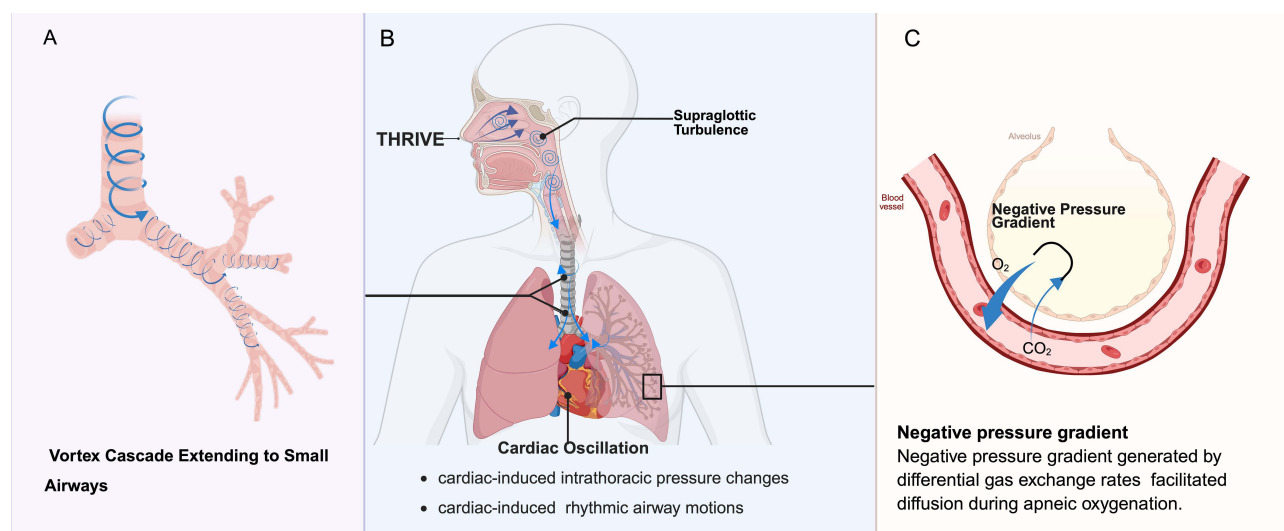


Figure 2 Mechanism of apneic oxygenation during transnasal humidified rapid-insufflation ventilatory exchange therapy. **(A)** The turbulent flow formed by high-flow gas in the nasopharyngeal cavity. **(B)** The interaction between cardiac oscillations and the turbulent flow facilitates the transport of carbon dioxide from the lungs to the nasal or oral cavity. **(C)** The negative pressure gradient generated by differential gas exchange rates facilitates gas diffusion during apneic oxygenation. In the figure, arrows indicate the direction of gas flow. Curved arrows and vortex symbols represent turbulence within the airway. The box outlines the alveolar region where differential gas exchange occurs. The thickness of the arrows represents the volume of gas participating in exchange process.

Abbreviations: COT, conventional oxygen therapy; HFNC, high-flow nasal cannula.

apnea time of 17 minutes.³⁷ No patients experienced oxygen saturation below 90% or hypercapnia. In the study, two patients used THRIVE throughout the entire surgical process, with safe apnea times of 32 minutes and 65 minutes. This finding showed that effective apneic oxygenation of THRIVE allowed it to ventilate during laryngoscopy, significantly extending the safe apnea time and providing more operating time for airway management in patients with difficult airways, thus improving the safety of anesthesia induction and airway management. Many studies have confirmed that THRIVE can significantly prolong safe apnea time (Table 2). The additional application of THRIVE during laryngoscopy prolonged the time when oxygen saturation was $\geq 95\%$ and reduced the minimum pulse oxygen saturation during laryngoscopy.³⁸ A prospective multicenter study independently evaluated the effectiveness of THRIVE technology in apneic oxygenation. Compared with preoxygenation using a facemask alone, patients who received a facemask combined with THRIVE showed a lower incidence of oxygen saturation decreasing to $<95\%$.⁷ Applying THRIVE to the entire stage of preoxygenation (both spontaneous breathing and apneic oxygenation) significantly improved the safe apnea time and extended the safety margin of airway management. In an RCT published in 2023, THRIVE was proven to effectively reduce the risk of desaturation during anesthesia induction in obese individuals. Fourteen patients (14/39) in the mask group experienced a desaturation within 18 minutes, compared with only five patients (5/41) in the THRIVE group.³⁹ THRIVE has achieved inspiring therapeutic results in various populations, including pediatric patients⁴⁰ and patients with morbidly obesity,^{39,41} obstructive sleep apnea,⁴² critical illness,^{43,44} and head and neck cancer.⁴⁵

Nevertheless, the superiority of THRIVE over conventional facemasks remains contentious. Compared with conventional facemask, THRIVE offers the advantage of effective apneic oxygenation during endotracheal intubation; however, it is less efficient during spontaneous breathing. In an observational study, healthy volunteers received THRIVE treatment at a flow rate of 70 L/min and FiO_2 of 100% with the mouth closed for 3 minutes, but only half of them achieved the target end-tidal oxygen concentration (EtO_2) of 90%, with the median EtO_2 being 86%.⁴⁶ Similar results were observed in pregnant women.⁴⁸ THRIVE could not quickly and effectively achieve the target EtO_2 of 90% during spontaneous breathing. Besides, while some studies suggest that compared with conventional facemasks, THRIVE reduces the incidence of desaturation and improves the lowest SpO_2 during intubation, these benefits are not always evident in other studies. The PREOPTI-DAM RCT, conducted at the University Hospital of Nantes in France, found that compared with NIV, preoxygenation with THRIVE in obese patients provided lower EtO_2 after intubation and a higher rate of desaturation $<95\%$.⁴⁹ A meta-analysis involving 11 RCTs found that THRIVE was more effective than conventional mask therapy, but not as effective as NIV.⁵¹ The combination of THRIVE and NIV may be a more suitable choice for critically ill or complex patients. It is important to note that variations in control and intervention protocols – such as flow rates (30–70 L/min), preoxygenation duration (3–5 minutes), and patient positioning (supine to 45° head-up) – may influence outcomes. In addition, the threshold defining desaturation (90–95% SpO_2) differs across studies, contributing to heterogeneous findings. Despite these discrepancies, THRIVE remains a promising technique for anesthesia induction. Optimal flow rates and positioning require further investigation. A meta-analysis compared nine different therapies (nine combinations of preoxygenation techniques and positions) and identified THRIVE with head elevation as the top-ranked therapy for prolonging safe apnea time.¹² THRIVE remained the top-ranked oxygenation regimen even without the consideration of position. In terms of desaturation, although THRIVE was not superior to NIV it was better than non-pressure facemasks.¹²

There have been concerns regarding the potential risks of gastric insufflation and aspiration during THRIVE therapy in preoxygenation. However, according to relevant research, the PEEP generated by THRIVE, even at a flow rate of up to 80 L/min with the patient's mouth closed, was still below 10 cmH_2O .¹⁷ Given that the lower esophageal sphincter can form a pressure barrier of approximately 15–25 mmHg (20–34 cmH_2O) under normal conditions to prevent the reflux of gastric contents,⁵² the PEEP generated by THRIVE seemed insufficient to induce gastric insufflation or aspiration. In healthy fasting awake adults, THRIVE treatment at a flow rate of up to 70 L/min for 30 minutes did not increase the cross-sectional area of the gastric antrum,⁵³ which is considered as a reliable index for gastric content volume.⁵⁴ No gastric insufflation was observed among 60 participants.⁵³ However, sedatives and neuromuscular blocking drugs can reduce the tension of the upper and lower esophageal sphincters, altering the barrier pressure between the stomach and esophagus.⁵⁵ Quantitative computed tomography assessments revealed that the gastric gas volume after THRIVE treatment was approximately 24 cm, which was comparable with that in the conventional oxygenation group

Table 2 Summary of Current Trials Evaluating HFNC in Anesthesia Induction

Application	Design	Population (n)	Comparison	Primary Outcome	Results	Reference
Only spontaneous breathing						
	Prospective observational study	Healthy volunteers (n=21)	Only HFNO group, HFNO (70 L/min for 30 s)	Proportion of participants achieving EtO ₂ ≥90% after preoxygenation	Proportion with EtO ₂ ≥90% was 50%	[46]
	RCT	Healthy volunteers (n=50)	HFNO (60 L/min, FiO ₂ =100%) vs FM (12 L/min, FiO ₂ =100%)	EtO ₂ at the end of 3 min pre-oxygenation	Lower EtO ₂ in HFNO group (77%) than in FM group (89%)	[47]
	Prospective observational study	Healthy pregnant women (n=73)	Only HFNO group, HFNO (30 L/min for 30 s, and then 50 L/min for the next 150 s)	Proportion of participants achieving EtO ₂ ≥90% after preoxygenation	Proportion with EtO ₂ ≥90% was 60% and EtO ₂ ≥80% was 84%	[48]
Only apneic oxygenation						
	RCT	Obese men, BMI 30–35 kg/m ² (n=30)	THRIVE vs no supplemental oxygen, both with head up 25°	Duration of SpO ₂ ≥95%	Longer duration of SpO ₂ ≥95% in THRIVE group	[38]
	RCT	Adults (n=450)	THRIVE (60 L/min, FiO ₂ =100%) vs no ventilation (FM alone) during intubation	Lowest EtO ₂ value within the 2 min after tracheal intubation	Higher value of the lowest EtO ₂ value within the 2 min after tracheal intubation with THRIVE than with FM alone	[7]
	RCT	Obstructive sleep apnea patients (n=43)	HFNO (60 L/min, FiO ₂ =100%) vs no supplemental oxygen	Safe apnea time, interval from cessation of mechanical ventilation until SpO ₂ <95%	Longer safe apnea time in HFNO group	[42]
Total stage of preoxygenation (spontaneous breathing and apneic oxygenation)						
	RCT	Adults, BMI >40 kg/m ² (n=80)	HFNC (35–70 L/min) vs FM (15 L/min) at 45° mid-thoracic incline; 3 min for preoxygenation	Time to desaturation to 92%	Comparable safe apnea time between HFNC and FM groups (18 min); lower risks of desaturation with HFNC than with FM	[39]
	RCT	Infants and children aged up to 10 years (n=48)	THRIVE (flow was based on weight) vs FM, both FiO ₂ =100%	Time to desaturation to 92%	Longer apnea time in THRIVE group than in FM group	[40]
	RCT	Adults, BMI ≥40 kg/m ² (n=40)	Preoxygenation for 3 min: HFNC (40 L/min, FiO ₂ =100%) vs FM (FiO ₂ =100%); apnea period: HFNC (60 L/min, FiO ₂ =100%) vs no supplemental oxygen	Safe apnea time, time to desaturation to 95% or maximum 6 min	Longer safe apnea time and higher minimum peri-intubation SpO ₂ with HFNC than with FM	[41]
	RCT	Patients with head and neck cancer (n=52)	THRIVE (30–60 L/min, FiO ₂ =100%) vs FM (12 L/min, FiO ₂ =100%); 5 min for preoxygenation	PaO ₂ immediately after intubation	Higher PaO ₂ immediately after intubation in HFNC group than in FM group	[45]
	RCT	Adults, BMI >35 kg/m ² (n=100)	HFNC (60 L/min, FiO ₂ =100%) vs NIV, 4 min for preoxygenation	Lowest level of EtO ₂ within 2 min after intubation	Lower EtO ₂ after intubation and higher rate of desaturation <95% with HFNC than with NIV	[49]
	RCT	Pregnant women (n=34)	HFNO (50 L/min, FiO ₂ =100%) vs FM (10 L/min, FiO ₂ =100%); 3 min for preoxygenation, at a 15° left lateral tilt and a 30° head-up position	PaO ₂ immediately after intubation	Higher PaO ₂ in HFNO group than in FM group	[50]

Abbreviations: BMI, body mass index; EtO₂, end-tidal carbon dioxide concentration; FiO₂, inspired oxygen concentration; FM, facemask; HFNC, high-flow nasal cannula; HFNO, high-flow nasal oxygen; NIV, non-invasive ventilation; PaO₂, partial pressure of oxygen in artery; RCT, randomized controlled trial; SpO₂, peripheral capillary oxygen saturation; THRIVE, transnasal humidified rapid-insufflation ventilatory exchange.

(23.8 cm³).⁵⁴ Moreover, the volumes were insufficient to pose a risk of aspiration. Ultrasound assessments of the cross-sectional area of the gastric antrum did not show any change following preoxygenation and tracheal intubation among elderly patients using THRIVE.⁵⁶ No sonographic evidence of gastric insufflation, such as the “comet-tail sign”, was observed.⁵⁶ Compared with a pressure-controlled facemask ventilation group, elderly patients using THRIVE demonstrated smaller cross-sectional areas of the gastric antrum and a lower incidence of gastric insufflation.⁵⁷

Applications of HFNC During Tubeless Laryngopharyngeal Surgery

Microscopic laryngoscopic surgery is widely used for the examination and treatment of various throat diseases. Traditionally, mechanical ventilation with endotracheal intubation was applied for secure oxygenation in such surgery; however, the endotracheal tube often obstructed the surgical view, affecting operative access. To overcome this limitation, tubeless anesthetic techniques have been adopted, which provide a better view of surgical field for surgeons, but present new challenges for the anesthesiologists: sustaining stable peripheral oxygen saturation throughout the procedure and maintaining adequate depth of anesthesia at the same time. The THRIVE technique has been proven to provide effective apneic oxygenation and prolong the safe apneic time in various populations, including morbidly obese patients³⁹ and pediatric patients.⁴⁰ In recent years, the application of THRIVE has gradually expanded to tubeless upper airway surgery. Multiple observational studies conducted in adults have shown that the application of THRIVE techniques in micro-laryngoscopy surgery is feasible, achieving a good balance between the view of the surgical field and the patient’s oxygenation requirements, improving patients’ safety, and enabling uninterrupted procedures without surgical field obstruction.^{8,58,59} It can serve as an alternative to tracheal intubation or high-frequency jet ventilation.⁵⁹ However, in pediatric patients, evidence from RCTs did not support THRIVE as a better oxygenation therapy than standard nursing.^{60,61} Younger children and those undergoing longer anesthesia remained at high risk of requiring intraoperative rescue ventilation.⁶¹

Furthermore, the high oxygen fraction provided by THRIVE also increases the risk of airway fires, especially in surgery using lasers or electrocautery.^{62,63} It was observed that even in the absence of combustible materials such as PVC endotracheal tubes or gauze, native tissues may act as a fuel under laser energy.^{62,63} Continuous laser application, low gas flow rates, and high oxygenation fractions were reported as risk factors. It was advised to reduce oxygenation fractions appropriately prior to laser use to mitigate airway fires.⁶³ Additional protective measures included safety training on lasers, minimizing laser energy, eye protection, covering exposed facial and neck areas with wet gauze, using non-flammable airway equipment, and irrigating the surgical site with 0.9% saline in case of fire.⁶²

Another concern about THRIVE is the accumulation of carbon dioxide (CO₂). Although THRIVE facilitates apneic oxygenation, its efficiency in eliminating CO₂ during apneic oxygenation remains inadequate to match metabolic CO₂ production,⁶⁴ posing risks of hypercapnia and acidosis, which limit the application of THRIVE for long-term surgery. During 30-minute tubeless surgery with THRIVE, PaCO₂ was observed to increase at an average rate of 1.8 mmHg/min – more than twice that observed in spontaneously breathing patients (0.8 mmHg/min).⁶⁵ In addition, the characteristic of the open breathing circuit created technical challenges for monitoring intraoperative end-tidal CO₂ during THRIVE therapy. Transcutaneous CO₂ monitoring may offer an alternative solution. A novel THRIVE device equipped with a CO₂ sampling tube has been developed to capture exhaled gas from the nose or mouth; however, the measured end-tidal CO₂ may underestimate the true values, limiting its reliability for detecting hypercapnia. This device would therefore be primarily reserved for detecting apneic events or airway obstruction.⁶⁶

Applications of HFNC During Postoperative Recovery

COT, such as the nasal cannula or venturi mask, is the main technique for postoperative respiratory care. However, COT cannot supply gas with a stable inspiratory oxygen fraction or provide ventilatory support. When COT fails, NIV or continuous positive airway pressure (CPAP) is applied. Although NIV and CPAP can effectively improve postoperative oxygenation, reducing the incidence of hypoxemia and reintubation,^{67,68} the requirements for secure mask fitting often result in poor tolerance, skin injury, communication difficulties, and impaired airway secretion clearance. In contrast, HFNC, as a new oxygen delivery technique, can overcome these limitations.⁶⁹ With high-flow gases continuously flushing the airway, HFNC helps to reduce the rebreathing of exhaled gas and stabilize the FiO₂. Warmed and humidified oxygen

supplied by HFNC enhances mucociliary clearance function and facilitates the removal of airway secretions. With its superior patient comfort, HFNC represents a promising approach to postoperative respiratory care in extubated patients.

HFNC has shown efficacy in both general populations and critically ill patients at low to medium risk of extubation failure (Table 3). Compared with COT, HFNC improves post-extubation oxygenation, and reduces the incidence of postoperative hypoxemia and reintubation. Among patients undergoing gynecological surgery, those receiving pre-emptive HFNC within 2 hours after extubation showed a higher oxygenation index and less postoperative atelectasis, assessed by lung ultrasound scores and end-expiratory diaphragmatic thickness.⁷⁰ Multiple RCTs conducted in various populations, including elderly patients,⁷¹ obese patients,⁷² and esophageal cancer patients,⁷³ have confirmed the benefits of HFNC in promoting postoperative oxygenation and improving patient prognosis.

Among patients with medium to high risks of postoperative pulmonary complications (PPCs), clinical practice data on the efficacy of HFNC are inconsistent. In patients undergoing thoracoscopic lobectomy, HFNC therapy was confirmed to improve post-extubation arterial oxygenation pressure (PaO_2), $\text{PaO}_2/\text{FiO}_2$, and arterial oxygen saturation (SaO_2)/ FiO_2 , effectively reducing the incidence of postoperative hypoxemia and decreasing the need for salvage NIV and reintubation.⁷⁴ Besides, prophylactic HFNC therapy after cardiothoracic surgery has been proven to reduce the requirement for escalated respiratory support and reintubation.⁷⁷ Data from a multicenter, randomized trial in cardiothoracic patients at risk of respiratory failure indicated that HFNC demonstrated comparable therapeutic effects to bilevel positive airway pressure but with a lower incidence of skin rupture.⁶⁹ Even in patients with hypoxemia, HFNC therapy following extubation has been shown to effectively reduce the need for rescue NIV.⁷⁸ While multiple studies have reported the advantages of HFNC therapy, there have still been some controversial results. In a study of 155 elective cardiac surgery patients with a body mass index (BMI) $\geq 30 \text{ kg/m}^2$, Corley et al found that postoperative HFNC therapy did not improve $\text{PaO}_2/\text{FiO}_2$ at 24 hours post-extubation or reduce the incidence of early atelectasis.⁷⁵ Similarly, the OPERA trial, a multicenter RCT conducted across three university hospitals in France, indicated that among patients with a high risk of PPCs, prophylactic HFNC did not prevent postoperative hypoxemia within 24 hours or reduce pulmonary complications.⁷⁶ It should be noted that the risk of extubation failure increased with the number of risk factors. Studies in critical patients concluded that in patients with four or more risk factors for extubation failure, prophylactic NIV combined with active humidification may be superior to HFNC, leading to better respiratory outcomes.⁷⁹ Therefore, it is essential to conduct a careful and individualized assessment of a patient's condition, risk factors for extubation failure and potential PPCs before selecting an oxygen therapy strategy, and to escalate respiratory support in a timely manner, as needed. The guidelines from the European Respiratory Society (ERS) recommend the use of HFNC or COT for patients with a low risk of PPCs, and HFNC or NIV for patients with a high risk of PPCs for postoperative oxygen therapy.⁸⁰ These recommendations highlight the broad applicability of HFNC for postoperative oxygen therapy across the entire population, with outstanding performance in balancing oxygenation effects and patient comfort.

There remains a challenging clinical problem in the application of HFNC for postoperative oxygen therapy: potential intubation delay following HFNC failure. Such delays may exacerbate respiratory muscle fatigue and induce cardiopulmonary dysfunction, increasing the risks of adverse events. Evidence indicates that delayed intubation following HFNC failure (48 hours after initiating HFNC) is associated with higher intensive care unit (ICU) mortality and longer mechanical ventilation duration.⁸¹ These findings highlight the necessity of closely monitoring the efficacy of oxygen therapy and promptly adjusting oxygen therapy interventions. Clinical symptoms such as persistent tachypnea, hypoxemia, and thoracoabdominal asynchrony¹³ may indicate the need to escalate respiratory therapy, but solely relying on clinical signs may lead to delayed decision making. Reliable predictive tools to evaluate the efficacy of HFNC are urgently required. Roca et al proposed the respiratory rate oxidation index (ROX index, calculated as the ratio of $\text{SpO}_2/\text{FiO}_2$ to respiratory rate) to predict the effectiveness of HFNC therapy.⁸² A ROX index ≥ 4.88 was an important predictor of successful HFNC therapy for pneumonia patients.⁸² Conversely, ROX indices of < 2.85 at 2 hours, < 3.47 at 6 hours, and < 3.85 at 12 hours indicated HFNC failure, with specificities of 99.2%, 99.2%, and 98.4%, respectively.⁸³ Other modified indices, such as the mROX⁸⁴ ($\text{PaO}_2/\text{FiO}_2$ to respiratory rate ratio) and ROX-HR⁸⁵ (ROX index to heart rate ratio), have also shown utility in predicting HFNC failure among patients with acute hypoxemia. Machine learning technologies have enabled the integration of multiple clinical indicators to predict HFNC failure and identify more complex and individualized thresholds for escalating respiratory support. For instance, a support vector machine-based

Table 3 Summary of Current Trials Evaluating HFNC Oxygenation During Postoperative Recovery

Surgery	Design	Population (n)	Comparison	Primary Outcome	Results	Reference
Cardiothoracic surgery	RCT	ARF or with risks of ARF after extubation (n=830)	HFNC (50 L/min, FiO ₂ =50%) vs BiPAP (pressure support level=8 cmH ₂ O; PEEP=4 cmH ₂ O; FiO ₂ =50%)	Treatment failure (reintubation, switch to the other study treatment, or premature treatment discontinuation)	No differences in treatment failure between HFNC group and BiPAP group	[69]
Major gynecological surgery	RCT	Female adult patients (n=83)	HFNC (60 L/min) vs COT; FiO ₂ was initially set at 40% and then titrated to maintain 94% < SpO ₂ ≤98%	PaO ₂ /FiO ₂ ratio after 2 h of treatment	Higher PaO ₂ /FiO ₂ ratio with HFNC than with COT	[70]
Orthopedic surgery	RCT	≥65 years old (n=60)	HFNC (40 L/min, FiO ₂ =60%) vs COT (4 L/min; FiO ₂ =60%)	PaO ₂ 1 h after extubation	Higher PaO ₂ with HFNC than with COT	[71]
Laparoscopic bariatric surgery	RCT	Adults with BMI ≥35 kg/m ² , ASA II–III (n=69)	HFNC (60 L/min, FiO ₂ =50%) vs COT (15 L/min; FiO ₂ =50%)	Incidence of hypoxemia (PaO ₂ /FiO ₂ ratio <300 mmHg) 3 h after extubation	Lower incidence of postoperative hypoxemia in HFNC group than in COT group	[72]
Esophagectomy	Retrospective observational study	Postoperative hypoxemia (PaO ₂ /FiO ₂ ratio <300 mmHg or SaO ₂ <92%, RR >30 breaths/min) (n=177)	HFNC (30–40 L/min) vs COT; FiO ₂ was titrated to maintain SpO ₂ ≥98%	Clinical outcomes after oxygen therapy	Higher PaO ₂ on postoperative day 1–4 in HFNC group than in COT group	[73]
Thoracoscopic lobectomy	RCT	Adults, ARISCAT score ≥26 (n=64)	HFNC (35–60 L/min) vs COT; FiO ₂ (45–100%) was titrated to maintain SpO ₂ ≥95%	Incidence of hypoxemia (PaO ₂ /FiO ₂ ratio <300 mmHg) in the first 72 h after extubation	Lower incidence of postoperative hypoxemia in HFNC group than in COT group	[74]
Cardiac surgery	RCT	Adults with BMI ≥30 kg/m ² (n=155)	HFNC (35–50 L/min) vs COT (2–6 L/min); FiO ₂ was titrated to maintain SpO ₂ ≥95%	Atelectasis scores based on chest X-ray	No difference in atelectasis scores on postoperative day 1 or 5 between HFNC group and COT group; no difference in PaO ₂ /FiO ₂ ratio 24 h post-extubation between groups	[75]
Major abdominal surgery	RCT	Adults, ARISCAT score ≥26 (n=220)	HFNC (50–60 L/min) vs COT; FiO ₂ was titrated to maintain SpO ₂ ≥95%	Incidence of hypoxemia (PaO ₂ /FiO ₂ ratio <300 mmHg) 1 h after extubation	Comparable incidence of post-extubation hypoxemia between HFNC group (21%) and COT group (24%)	[76]

Abbreviations: ARF, acute respiratory failure; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; ASA, American Society of Anesthesiologists physical status classification; BiPAP, bilevel positive airway pressure; BMI, body mass index; COT, conventional oxygen therapy; FiO₂, inspired oxygen concentration; HFNC, high-flow nasal cannula; PaO₂, partial pressure of oxygen in artery; PEEP, positive end-expiratory pressure; RCT, randomized controlled trial; RR, respiratory rate; SaO₂, arterial oxygen saturation.

model achieved an accuracy of 83%, a sensitivity of 84%, a specificity of 82%, and an area under the curve of 0.82 in external validation.⁸⁶ Given the differences between perioperative respiratory management and ICU clinical practice, additional studies are needed to validate the predictive performance and refine relative interpretations of these predictive tools in different clinical settings. Decision timepoints should be refined and key clinical parameters such as PaO₂ and PaCO₂ should also be incorporated to adapt to perioperative clinical practice. Future research should focus on more comprehensive and perioperative-specific models.

Evidence Assessments and Clinical Recommendations for Perioperative Oxygen Therapy

A preliminary evaluation of the available evidence was conducted (Table 4). The application of HFNC for procedural sedation is supported by multiple high-quality RCTs and rigorous meta-analyses, representing the indication with the

Table 4 Summary of Evidence Assessments Across Perioperative Settings

Perioperative Setting	Studies Included in the Review	Methodological Assessment	Inconsistency in Results	Overall Evidence Assessment
Procedural sedation	12 RCTs, 3 meta-analyses	7 rigorous, small-scale RCTs; 1 small-scale RCT with unclear risk of bias in randomization and allocation concealment; 1 rigorous, medium-scale RCT; 3 high-quality, large-scale RCTs; 1 methodologically rigorous meta-analysis with heterogeneity concerns; 2 methodologically rigorous meta-analyses	Most studies reported HFNC superior to COT; only two small-scale RCTs (in children and morbidly obese adults) reported comparable outcomes	Strong evidence from multiple rigorous RCTs and meta-analyses supported the superiority of HFNC over COT, with minor inconsistencies limited to specific subpopulations
Anesthesia induction				
Only spontaneous breathing	1 RCT, 2 observational studies	Small-scale trials; predominantly observational studies; single RCT with unclear blinding risk	Consistent evidence indicated HFNC was less efficient during spontaneous breathing than COT	Moderate evidence from small-scale and observational studies consistently indicated HFNC was inferior to COT in efficiency
Only apneic oxygenation	2 RCTs, 1 non-randomized interventional study	2 small-scale RCTs; 1 large-scale multicenter trial with potential risk of bias in randomization	Consistent evidence demonstrated HFNC effectively prolonged safe apnea time during apneic oxygenation, superior to COT	Robust evidence from interventional studies demonstrated HFNC effectively prolonged safe apnea time, despite some methodological concerns
Total stage of preoxygenation	6 RCTs, 2 meta-analyses	1 small-scale RCT with risk of bias in outcome measurement; 4 rigorous, small-scale RCTs; 1 rigorous, medium-scale RCT; 2 methodologically rigorous meta-analyses with heterogeneity concerns	Most studies indicated HFNC was superior to COT; only small-scale RCT in morbidly obese adults reported comparable outcomes	Robust evidence overall favored HFNC over COT, with comparable outcomes only noted in specific populations (eg, morbidly obese adults)
Tubeless laryngopharyngeal surgery	1 RCT, 3 observational studies, 1 systematic review	1 high-quality, large-scale RCT; 3 small-scale observational studies; 1 meta-analysis with potential selective bias	Population dependent: HFNC superior to COT in adults but inferior in children	Moderate evidence with population-dependent outcomes: superior to COT in adults, inferior in children based on a high-quality RCT
Postoperative recovery	7 RCTs, 1 observational study	4 rigorous, small-scale RCTs; 2 rigorous, medium-scale RCTs; 1 high-quality, large-scale RCT; 1 observational study with potential selective bias	Consistent superiority of HFNC over COT in general patient populations; in patients with high-risk postoperative complications: one small RCT reported superior results with HFNC, while two medium-sized RCTs reported comparable results to COT	Robust evidence supported HFNC superiority over COT in general patients; limited evidence in patients with high-risk postoperative complications owing to inconsistent findings

Abbreviations: COT, conventional oxygen therapy; HFNC, high-flow nasal cannula; RCT, randomized controlled trial.

Table 5 Evidence-Based Clinical Practice Recommendations for Perioperative HFNC

Perioperative Setting	Patients	Recommendations
Procedural sedation		
	Adult patients Pediatric or morbidly obese patients	Recommend HFNC as superior to COT Recommend HFNC as a supplement to COT
Anesthesia induction		
Only spontaneous breathing Only apneic oxygenation	All patients All patients	Recommend facemask Recommend HFNC as superior to facemask
Total stage of preoxygenation		
	General patients Critical or complex patients	Recommend HFNC as superior to facemask Recommend the combined use of HFNC and NIV
Tubeless laryngopharyngeal surgery		
	Adult patients Pediatric patients	Recommend HFNC as supplement to routine care Not recommended for HFNC
Postoperative recovery		
	Patients with low risk of PPCs Patients with high risk of PPCs	HFNC or COT HFNC or NIV; individualized assessment is suggested

Abbreviations: COT, conventional oxygen therapy; HFNC, high-flow nasal cannula; NIV, non-invasive ventilation; PPCs, postoperative pulmonary complications.

strongest evidence.^{5,9–11} Synthesis of these evaluations informed the summarized recommendations for perioperative oxygen therapy across various clinical scenarios (Table 5). For most perioperative scenarios, HFNC was recommended as an alternative or preferred option over COT, with the exception of pediatric tubeless surgery.^{5,12,60,80} Besides, individualized assessments remained essential. For patients at high risk of PPCs, HFNC or NIV was recommended for oxygen therapy during postoperative recovery, and NIV combined with active humidification may be optimal for critically ill patients.^{79,81} It should be acknowledged that the assessments of evidence strength in Table 4 were performed via a structured descriptive synthesis based on three key dimensions: study design, methodological rigor, and consistency of findings. As a narrative review, this work carries inherent limitations. A systematic literature analysis and formal evidence grading (for example, the Grading of Recommendations, Assessment, Development, and Evaluation framework)⁸⁷ were not performed, nor were statistical evaluations of publication bias, imprecision, or heterogeneity feasible. Consequently, the evidence assessments remain descriptive and qualitative. Definitive evidence strengths require confirmation through systematic reviews, and clinical judgment remains paramount.

Conclusion

As an emerging respiratory support technology, HFNC addresses a key unmet need in perioperative care: providing reliable, non-invasive oxygenation without interfering with procedural access or compromising patient comfort. Multiple studies indicate that HFNC has demonstrated considerable potential across various perioperative settings, with the strongest evidence in applications during procedural sedation. Its unique efficacy during apneic oxygenation offers a valuable alternative for oxygenation during laryngoscopy, tracheal intubation, and brief tubeless surgery. However, heterogeneity in oxygen flow rates, fractions, and treatment durations across studies limits comparability, and the optimal HFNC protocol remains to be established. Challenges include balancing the benefits of high-flow therapy against potential barotrauma risks and weighing oxygenation efficacy against adverse effects associated with high FiO₂ exposure. Clinically, HFNC also faces challenges such as risk of CO₂ retention during anesthesia, limitations of EtCO₂ monitoring, and the potential for delayed intubation in patients at high risk of PPCs. In summary, based on existing evidence, HFNC should be considered as a valuable and recommended technique in perioperative respiratory management. Future

research should focus on optimizing clinical protocols, developing reliable predictive models, and validating these through large-scale, multicenter RCTs to advance evidence-based and precise strategies for perioperative respiratory management.

Abbreviations

BMI, body mass index; COT, conventional oxygen therapy; CPAP, continuous positive airway pressure; EtO₂, end-tidal oxygen concentration; FiO₂, inspired oxygen concentration; HFNC, high-flow nasal cannula oxygen therapy; ICU, intensive care unit; NIV, non-invasive ventilation; PaCO₂, arterial carbon dioxide pressure; PaO₂, arterial oxygen pressure; PEEP, positive end-expiratory pressure; PPCs, postoperative pulmonary complications; ROX index, respiratory rate oxygenation index; mROX, modified respiratory rate oxygenation index; ROX-HR, respiratory rate oxygenation index to heart rate ratio; SaO₂, arterial oxygen saturation; SpO₂, peripheral oxygen saturation; THRIVE, transnasal humidified rapid-insufflation ventilatory exchange.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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