Review

High-Flow Nasal Oxygen Therapy for Perioperative Respiratory Optimization and Peri-Oxygenation in Patients with Chronic Cardio-Respiratory Disease: A Comprehensive Evidence Review

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High-Flow Nasal Oxygen Therapy for Perioperative Respiratory Optimization and Peri-Oxygenation in Patients with Chronic Cardio-Respiratory Disease: A Comprehensive Evidence Review

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Abstract

Background: Patients with chronic cardio-respiratory diseases face substantially elevated perioperative complication risks. High-flow nasal oxygen (HFNO) therapy has emerged as a promising non-invasive respiratory support modality, yet evidence specific to this high-risk population has not been comprehensively synthesized. **Objectives:** To systematically evaluate HFNO effectiveness across the perioperative continuum—including pre-oxygenation, apneic oxygenation, and post-extubation support—in patients with chronic obstructive pulmonary disease, heart failure, interstitial lung disease, obesity, and related conditions. We aimed to compare HFNO with alternative modalities and provide evidence-based implementation guidance. **Methods:** We conducted a comprehensive narrative review with systematic search of major databases including PubMed, Embase, and the Cochrane Library for randomized controlled trials, systematic reviews, and observational studies involving adult patients with chronic cardio-respiratory diseases undergoing surgery with HFNO intervention at any perioperative phase. Quality assessment using established tools was performed with structured narrative synthesis organized by perioperative phase and disease population. **Results:** The review synthesizes evidence across multiple perioperative applications, comparing HFNO effectiveness with conventional oxygen therapy and non-invasive ventilation. Disease-specific considerations for chronic obstructive pulmonary disease, heart failure, obesity and obstructive sleep apnea, interstitial lung disease, and thoracic surgery populations are delineated. Evidence-based clinical algorithms for patient selection, protocol optimization, and escalation strategies are provided. Cost-effectiveness, implementation barriers, training requirements, and integration into Enhanced Recovery pathways are addressed. **Conclusions:** HFNO represents a valuable non-pharmacological intervention for perioperative respiratory optimization in chronic cardio-respiratory disease patients. This comprehensive synthesis provides clinicians with evidence-based guidance for implementation while identifying critical research gaps. Proper patient selection and protocol optimization can reduce postoperative pulmonary complications, prevent reintubation, and improve outcomes in this high-risk population. Future research should focus on personalized approaches, long-term outcome assessment, and implementation science.

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1. Introduction

Maintaining adequate perioperative oxygenation is the cornerstone of safe anesthetic management. Each year, approximately 310 million surgical procedures are performed worldwide, encompassing anesthetic approaches ranging from general anesthesia to procedural sedation, and exposing patients to the risk of hypoxemia with potential complications including cerebral hypoxia, cardiac arrest, and death [1]. Hypoxemia is a primary driver of postoperative pulmonary complications, contributing significantly to post-surgical morbidity and mortality, particularly in patients with pre-existing pulmonary disease.

Multiple strategies are available to optimize oxygenation and ventilation in the perioperative period, ranging from low-flow systems (nasal cannulae, simple face masks) to higher-flow oxygen delivery devices (Venturi masks, non-rebreather masks) and high-flow nasal oxygen (HFNO).

Conventional oxygen therapy (COT)—encompassing nasal cannulae, face masks, Venturi masks, and non-rebreather masks with reservoir—has long been considered the first-line treatment for hypoxemic patients. Low-flow nasal cannulae are widely used in the perioperative setting; however, oxygen delivery is inherently limited, with a FiO_2 ranging from 24% to 44%, and flow rates should not exceed 6 $L \cdot min^{-1}$, beyond which further FiO_2 increase is prevented by room-air dilution [2]. During inspiration, inhaled air is warmed to body temperature and humidified along the upper airway; however, when supplemental oxygen is delivered via a bubble humidifier, absolute humidity remains low. This leads to dryness and irritation of the nasal and oropharyngeal mucosa, impaired mucociliary clearance, and patient discomfort [3,4]. Furthermore, delivery of unconditioned gas increases upper airway resistance and reduces inspiratory flow [2–4]. In patients with specific comorbidities—such as obesity or obstructive sleep apnea—or with pre-existing pulmonary disease, low-flow oxygen delivery may prove insufficient to meet metabolic demands.

HFNO overcomes many of the limitations of COT while maintaining good patient tolerability, and has opened new frontiers in respiratory support across diverse clinical contexts.

1.1. High-Flow Nasal Cannula and New Frontiers

HFNO therapy is widely used in intensive care units as an alternative to non-invasive ventilation for hypoxemic patients with acute respiratory failure and a PaO_2/FiO_2 ratio below 200 mmHg. Given the multiple benefits demonstrated in the critical care setting, the past decade has seen numerous studies validating its use in perioperative contexts as well [5,6].

The HFNO system represents a versatile oxygenation strategy applicable to multiple phases of anesthetic management. In general anesthesia, its application extends from pre-oxygenation through endotracheal intubation, a phase commonly referred to as peri-oxygenation. HFNO has also been used during procedural sedation for gastrointestinal and thoracic endoscopy, as the basis for apneic oxygenation techniques such as Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE) in upper airway procedures [7], and as respiratory support during awake tracheal intubation [8].

HFNO delivers heated and fully humidified oxygen—maintained at 34–37 °C with 100% relative humidity (equivalent to 44 mg $H_2O \cdot L^{-1}$)—through dedicated wide-bore nasal cannulae at flow rates ranging from 20 to 70 $L \cdot min^{-1}$, with an adjustable FiO_2 from 0.21 to 1.0 [4,9,10]. The system comprises a soft silicone nasal interface with openings wider than those of conventional nasal cannulae, a flow meter, a heating element, a single heated inspiratory circuit with minimal condensation, an active humidifier, and an oxygen inlet (Figure 1).

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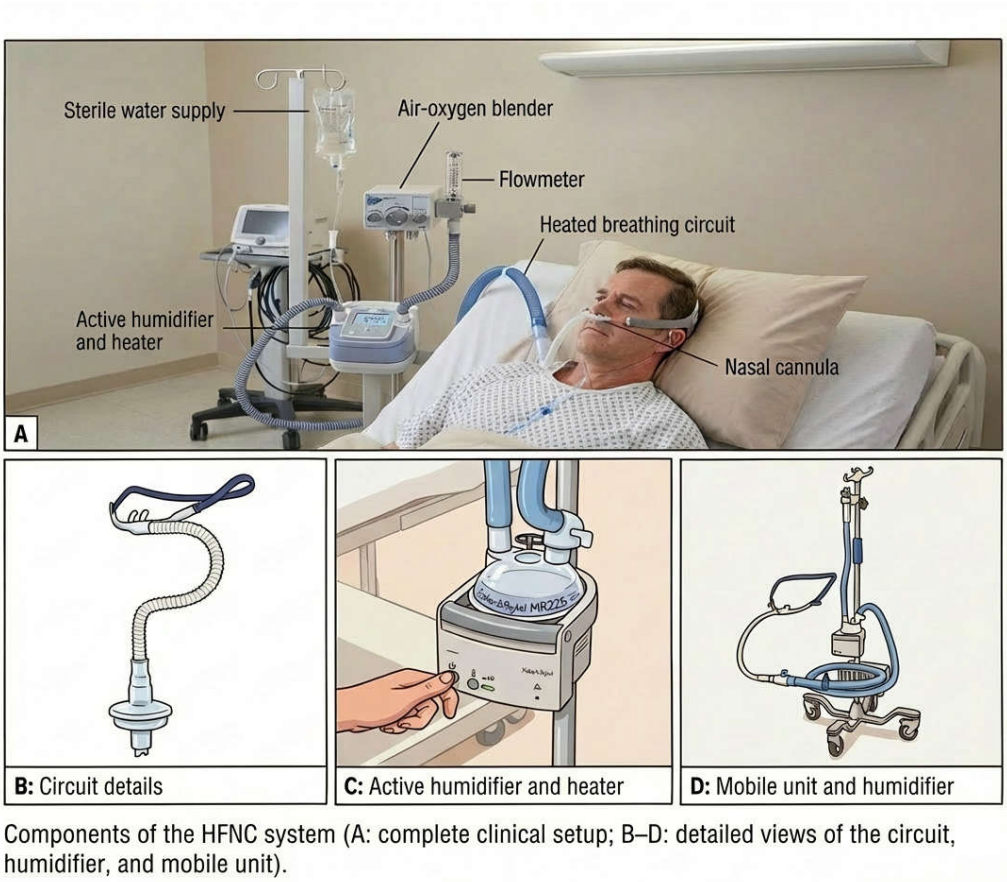

Figure 1. Components of the HFNO system. A: complete clinical setup; B–D: detailed views of the circuit, humidifier, and mobile unit.

1.2. Mechanism of Action and Benefits of HFNO

HFNO is a straightforward, comfortable, and well-tolerated method of oxygen administration (Table 1). At flow rates exceeding 60 L·min^{-1}, HFNO reduces anatomical dead space volume and promotes washout of expired carbon dioxide from the upper airways, thereby minimizing CO_2 rebreathing [9,11]. Because the delivered flow rate exceeds the patient's peak inspiratory flow, dilution of oxygen with ambient air is prevented, ensuring closer correspondence between the set and the delivered FiO_2. In addition, HFNO promotes a more favorable respiratory pattern by reducing respiratory rate, decreasing work of breathing, and increasing tidal volume [5,10]. Combined with optimal airway humidification and heating, these effects reduce inspiratory airway resistance and respiratory effort, lowering the patient's overall metabolic demand.

Table 1. Technical comparison of High-Flow Nasal Oxygen (HFNO), Conventional Oxygen Therapy (COT), and Non-Invasive Ventilation (NIV). Tolerability is expressed on a semiquantitative scale (+++ excellent, ++ good, + moderate). RH: relative humidity; PEEP: positive end-expiratory pressure.

PARAMETER	HFNO	CONVENTIONAL OXYGEN THERAPY	NIV
Flow rate (L·min^{-1})	20–70	1–15	Variable
FiO_2	0.21–1.0	0.24–0.90	0.21–1.0
Humidification	Active (100% RH, 44 mg H_2O·L^{-1})	Passive/absent	Variable
Gas temperature (°C)	34–37	Ambient	Ambient
Generated PEEP (cmH_2O)	2.7–7.4	0	Adjustable

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Interface	Wide-bore nasal cannulae	Face mask/nasal cannulae	Face/nasal mask
Patient tolerability	+++	++	+

Although HFNO does not form a closed circuit, the high flow rate limits expiratory air outflow, generating a low level of positive airway pressure of approximately 2.7–7.4 cmH_2O, analogous to positive end-expiratory pressure (PEEP) [11,12]. This promotes alveolar recruitment, reduces atelectasis and bronchospasm, and attenuates ventilation–perfusion mismatch [13,14]. Finally, the delivery of adequately heated and humidified gas prevents mucosal dryness, reduces the energy expenditure associated with airway gas conditioning, protects the mucociliary epithelium, and facilitates mucus clearance [4,8,10].

The clinical benefits of HFNO vary according to the interface used—nasal cannulae versus tracheostomy tube. Natalini and colleagues demonstrated that, in tracheostomized patients, a minimum flow rate of 50 $L \cdot min^{-1}$ is required to achieve adequate oxygenation and a meaningful reduction in work of breathing, as reflected by decreased respiratory rate and generation of minimal positive expiratory pressure [15]. In contrast, patients receiving HFNO via nasal cannulae achieve comparable effects at flow rates of 30 $L \cdot min^{-1}$. This difference reflects the fact that, in the setting of tracheal oxygen delivery, the reduction in anatomical dead space and inspiratory resistance is attenuated, necessitating higher flow rates to achieve equivalent clinical benefit.

1.3. Contraindications

HFNO is contraindicated in cases of severe nasal obstruction, profuse epistaxis, recent facial trauma, recent nasal surgery, significantly raised intracranial pressure, and skull base fractures due to the risk of pneumocephalus [16–18].

2. Hfno for Pre-Oxygenation

General anesthesia and endotracheal intubation are associated with potentially serious complications, including oxygen desaturation, hemodynamic instability, arrhythmias, hypoxic brain injury, cardiac arrest, and death. Perioperative hypoxemia may result from difficult oxygenation or mask ventilation, or from difficult and failed endotracheal intubation, particularly in patients with clinical or anatomical predictors of challenging airway management [19]. To mitigate the peri-intubation risk of desaturation, a reliable and continuous oxygen supplementation strategy is of paramount importance. HFNO, through effective pre-oxygenation and the possibility of being maintained in situ during airway instrumentation, can achieve this goal with a favorable benefit-to-risk profile [19–23].

2.1. Pre-Oxygenation: Conventional Oxygen Therapy Versus High-Flow Oxygen Therapy

Conventionally, pre-oxygenation in the operating room involves administration of 100% oxygen at a flow rate exceeding the patient's minute ventilation through a well-fitted face mask. Adequate denitrogenation of the expiratory reserve volume and functional residual capacity can be achieved with different techniques depending on patient cooperation and time constraints; under standard conditions, three to five minutes of tidal volume breathing is considered acceptable in healthy adults [19]. Adequate pre-oxygenation with a face mask allows a healthy adult to sustain an apneic interval of seven to ten minutes without developing hypoxemia [22,23].

With HFNO intratracheal FiO_2 increases proportionally with the delivered oxygen flow rate. One study demonstrated a significant rise in intratracheal FiO_2 from 67% to 93% as the flow rate increased from 15 to 45 $L \cdot min^{-1}$ [24], supporting the use of flows above 50 $L \cdot min^{-1}$ to maximize oxygenation. FiO_2 should be set to 1.0, and patients should be instructed to breathe with their mouth closed in order to maintain the nasopharyngeal positive pressure generated by HFNO [25].

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HFNO is generally well tolerated by awake patients, though some individuals experience discomfort at flow rates of 50–70 L·min^{-1}, in which case immediate flow reduction is recommended, with subsequent titration back to 50–70 L·min^{-1} once consciousness is lost [3]. A recent study suggests that the optimal flow rate for HFNO pre-oxygenation in elective surgical patients is 45 L·min^{-1}, as higher values offer limited additional extension of safe apnea time while increasing patient discomfort [26].

In pediatric patients, flow rate is weight-based, set at 2 L·kg^{-1}·min^{-1} according to the following thresholds: 0–15 kg, 35 L·min^{-1}; 15–30 kg, 40 L·min^{-1}; 30–50 kg, 50 L·min^{-1} [27,28].

2.2. Pre-Oxygenation of the Obese Patient

A body mass index greater than 35 kg·m^{-2} is an independent predictor of difficult mask ventilation and, in some cases, difficult intubation. Conventional face mask pre-oxygenation is of limited benefit in this population, as obesity-related pathophysiological changes substantially reduce safe apnea time [23,29].

Obesity is associated with a reduction in respiratory system compliance of up to 35%. Increased thoracic and abdominal mass raises pleural pressure and restricts chest wall excursion, while increased intra-abdominal volume and visceral fat elevate the diaphragm, reducing its mechanical efficiency to approximately half that observed in lean individuals [23,30]. These changes increase metabolic oxygen demand while simultaneously reducing expiratory reserve volume and functional residual capacity, promoting atelectasis, decreasing tidal volume, and increasing respiratory rate [23,31].

Appropriate patient positioning during pre-oxygenation is essential to extend safe apnea time and reduce the risk of pulmonary aspiration. Elevating the head to a 25-degree incline and optimizing airway alignment through targeted pillow placement—the so-called ramped position—is recommended.

The optimal pre-oxygenation strategy in patients with obesity is positive airway pressure, with or without pressure support [29]. When non-invasive ventilation (NIV) is unavailable, HFNO can be used as a standalone strategy or as a supplement during face mask pre-oxygenation to compensate for mask leaks while generating a minimum level of continuous positive airway pressure, provided the patient breathes with mouth closed (FiO_2 1.0, 60 L·min^{-1}). In a randomized controlled trial, Wu and colleagues compared HFNO versus face mask alone in 80 obese patients, demonstrating higher partial pressure of arterial oxygen and a significantly lower rate of peri-intubation desaturation events in the HFNO group [32]. A key advantage of HFNO is that it can remain in place following induction of anesthesia—unlike a face mask, which must be removed before laryngoscopy—thereby enabling uninterrupted apneic oxygenation during airway instrumentation (Figure 2).

Schutzer-Weissmann and colleagues demonstrated an extension of safe apnea time to 18 minutes without desaturation in obese patients pre-oxygenated with HFNO [33]. Heinrich and colleagues confirmed the efficacy of HFNO at FiO_2 1.0 and 50 L·min^{-1} in obese patients undergoing bariatric surgery, comparing it with continuous positive airway pressure at 7 cmH_2O/FiO_2 1.0 and face mask at 12 L·min^{-1}/FiO_2 1.0 [34]. The primary endpoint—PaO_2 measured at 1, 3, 5, and 7 minutes from rapid sequence induction and intubation (RSII)—showed that HFNO significantly improved oxygenation at 5 and 7 minutes compared to face mask, without a significant difference relative to CPAP. However, a recent systematic review [35] indicates that, while positioning optimization remains the most effective preparation strategy, there may be no difference between HFNO and conventional face mask pre-oxygenation in preventing oxygen desaturation below 92% before intubation in elective obese surgical patients.

Recent studies [36,37] suggest that HFNO pre-oxygenation may also be beneficial in patients with obstructive sleep apnea (OSA), who are particularly prone to difficult mask ventilation and early desaturation. When left in place following induction, HFNO prolonged safe apnea time and reduced the incidence of desaturation episodes in this population.

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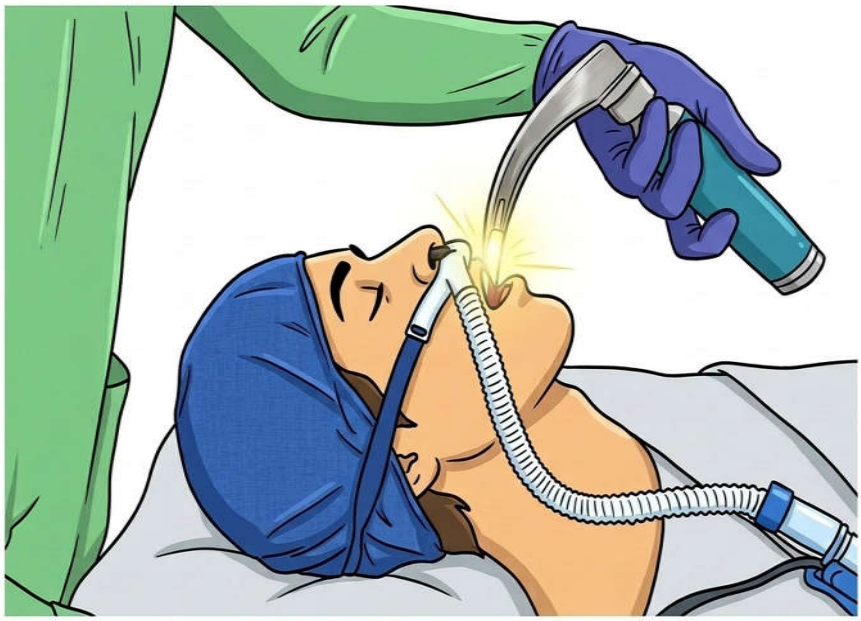

Figure 2. High-Flow Nasal Oxygen During Direct Laryngoscopy. HFNO cannulae remain in situ during laryngoscopy, enabling uninterrupted apneic oxygenation with heated, humidified oxygen throughout the peri-intubation period—a key advantage over facemask or NIV-based strategies.

2.3. Pre-Oxygenation of the Pregnant Patient

The pregnant patient requiring general anesthesia represents a rare but clinically distinctive scenario. During pregnancy, oxygen consumption increases by approximately 20%, while functional residual capacity decreases by 20% as a consequence of diaphragmatic elevation by the gravid uterus [37,38]. These reciprocal physiological changes create a state of vulnerability in which desaturation can occur within 2–3 minutes of apnea, compared to 7–10 minutes in non-pregnant adults [37,38]. The situation becomes particularly critical during obstetric hemorrhage, where increased metabolic demands, reduced oxygen reserve, and potential hypovolemia compound the risk of rapid desaturation [39]. Pregnancy-related airway changes—including progression of Mallampati score, mucosal edema, and heightened aspiration risk—further complicate airway management [39].

In this context, HFNO offers clinically relevant advantages over conventional approaches. Zhou and colleagues demonstrated that HFNO maintains superior maternal oxygenation during RSII compared to conventional face mask pre-oxygenation [38]. The generation of positive nasopharyngeal pressure [12,25] without the need for mask removal allows continuous oxygenation throughout airway assessment and instrumentation.

High-risk obstetric patients—including those with pre-eclampsia complicated by pulmonary edema, obesity and obstructive sleep apnea [36,37], and those undergoing emergency cesarean section—may derive extended benefit from HFNO-based pre-oxygenation.

Current guidelines suggest the use of HFNO or low-flow nasal cannulae during the pre-intubation phase, although the supporting evidence base remains limited [39]. A recent systematic review including 11 studies [40] concluded that the advantages of perioperative HFNO over COT in the obstetric population remain uncertain, underscoring the need for further adequately powered trials in this specific setting.

2.4. Pre-Oxygenation of Critically Ill Patients

Critically ill patients represent a particularly fragile population: recent studies highlight a relevant incidence of cardiovascular complications (>40%) and hypoxemic events (9%) during airway

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management, with a 3.1% incidence of cardiac arrest [41,42]. The risk of complications is further increased in critically ill patients with obesity, particularly with respect to hypoxemia [43].

The optimal pre-oxygenation strategy in this population requires prior hemodynamic optimization and thorough team preparation [44], and should be based primarily on positive airway pressure, ideally combined with pressure support [45].

HFNO alone has been shown to be inferior to NIV as a pre-oxygenation strategy in critically ill patients [46], and its use should therefore be reserved for cases in which NIV is contraindicated or in non-hypoxemic patients who require intubation [47]. While HFNO lacks the alveolar recruiting effect of sustained positive airway pressure and pressure support, it may be used in combination with NIV in severely hypoxemic patients to maximize the benefits of both techniques, including the provision of apneic oxygenation during airway instrumentation [48].

Notably, despite robust evidence supporting its superiority, NIV-based pre-oxygenation remains poorly implemented in intensive care units [44], and HFNO may nonetheless represent a meaningful advantage over conventional face mask pre-oxygenation in this setting [45].

3. Apneic Oxygenation with HFNO

Apneic oxygenation involves the continuous delivery of oxygen at variable flow rates during the phase immediately following induction of general anesthesia and preceding endotracheal intubation, when the patient's respiratory drive and neuromuscular activity are suppressed. The primary aim is to maintain adequate arterial oxygenation and delay the onset of desaturation, particularly in patients presenting with predictors of difficult airway management, reduced functional residual capacity, increased metabolic oxygen demand, or pre-existing respiratory disease [49,50].

The physiological basis of apneic oxygenation is the principle of apneic mass-flow diffusion. During apnea, oxygen previously accumulated in the nasopharynx, oropharynx, and alveolar space continues to diffuse passively across the alveolar-capillary membrane into the bloodstream at a rate of approximately 250 mL·min^{-1}. This net oxygen uptake generates a sub-atmospheric alveolar pressure, creating a sustained pressure gradient from the upper airways toward the alveoli that supports passive oxygen delivery in the absence of active ventilation [49,50] (Figure 3).

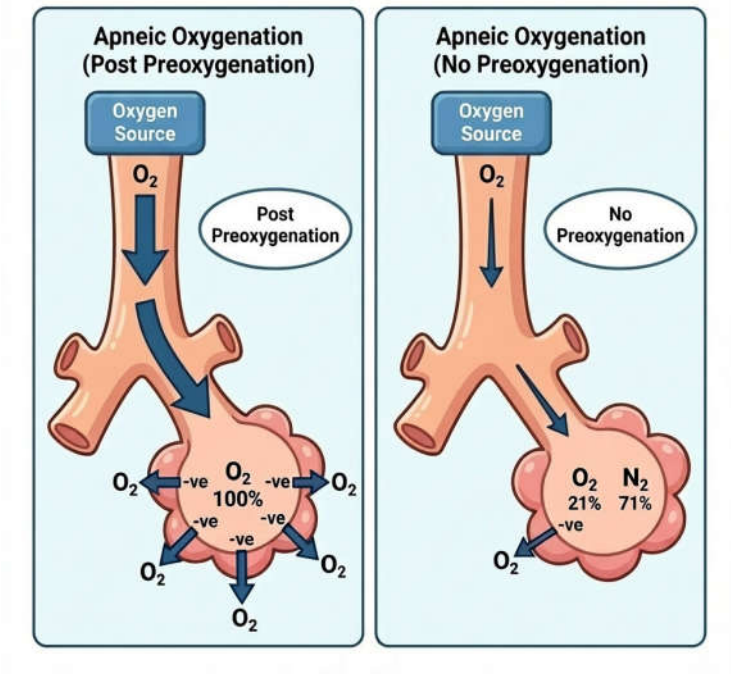

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Figure 3. Apneic Oxygenation. Schematic comparison of apneic oxygenation efficacy with (**left**) versus without (**right**) adequate preoxygenation, illustrating the impact of alveolar gas composition on passive oxygen diffusion gradient during apnea.

Maintenance of upper airway patency is a prerequisite for effective apneic oxygenation and may be achieved through jaw thrust, mandibular subluxation, or placement of a nasopharyngeal airway. Oxygen may be delivered via nasal cannulae, nasopharyngeal catheters, or oropharyngeal catheters at conventional low flow rates of 3–10 L·min^{-1}. HFNO, delivering heated and humidified oxygen at flow rates of 30–70 L·min^{-1}, offers substantially extended safe apnea time compared to these alternatives, with the additional benefits of positive nasopharyngeal pressure generation and partial CO_2 washout from the upper airway dead space [49,50].

3.1. Apneic Oxygenation in the Obese Patient

HFNO finds particular application in patients with severe obesity, obstructive sleep apnea, chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, neuromuscular disease, and pregnancy—all conditions in which functional residual capacity is reduced and/or upper airway patency is compromised. In patients with OSA, oxygen flows exceeding 20 L·min^{-1} reduce the apnea-hypopnea index by 64%; flows exceeding 35 L·min^{-1} generate a positive nasal end-expiratory pressure of 3–5 mmHg, sufficient to prevent upper airway collapse [36].

Wong and colleagues demonstrated the efficacy of HFNO in severely obese patients (BMI >40 kg·m^{-2}), showing a significant extension of safe apnea time to 4.3 minutes compared to 1.3 minutes in the control group [51]. Patel and colleagues described the technique of transnasal humidified rapid-insufflation ventilatory exchange (THRIVE)—HFNO delivered at 70 L·min^{-1} with FiO_2 1.0, initiated ten minutes before induction and maintained without interruption until airway securement—in a cohort that included patients with obesity and OSA among those with anticipated difficult airway management [52]. This approach yielded a mean apnea time of 14 minutes (median 9–19, range 5–65 minutes) without episodes of desaturation below 90% or clinically significant CO_2-related adverse events; the $EtCO_2$ increase rate was 0.15 kPa·min^{-1}.

The OPTIMASK study compared face mask alone versus combined face mask and HFNO during pre-oxygenation, with HFNO maintained through the apneic phase until intubation [53]. In 450 patients undergoing general anesthesia regardless of BMI, end-tidal oxygen values at the time of intubation were significantly higher in the combined face mask and HFNO group than in those receiving face mask alone, confirming the additive benefit of maintaining HFNO through the apneic interval.

3.2. Apneic Oxygenation in the Pediatric Patient

Compared to adults, children are at substantially greater risk of rapid arterial oxygen desaturation following cessation of ventilation, owing to reduced functional residual capacity, higher mass-specific oxygen consumption, and a predisposition to upper airway collapse [54]. One study demonstrated that mean time to desaturation below 90% SpO_2 was 160 seconds in children, 382 seconds in adolescents, and as short as 97 seconds in neonates, with an incidence of desaturation episodes of 4–10% during induction of general anesthesia and up to 20% during endotracheal intubation [54]. These figures underscore the importance of effective apneic oxygenation strategies in this population.

A study involving 48 children under ten years of age with normal airways compared HFNO with face mask pre-oxygenation [27]. HFNO was delivered at 2 L·kg^{-1}·min^{-1} with flow rates of 35, 40, or 50 L·min^{-1} stratified by body weight. Safe apnea time with SpO_2 above 92% was doubled in the HFNO group, reaching approximately ten minutes; beyond this threshold, progressive hypercapnia becomes the primary limiting factor [28]. For this reason, HFNO in children is considered safe for short surgical procedures with an anticipated apneic interval of 5–6 minutes, after which CO_2 monitoring and clinical reassessment are mandatory.

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3.3. Apneic Oxygenation in Laryngeal Surgery

Airway surgery presents a unique operational challenge in which the anesthesiologist and surgeon share the same operative field. Available ventilation and oxygenation strategies include transtracheal or transglottic jet ventilation, controlled mechanical ventilation through a small-diameter endotracheal tube, and apneic oxygenation [55]. HFNO has been described for laryngeal microsurgery under both deep sedation and general anesthesia with neuromuscular blockade—so-called non-intubated deep paralysis [56,57]—including in cases of difficult airway secondary to severe supraglottic-pharyngeal stenosis [58]. For short-duration procedures such as vocal cord microsurgery, HFNO avoids endotracheal intubation entirely [59]; it has also been validated as an effective oxygenation method for procedures of longer duration, including open laryngeal surgery [55].

A relevant advantage of HFNO over conventional low-flow nasal cannulae in this setting is its superior CO_2 clearance capacity. In adults, apneic oxygenation delivered at 70–80 $L \cdot min^{-1}$ results in an $EtCO_2$ increase of 0.12–0.17 $kPa \cdot min^{-1}$, while during spontaneous breathing under HFNO the rate of CO_2 rise is minimal, at approximately 0.03 $kPa \cdot min^{-1}$ [60]. The rate of CO_2 accumulation during apnea is greatest in the first 1–2 minutes and subsequently diminishes [61]. Transient respiratory acidosis resulting from apneic CO_2 accumulation does not represent a significant clinical risk under these conditions, as moderate hypercapnia has not been associated with arrhythmias or clinically meaningful sympathetic nervous system stimulation [62]. The precise mechanism of CO_2 washout during HFNO use remains incompletely understood; cardiogenic oscillations, gas mixing within the anatomical dead space, and micro-ventilation induced by pharyngeal pressure variations have been proposed as contributing mechanisms [63]. In children, CO_2 accumulation is substantially faster: in pediatric patients weighing 10–20 kg, transcutaneous PCO_2 rises at approximately 0.55 $kPa \cdot min^{-1}$ [28,64]. Continuous CO_2 monitoring—using transcutaneous sensors or dedicated nasal cannulae capable of $EtCO_2$ sampling—is therefore strongly recommended throughout procedures employing apneic oxygenation [65].

The most serious complication specific to head and neck surgery is airway fire, resulting from the concurrent presence of energy sources such as laser or electrocautery, an oxidizer-enriched atmosphere, and combustible materials. Over 80% of fires occurring in the operating room involve the head, neck, or upper chest [66]. A closed delivery circuit, such as a cuffed endotracheal tube, substantially reduces fire risk; however, its presence may preclude adequate surgical access to the posterior larynx, trachea, or distal airways. In such cases, tubeless airway management incorporating HFNO or THRIVE may be the only viable option.

High FiO_2 is widely recognized as a fire risk amplifier, while the relationship between high flow rate and ignition risk is less clearly established: increased flow delivers more oxygen to the surgical site, but the heightened absolute humidity of HFNO may conversely exert a suppressive effect on combustion [66–68]. Intermittent use of HFNO and systematic FiO_2 reduction whenever an energy source is active are therefore recommended. The use of HFNO in the presence of an ignition source during head and neck surgery carries a significant risk of airway fire, a concern formally highlighted in the anaesthesia literature [69]. Current safety recommendations advise limiting FiO_2 to 0.3 when an ignition source is present, with definitive airway securement required should a higher inspired oxygen fraction become clinically necessary [67,69].

3.4. Complications of Apneic Oxygenation

The principal limitation of apneic oxygenation—whether delivered via HFNO or conventional devices—is progressive hypercapnia. During apnea, $PaCO_2$ rises at approximately 3 $mmHg \cdot min^{-1}$ until reaching a plateau of around 65 mmHg [61]. High-flow HFNO (up to 70 $L \cdot min^{-1}$) attenuates this accumulation through enhanced dead-space CO_2 washout [60], though continuous monitoring of transcutaneous or end-tidal PCO_2 remains essential, and is of particular importance in the pediatric population in whom hypercapnia develops at a substantially accelerated rate.

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The risk of gastric insufflation with HFNO is considered theoretical. The positive nasopharyngeal pressure generated by HFNO with the patient's mouth closed is proportional to the delivered flow rate but remains well below the lower esophageal sphincter opening pressure. No clinically significant complications—including gastric insufflation, regurgitation, or pulmonary aspiration of gastric contents—have been reported in association with HFNO use, even in severely obese patients. A recent systematic review found no increase in gastric volume attributable to HFNO, though the supporting evidence was graded as low certainty [70].

4. HFNO for Awake Tracheal Intubation

Awake tracheal intubation (ATI) remains the gold-standard technique when difficult mask ventilation and difficult intubation are simultaneously anticipated. More recently, the emerging concept of the physiologically difficult airway has broadened the indications for ATI beyond purely anatomical considerations, positioning it as a clinically appropriate alternative to rapid sequence induction and intubation (RSII) in hemodynamically fragile patients in whom the cardiovascular consequences of induction agents—vasodilation, myocardial depression, or loss of sympathetic tone—may precipitate circulatory collapse [71,72]. Candidates for this approach include patients with critically reduced respiratory reserve, such as those with morbid obesity, advanced pregnancy, or obstructive sleep apnea [73], as well as patients undergoing complex thyroid [74], head and neck [55], or maxillofacial surgery [75] in whom airway distortion, compression, or restricted mouth opening makes post-induction intubation unreliable.

HFNO at flow rates of 40–70 $L \cdot min^{-1}$ has been widely adopted as a supportive technique during ATI, providing concurrent benefits across multiple physiological domains [76,77]. First, continuous delivery of high-flow humidified oxygen at FiO_2 1.0 maintains arterial oxygenation throughout the procedure, providing a meaningful safety margin in the event of a prolonged or technically challenging bronchoscopic passage. Second, the positive nasopharyngeal pressure generated by high-flow delivery partially stents the upper airway, attenuating the tendency toward pharyngeal collapse that may accompany deep sedation or topicalization-induced loss of muscle tone. Third, the thermal conditioning of inspired gas—warmed to 37 °C and fully humidified—reduces mucosal drying and irritation caused by prolonged breathing through an open mouth during the procedural preparation phase, improving patient comfort and reducing the perception of dyspnea [76,77].

From a practical standpoint, the nasal cannulae used for HFNO delivery do not impede passage of the flexible bronchoscope through the nasal or oral route, and the two devices may be used simultaneously without mutual interference. Asymmetric nasal cannula designs—in which one prong is shorter or absent—are also available and may be employed to further optimize access. When ATI is performed using a videolaryngoscope rather than a flexible bronchoscope, the benefits of HFNO are fully preserved, as the cannulae remain in situ and continue to deliver oxygenation and positive pressure throughout laryngoscopy and tube passage [76,77].

5. HFNO in the Postoperative Setting

General anesthesia, the type and duration of surgical intervention, postoperative pain, and residual neuromuscular blockade each contribute to clinically significant alterations in respiratory physiology, increasing the risk of postoperative hypoxemia and pulmonary complications. In this context, supplemental oxygen therapy following extubation is a well-established component of postoperative care. Recent evidence suggests that in patients with pre-existing pulmonary disease, HFNO may offer advantages over NIV in terms of clinical outcomes, complication rates, and therapy adherence [78–82].

However, HFNO is not universally appropriate for all patients at risk of postoperative acute respiratory failure. Current evidence and guidelines support non-invasive ventilation as the first-line ventilatory support strategy in patients who develop postoperative acute respiratory failure,

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particularly in the presence of hypercapnia or significant hypoxemia requiring positive airway pressure above that achievable with HFNO alone [83].

Futier and colleagues conducted a multicenter randomized controlled trial enrolling 220 patients undergoing major abdominal surgery with moderate-to-high risk of postoperative pulmonary complications, comparing post-extubation HFNO with conventional oxygen therapy [84]. The proportion of patients presenting with hypoxemia at one hour after extubation was comparable between the two groups, and early application of HFNO did not reduce the overall risk of developing postoperative pulmonary complications relative to COT. A reduction in pulmonary complications was observed only in the subgroup of patients who received HFNO in conjunction with intraoperative protective ventilation and recruitment maneuvers, suggesting that the benefit of HFNO in the postoperative setting may be contingent on the quality of intraoperative lung management rather than representing an independent effect of post-extubation HFNO alone.

The role of HFNO in mildly hypercapnic acute respiratory failure remains an area of active scientific debate, without clear consensus on its indications in this specific clinical scenario. A recent survey further highlights significant variability in HFNO clinical practice, which is frequently inconsistent with available guidelines and current real-world evidence [85].

6. HFNO in Procedural Sedation

Procedural sedation refers to the administration of hypnotic and/or analgesic agents to reduce the level of consciousness, anxiety, and pain during diagnostic or therapeutic procedures. It reliably produces retrograde amnesia, reducing the elaboration of unpleasant procedural memories [86], while the patient's spontaneous respiratory drive is typically preserved. Optimal monitoring during procedural sedation should include continuous pulse oximetry, electrocardiography, capnography, and assessment of sedation depth. Oversedation may nevertheless result in respiratory depression, loss of upper airway patency, and oxygen desaturation [87], with the risk being substantially amplified in physiologically fragile patients [88–90]. In this setting, HFNO represents a clinically valuable tool both to prevent hypoxemia and to attenuate hypercapnia resulting from sedation-induced hypoventilation.

Many respiratory and gastrointestinal procedures are performed under procedural sedation, and the airway management challenges differ in character between these two domains. In gastrointestinal endoscopy, the primary concern is sedation-induced upper airway obstruction and desaturation in patients sharing the operative field with the endoscope. Nay and colleagues demonstrated that HFNO significantly reduced desaturation episodes—defined as SpO_2 below 92%—compared to conventional oxygen therapy in patients undergoing gastrointestinal endoscopic procedures under deep sedation [91]. Subsequent studies confirmed the applicability of HFNO across a range of gastrointestinal procedures, including endoscopic retrograde cholangiopancreatography [88,89], with specific evidence supporting its use in obese patients [92] and in the pediatric population [93]. A randomized controlled trial demonstrated that HFNO was effective in preventing hypoxemia compared to COT in this context [94]. A recent systematic review concluded that, when compared with COT, HFNO results in fewer hypoxemic events, with the magnitude of benefit varying according to the specific procedure and patient population [95,96].

Respiratory endoscopy presents analogous challenges, with the additional complexity of the anesthesiologist and endoscopist sharing the same operative field. An increasing body of evidence—including multiple clinical studies and meta-analyses—has compared COT, HFNO, and NIV during diagnostic and procedural bronchoscopy, including endobronchial ultrasound (EBUS), transbronchial needle aspiration (TBNA), and bronchoalveolar lavage (BAL) [97–107]. HFNO has consistently demonstrated superiority over COT in terms of oxygenation maintenance, reduction of desaturation episodes, and reduction of procedure interruptions due to hypoxemia. When HFNO is compared directly with NIV, the latter provides greater oxygenation support, particularly in severely hypoxemic patients, in whom NIV remains the preferred strategy [107].

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7. HFNO in Emergency and Trauma Settings

The principles of HFNO application during difficult airway management extend naturally to emergency and trauma scenarios, where the simultaneous convergence of hemodynamic instability, potentially challenging airway anatomy, and extreme time pressure creates conditions of maximal procedural risk [72]. In trauma patients requiring RSII, the concept of the physiologically difficult airway [71] is particularly relevant, as the goal of securing the airway must be pursued while preserving—or at minimum not further compromising—an already tenuous cardiovascular and respiratory equilibrium.

In this context, HFNO offers several simultaneous physiological benefits: it maintains adequate oxygen delivery in patients with already reduced oxygen-carrying capacity, provides continuous oxygenation during laryngoscopy without requiring mask removal [108–110], generates positive airway pressure that supports alveolar recruitment [11,12], and extends safe apnea time even in the presence of hypovolemia [52,57,58]. In patients with traumatic brain injury requiring strict blood pressure control to preserve cerebral perfusion pressure, even brief episodes of desaturation can worsen secondary brain injury, making uninterrupted oxygenation a priority throughout the peri-intubation period. In thoracic trauma complicated by pulmonary contusion, maintaining adequate oxygenation while minimizing ventilation-perfusion mismatch before definitive airway securement represents a critical challenge that HFNO is well positioned to help address [72].

The value of HFNO in this setting is further supported by its role in extending safe apnea time [52,57,58] and preventing desaturation [36,37,108]—both particularly important in the trauma operating room, where first-pass intubation success is essential and opportunities for reattempt may be progressively constrained by ongoing physiological deterioration. Raineri and colleagues evaluated the efficacy and safety of HFNO in 45 patients undergoing RSII for urgent abdominal surgery [34], recording a significant increase in oxygen saturation at all time points compared to baseline, with a minimum SpO_2 of 96%, a maximum apnea time of 12 minutes, and an $EtCO_2$ at the time of intubation of 36 mmHg. A recent systematic review and meta-analysis further supports these findings, concluding that HFNO may be superior to face mask for both pre-oxygenation and apneic oxygenation during RSII in emergency surgeries, particularly with respect to oxygenation maintenance [110].

Several practical considerations are specific to the trauma context. The nasal interface used for HFNO does not require cervical manipulation, facilitating oxygenation in patients requiring manual inline stabilization of the cervical spine. Unlike NIV masks, HFNO does not need to be removed before laryngoscopy, eliminating any interruption in oxygen delivery at the most critical moment of the procedure. In hemorrhagic shock, the maintenance of oxygen delivery assumes heightened clinical importance given the reduction in oxygen-carrying capacity imposed by blood loss. In polytrauma scenarios, the hands-free, continuous nature of HFNO delivery is operationally advantageous when the clinical team is simultaneously managing multiple life-threatening injuries [72].

While specific randomized controlled trials in trauma populations remain limited, the physiological rationale is compelling, and extrapolation from the emergency department intubation literature [111] and studies in critically ill ICU populations [108,111–113] supports the consideration of HFNO as a valuable adjunct within trauma airway management protocols. A large trial currently ongoing is specifically addressing the safety and efficacy of HFNO for pre-oxygenation and apneic oxygenation during emergency RSII [112].

8. Inflammatory Modulation and Immunological Considerations in Perioperative Respiratory Support

Beyond its direct physiological benefits, emerging evidence suggests that HFNO may form part of a broader perioperative strategy capable of influencing systemic inflammatory responses, with potential implications for postoperative outcomes.

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A randomized controlled trial indicates that the application of HFNC in senior patients could improve respiratory humidification, reduce the number of sputum aspirations and improve anti-inflammatory effects [78]. This observation illustrates a broader principle of perioperative medicine: anesthetic and perioperative management decisions may exert effects on inflammatory cascades that extend well beyond their primary intended targets.

The relevance of this principle to HFNO lies in the well-established interconnection between respiratory mechanics, inflammatory signaling, and postoperative pulmonary complications. Atelectasis formation, hypoxemia, and ventilation-perfusion mismatch are each recognized triggers of inflammatory cytokine release [79,80], whereas protective ventilation strategies have been shown to attenuate cytokine production [83]. By preventing atelectasis [11–14], ensuring adequate arterial oxygenation [36,37,51], and reducing the work of breathing [9,10], HFNO may secondarily dampen the inflammatory responses that contribute to postoperative pulmonary morbidity. The optimization of mucociliary clearance—a direct consequence of the heated, fully humidified gas delivered by HFNO [4,8]—may represent an additional mechanism through which HFNO attenuates the local inflammatory burden in the conducting airways during the perioperative period.

Perioperative management is most usefully viewed as an integrated whole: the choice of anesthetic technique, intraoperative ventilation strategy, and postoperative respiratory support modality may converge to either amplify or mitigate systemic inflammatory responses. This consideration may carry particular weight in patients with pre-existing chronic cardiorespiratory disease—such as COPD or heart failure—in whom baseline systemic inflammation is already elevated and perioperative insults may lower the threshold for clinically significant inflammatory escalation. Should the anti-inflammatory potential of HFNO be further substantiated by prospective data, this mechanism may also have meaningful implications for Enhanced Recovery After Surgery (ERAS) protocols, pre- and post-operative rehabilitation strategies, and multimodal perioperative management—including analgesic optimization—in which HFNO could be readily implemented as a low-risk, high-compliance adjunct.

It must be acknowledged that the evidence linking HFNO specifically to perioperative inflammatory modulation remains largely inferential at this stage, extrapolated from mechanistic studies of atelectasis, hypoxemia, and ventilation-induced injury rather than from dedicated clinical trials. This represents an area in which prospective investigation is both scientifically warranted and clinically relevant.

9. Monitoring Considerations

Advances in perioperative monitoring continue to expand the parameters available for clinical assessment beyond traditional vital signs and gas exchange indices. In the context of HFNO, appropriate monitoring serves a dual purpose: it enables early detection of clinical deterioration—particularly hypoxemia and hypercapnia—and it may inform real-time titration of flow rate and FiO_2 to the individual patient's physiological state.

Among currently available monitoring adjuncts, transcutaneous CO_2 monitoring holds particular relevance during laryngeal surgery and in pediatric applications, where the risk of clinically significant hypercapnia is elevated and end-tidal CO_2 sampling via conventional capnography may be unreliable or technically unfeasible [64,65]. Electrical impedance tomography offers the potential for non-invasive, real-time visualization of regional ventilation distribution and changes in end-expiratory lung volume, which may prove valuable in guiding HFNO settings during complex procedures or in patients with heterogeneous lung disease [13].

Looking further ahead, future extended applications of HFNO may benefit from integration with monitoring systems capable of detecting subtle early changes in autonomic balance, respiratory drive, or work of breathing that precede overt desaturation or respiratory failure. Respiratory rate variability analysis and diaphragmatic ultrasonography—the latter providing a non-invasive, bedside assessment of diaphragmatic function and effort—represent investigational tools with potential applicability in this domain, though their routine clinical use remains to be validated.

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While the integration of these advanced monitoring modalities into standard HFNO practice is not currently supported by sufficient evidence to justify routine adoption, their incorporation into clinical research protocols represents a scientifically valuable direction. Prospective data derived from such protocols may help define optimal HFNO parameters for specific patient populations and clinical scenarios, ultimately enabling more personalized and physiologically targeted approaches to perioperative respiratory support.

10. Conclusions

HFNO is a respiratory support technique that delivers a controlled concentration of heated and humidified oxygen at high flow rates. By virtue of its numerous physiological benefits, its clinical application has progressively expanded beyond its original intensive care context into the perioperative setting, where it has demonstrated efficacy in reducing desaturation episodes across specific phases of general anesthesia and in critically ill patients [77,108].

The ability to deliver continuous, uninterrupted oxygenation during laryngoscopy, endotracheal intubation, and supraglottic device positioning maintains adequate patient oxygenation throughout the peri-intubation period, allowing the clinician to concentrate on procedural execution and thereby improving first-pass success rates [35]. HFNO has also been shown to be a valuable adjunct during awake tracheal intubation, extending its utility to the most challenging airway management scenarios (Table 2).

Table 2. Comparative summary of Conventional Oxygen Therapy (COT), High-Flow Nasal Oxygen (HFNO), and Non-Invasive Ventilation (NIV) across perioperative indications. Ratings reflect current evidence synthesis: +++ preferred strategy with strong evidence; ++ effective alternative with moderate-to-high evidence; + applicable with limited evidence or as adjunct; – not indicated or insufficient evidence. Indications are organized according to perioperative phase as addressed in the present review.

INDICATION	COT	HFNO	NIV
Preoxygenation			
— Healthy individuals	+	+++	–
— Pediatric	+	++	–
— Pregnancy	++	++	–
— Obese (BMI >35 kg·m^{-2})	+	+	++
— Critically ill (moderate hypoxemia)	+	+	++
— Critically ill (severe hypoxemia)	–	–	+++
Rapid Sequence Induction/Intubation	+	++	+
Apneic oxygenation	+	+++	–
Procedural sedation	+	++	+
Post-extubation respiratory support	–	++	+++

In the domain of procedural sedation, HFNO has consistently demonstrated improvements in oxygenation, procedural safety, and patient tolerability during gastrointestinal and respiratory endoscopic procedures performed under deep sedation, reducing the frequency of operator interruptions required to manage hypoxemia. Beyond its role as a pre-oxygenation tool, THRIVE may be employed as a primary apneic oxygenation technique during selected procedures, further extending its clinical applicability.

Finally, the potential anti-inflammatory properties of HFNO—mediated through atelectasis prevention, reduction of alveolar mechanical stress, optimization of mucociliary function, and attenuation of hypoxemia-driven cytokine release—suggest that it may constitute a meaningful component within evolving multimodal perioperative optimization strategies. Integration with metabolic management, multimodal analgesia, trauma resuscitation protocols, and pre- and post-operative rehabilitation, within the framework of a holistic and physiologically integrated model of perioperative care, represents a promising direction for future clinical development.

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Several important areas warrant further investigation. Prospective studies should address the development of personalized HFNO protocols—defining optimal flow rates, FiO_2 settings, and duration of application tailored to specific patient phenotypes and surgical procedures. Long-term outcome data examining 30-day and 90-day morbidity—rather than immediate oxygenation parameters alone—are needed to fully characterize the clinical impact of perioperative HFNO use. Comprehensive cost-effectiveness analyses, incorporating equipment and consumable costs alongside the potential reduction in complications and healthcare resource utilization, will be essential to support implementation at an institutional and health system level. Head-to-head trials comparing HFNO with NIV in well-defined high-risk surgical populations are required to establish clear modality selection criteria. Dedicated mechanistic studies investigating the anti-inflammatory and immunomodulatory effects of HFNO will be necessary to characterize the benefits of this technique beyond oxygenation. Finally, implementation science research addressing barriers to adoption, training requirements, and strategies for integration into existing perioperative workflows will be critical to translating the available evidence into consistent clinical practice.

The perioperative application of HFNO exemplifies how technological innovation, when grounded in deepening physiological understanding and embedded within comprehensive care pathways, can meaningfully improve outcomes in vulnerable patient populations. As evidence continues to accumulate and clinical experience expands, HFNO is poised to become a standard component of perioperative respiratory management—contributing to the broader goals of enhanced surgical safety, reduced postoperative complications, and improved patient-centered outcomes.

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