High-flow nasal oxygenation for anesthetic management

Takashi Asai¹ and Hyun Joo Kim²

¹ M.D., Ph.D., Department of Anesthesiology, Dokkyo Medical University Saitama Medical Center, Koshigaya City, Japan
² M.D., Ph.D., Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul, Korea

Running title
High-flow nasal oxygenation

Corresponding author
Hyun Joo Kim, M.D., Ph.D.
Assistant Professor, Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Republic of Korea. Tel: (+82) 2-2228-2420. Fax: (+82) 2-2227-7897. Email: jjollong@gmail.com

Previous presentation in conferences
None

Conflict of interest
No potential conflict of interest relevant to this article was reported.

Funding
None

Acknowledgments
None

IRB number
Not applicable

Clinical trial registration number
Not applicable
High-flow nasal oxygenation for anesthetic management

Running title: High-flow nasal oxygenation in anesthesia
Abstract

High-flow nasal oxygenation (HFNO) is a promising new technique for anesthesiologists. The introduction of HFNO during induction of anesthesia and during upper airway surgery has been initiated and its applications have been rapidly growing. The advantages include its easy setting, high tolerability, its ability to produce positive airway pressure, a high fraction of inspired oxygen (FiO₂) and some clearance of carbon dioxide. HFNO via nasal cannula can provide oxygen, both in patients breathing spontaneously and in those being apnea, and does not interfere with bag-mask ventilation, attempts at laryngoscopy for tracheal intubation and surgical procedures to the airway. In this review, we describe techniques of the HFNO, and advantages and disadvantages of HFNO, based on the current state of knowledge.

Keywords: Airway surgery; Endotracheal intubation; High-flow nasal oxygenation; Hypoxemia.
Introduction

Airway management is an essential skill required for all the anesthesiologists. Anesthesiologists need to be continuously updated with developments of new airway devices and techniques, as airway management methods are still not optimal [1]. Among these developments, high-flow nasal oxygenation (HFNO) is especially prominent. Although this technique is spreading globally, there are some controversies regarding the indications and advantages of the required skills. Therefore, in this narrative review, we focus on new emerging airway management skill of HFNO and describe the potential role of the HFNO, based on the current state of knowledge.
High-flow nasal oxygenation (HFNO)

HFNO is a method that provides oxygen at a high flow rate over 15 L/min (which is the maximum flow rate for a conventional nasal cannula) through the patient’s nasal opening [2]. The device is able to titrate fractional inspired oxygen (FiO₂) up to 1.0 and consistently deliver highly oxygenated flow to the alveoli, because the device can provide higher flow rates than usual inspiratory flow, and can reduce entrainment of room air [2]. The HFNO generates a low level of continuous positive airway pressure of 2.7–7.4 cmH₂O, washout of the nasopharyngeal dead space, reduction of nasopharyngeal resistance, increased alveolar recruitment, decreased work of breathing, and prevention of atelectasis and bronchospasm [2–4]. Specially designed equipment is required for HFNO, because the oxygen flow should be at adequately high temperatures and humidity, which avoids patients feeling dryness in the nasal cavity and promotes tolerance of the high-flow rate [3]. Additionally, humidified and heated inspired oxygen lessens the energy cost for gas conditioning [5], prevents mucociliary damage, and facilitates mucociliary clearance [3,6].

Traditional use of HFNO

HFNO has proven highly effective for patients admitted in the intensive care unit (ICU) [7] or post-anesthetic care unit after surgery [3]. It is clear that HFNO enhances oxygenation in patients who have hypoxemic acute respiratory failure and helps to avert re-intubation after extubation in ICU [3]. A meta-analysis reported that HFNO used postoperatively reduced the length of hospital stay in adult patients [8]. After this meta-analysis report, one study has confirmed that postoperative HFNO reduced the length of hospital stay, and the incidence of re-admission to the ICU of cardiac surgical patients with pre-existing respiratory disease [7].

The reported side effects from trials were minor, such as noise, feeling hot, and runny nose [3]. The nasal interface is composed of soft silicone with a wider bore compared to that of traditional
nasal prongs. HFNO is generally well tolerated compared to other means of oxygen supplementation such as a low-flow nasal cannula or a facemask [9], and that patients may tolerate HFNO up to 100 L/min without any discomfort, and some may even fall asleep [4].

HFNO has potential contraindications including severe nasal obstruction, copious nasal bleeding, recent nasal trauma, recent nasal surgery, significantly raised intracranial pressure, and base of skull fracture [10].

Use for anesthesia management

Recently, HFNO has been applied during anesthesia management, including at the anesthetic induction period and intraoperative period (Fig. 1). For this, equipment with different characteristics (Optiflow™; Fisher & Paykel Healthcare, New Zealand) has been developed. Optiflow consists of a flow meter, humidifier, and heating system, heated non-condensing circuit, nasal cannula, head strap, and oxygen connector for gas supply (Fig. 2). Different to Airvo (Airvo™ system, Fisher & Paykel Healthcare Ltd., New Zealand) for the use in the ICU, FiO₂ is fixed at 1.0 to facilitate installation of the device within 2–3 min [11]. The oxygen flow rate can be increased up to 70 L/min which is more than that of Airvo (2–60 L/min). Due to the FiO₂ of 1.0 and higher flow rate, Optiflow is indicated mostly for adults and children who weigh more than 10 kg. Airvo is more appropriate than Optiflow for children less than 10 kg due to the proper titration of FiO₂ less than 1.0 (range: 21–100%) and flow rate less than 20 L/min. The heating and active humidifying of oxygen flow of Optiflow is similar to that of Airvo (37°C and 44 mgH₂O/L). It is recommended that this equipment is turned on approximately 5 min before use to ensure adequate humidification and heating [10].
Conventional oxygenation methods

When general anesthesia is induced and a neuromuscular blocking agent is given, there is a risk of hypoxemia after induction of anesthesia, if facemask ventilation is inadequate and tracheal intubation is difficult or has failed. If difficult oxygenation occurs during induction of anesthesia, there is a high risk of severe complications, such as hemodynamic instability, dysrhythmias, hypoxic brain injury, cardiac arrest, and even death [12]. One effective method to minimize hypoxemia-related complications during induction of anesthesia is adequate oxygenation.

Oxygenation during induction of anesthesia can be divided into two phases, based on the time points: pre-oxygenation and per-oxygenation. Preoxygenation is defined as administration of oxygen before induction of anesthesia, and its purpose is to maximize a “safe” apnea time (apnea time without hypoxemia) after induction of anesthesia, and to delay the onset of hypoxemia if airway management is unexpectedly difficult [12,13]. Peroxygenation is oxygenation from induction of anesthesia to completion of securing the airway. After induction of anesthesia, patient’s spontaneous breathing can either be maintained or stopped. In the latter case, a usual method is intermittent positive pressure ventilation via a facemask. If this is not possible, an alternative method is insufflation of oxygen to the pharyngeal cavity, and this method is called “apneic oxygenation”.

Preoxygenation via a facemask

In adults, the conventional method of preoxygenation is to provide oxygen of FiO\textsubscript{2} of 1.0 with flow rate of 10–12 L/min through a tightly fitting facemask over the patient’s nose and mouth [14,15]. The duration of preoxygenation should be titrated to denitrogenate expiratory reserve and residual lung volume [16]. Adequate preoxygenation is now recommended to be confirmed by the end-tidal oxygen partial pressure (EtO\textsubscript{2}) exceeding 90%. In healthy adults, this endpoint can be
achieved within 3 to 5 min when using tidal volume breathing through a facemask [17].

During preoxygenation, the method of patient’s breathing is crucial, and this affects the needed time of adequate oxygenation [16]. The two most representative methods are tidal volume breathing for 3 min and vital capacity breathing of 8 breaths within 60 sec [18]. Adequate preoxygenation enables a healthy adult to endure apnea without hypoxemia for about 7–10 min [18].

**Apneic oxygenation**

Apneic oxygenation can be employed to delay further the onset of desaturation. Apneic oxygenation can provide additional time to consider and attempt alternative airway management options when the airway is not easily secured. During this less stressful condition, it is critical for the physician to concentrate on an emergency situation and make a right decision for the patient’s safety.

The concept of apneic oxygenation was established in 1908 [19]. The underlying physiology involves passive movement of oxygen from the nasopharynx or the oropharynx to the alveoli; oxygen is taken up into the bloodstream even without active lung expansion [20,21]. This gas movement occurs because the oxygen and carbon dioxide differ in the flow rates of absorption and excretion between the alveoli and bloodstream (O₂ 250 ml/min and CO₂ 8–20 ml/min). This creates a sub-atmospheric pressure in the alveoli, and a pressure gradient between the upper airway and the alveoli. Because of this, oxygen is drawn from the pharynx into the alveoli. Therefore, if oxygenation is insufflated into the nasal or oral (buccal) route, this would prevent rapid desaturation even when the patient is being apneic [22]. Several available equipment such as nasal prongs, a nasopharyngeal catheter, an oropharyngeal catheter, an adapted Ring-Adair-Elwin (RAE) tube, and a modified laryngoscope currently exist for this purpose.
Oxygenation insufflation via a nasal cannula or prongs

Apneic oxygenation through a nasal catheter or prongs, with oxygen flow rate of 3–10 L/min, is generally useful in delaying desaturation in adult patients with physical status of American Society of Anesthesiologists (ASA) 1 or 2 [23]. In a retrospective study of 728 patients [24], the incidence of desaturation (peripheral capillary oxygen saturation (SpO$_2$) < 93%) was decreased from 23% to 17%, by implementation of apneic oxygenation (with oxygen flow rate of 15 L/min) via a nasal cannula. Likewise, in a study of 127 patients with intracranial hemorrhage that required rapid-sequence induction of anesthesia in the emergency department [25], nasal prongs with oxygen flow of 5–15 L/min during apnea reduced the incidence of desaturation (SpO$_2$ < 90%) from 29% to 7%. In obese patients (with the mean body mass index (BMI): 31.2 kg/m$^2$), nasal prongs with oxygen flow of 5 L/min extended the safe apnea time (SpO$_2$ ≥ 95%) from 3.5 to 5.3 min [26]. Nasal prongs with oxygen flow of 10 L/min, together with oxygen 15 L/min via a facemask for 3 min, increased the EtO$_2$, even when there was gas leakage around the facemask [27].

Oxygenation insufflation via a pharyngeal tube

One study [28] of 56 adult patients of ASA 1–2 has shown that administration of oxygen 5 L/min via a nasopharyngeal catheter was superior to oxygenation via nasal prongs, in preventing desaturation, possibly because a nasopharyngeal catheter delivers oxygen more effectively to the alveoli, because of the shorter distance from the oxygen outlet to the laryngeal inlet. Insufflation of oxygen at 10 L/min via a RAE tube, with its tip being placed into the oral cavity (buccal route), extended the median safe apnea time (tracheal oxygen concentrations > 94%) from 447 to 750 sec in adult patients [29]. However, in one of ten patients, SpO$_2$ decreased to less than 95% at 9.5 min, and in another patient, SpO$_2$ fell to less than 50%, due to the occlusion of the tip of the RAE tube by the soft tissues [29]. A similar study was performed, in obese patients with BMI of 30–40 kg/m$^2$,
in which apneic oxygenation of 10 L/min via a RAE tube of ID 3.5 mm extended the median safe
apnea time (SpO$_2$ $\geq$ 95%) from 296 to 750 sec [30]. In infants and small children without
cardiopulmonary disease, oxygen insufflation of 4 L/min through a tube, which was attached to the
side channel of a videolaryngoscope, extended the safe apnea time (SpO$_2$ $\geq$ 95%) by an average of
30 sec (mean time: from 131 to 166 sec) [31].

Limitations of conventional apneic oxygenation

Apneic oxygenation devices providing oxygen with a flow rate of less than 15 L/min have
several limitations. First, the resulting FiO$_2$ is unpredictable and limited due to the entrainment of
room air [22]. Second, the air flow is cold and dry, impairing mucociliary function and may
trigger bronchoconstriction. Third, the tip of a nasopharyngeal catheter or a RAE tube can be
misplaced or occluded by the surrounding tissues, resulting in unexpected desaturation. Fourth,
oxygen insufflation via a tube which is attached to the side channel of a laryngoscope can be
performed only when the laryngoscope is placed in the patient’s oropharynx. Lastly, when oxygen
insufflation is performed while the patient is being apnea, clearance of CO$_2$ from the body cannot
be expected [32].
HFNO during induction of anesthesia

The efficacy of HFNO therapy for extending safe apnea time before securing the airway has been examined in several clinical studies which can be categorized into preoxygenation, induction of general anesthesia, rapid-sequence induction, and awake tracheal intubation (Table 1).

Preoxygenation

Non-obese adults

One benefit of HFNO is that it can be easily and comfortably applied to an awake patient until anesthesia is induced. In ten awake adult volunteers, HFNO with oxygen flow of 60 L/min for 3 min was compared with oxygenation via a facemask (with oxygen flow of 10 L/min) [33]. The mean EtO\textsubscript{2} was similar (86 kPa for HFNO and 89 kPa for a facemask). Nevertheless, for HFNO, EtO\textsubscript{2} decreased to 49 kPa when volunteers opened their mouths, indicating that HFNO may be effective only with the mouth closed.

In another observational study of 21 awake adult volunteers, to whom HFNO with oxygen flow of 70 L/min was applied, while the volunteers were closing their mouths, the EtO\textsubscript{2} increased from 14–17% to 78–92% at 3 min [34]. Nevertheless, in the half of the volunteers EtO\textsubscript{2} did not reach 90%. In addition, one had discomfort and the test was stopped midway; additional four reported moderate discomfort (5 or 6 in a visual analogue scale). Although it may be technically difficult to measure EtO\textsubscript{2} accurately during the use of HFNO, it may be that HFNO may not reliably increase the EtO\textsubscript{2} by preoxygenation for 3 min. In addition, in patients with respiratory distress situations, patients inevitably need to breathe with an open mouth, and it may be difficult to follow closed mouth instructions [35]. Optimal parameters for application of HFNO such as the duration of preoxygenation, breathing pattern, or mouth status need to be determined. In reported studies, the duration of HFNO was differently applied 3 to 5 min before the start of induction [10,33,36–38].
To determine the optimal preoxygenation time during HFNO, new criteria such as oxygen reserve index sensor other than EtO₂ should be considered in future clinical trials.

**Obese adults**

In obese patients, when preoxygenation is carried out through a facemask, safe apnea time is as short as 1–3 min after preoxygenation compared with 7–10 min for healthy adult patients [18,39]. This is due to physiological changes such as decreased functional residual capacity, increased oxygen consumption, and increased closing volume [15]. In a study of 33 morbidly obese patients (BMI ≥ 35 kg/m²) [40], HFNO of 50 L/min with the patient’s mouth being closed was superior to facemask oxygenation in achieving high PaO₂. After 3 min of preoxygenation with 30° head up position, the median PaO₂ was 380 mmHg for the HFNO group, and 337 mmHg for the facemask group. None of the patients had complications due to epistaxis or gastric aspiration when using HFNO. Therefore, in obese patients, the efficacy of HFNO is increased by placing the patient to a head-up position.

**Pregnant women**

In obstetrics, it is particularly important to make sure that EtO₂ should be reached beyond 90%, using at least 3 min of tidal volume breathing of 100% oxygen [20,41], because the rate of difficult intubation may be 10 times higher than that in the general population [12,42]. In addition, safe apnea time is relatively short due to several changes such as airway edema, decreased functional residual capacity, increased oxygen consumption, emergency surgery, and higher risk of aspiration [41].

A computational modelling to simulate the effects of apneic oxygenation during rapid-sequence induction of anesthesia in obstetric women has indicated that the increase in FiO₂ up to 1.0 extends
safe apnea time [43]. A successful use of HFNO in a pregnant woman with severe cardiopulmonary disease has been reported [11]: a 27-year-old pregnant woman with acute respiratory distress syndrome and heart failure, required emergency Cesarean section. She had dyspnea and significant mouth breathing, and her SpO$_2$ was 80%. Oxygen 9 L/min via a facemask increased SpO$_2$ to 95%, and HFNO 70 L/min with FiO$_2$ 1.0 further increased SpO$_2$ to 98% within 5 min, even though the patient breathed mainly through the mouth. After induction of anesthesia, tracheal intubation was successfully performed with SpO$_2$ being maintained at 98%.

In contrast, one study has cast a doubt on efficacy of HFNO [36] in pregnant women: after HFNO for 3 min (30 L/min for 30 sec, followed by 50 L/min for 150 sec), EtO$_2$ of 90% was achieved in merely 44 of 73 (60%) of pregnant women. In addition, although HFNO received similar comfort scores as those of a facemask, only 56% of women preferred the HFNO to the facemask. These results are similar in non-pregnant patients.

**HFNO for apneic oxygenation**

After induction of anesthesia and neuromuscular blockade, oxygenation is usually performed by intermittent positive pressure ventilation via a facemask. When a facemask is used, the mask needs to be removed during attempts at tracheal intubation, and thus no oxygen is being supplied. If the time taking for tracheal intubation is prolonged and mask ventilation is difficult, such as difficulty in advancing a tracheal tube over a fiberoptic bronchoscope (which has successfully been inserted into the trachea), there is a risk of hypoxemia. Apneic oxygenation may be performed by insufflation oxygen through a RAE tube, a nasopharyngeal airway, or a short tracheal tube.

With HFNO, the nasal cannula does not need to be removed during attempts at laryngoscopy or fiberoptic bronchoscopy, or during insertion of a supraglottic airway, and keeps oxygenation more stable. Moreover, there is low probability of problems associated with incorrect positioning of the
device, which is more likely to occur with a buccal RAE tube. This prevents the need for clinicians to abandon ongoing intubation attempts too early due to the occurrence of desaturation, and allows them to focus on performing tracheal intubation and maneuvering it with sufficient time [44]. In addition, the nasal cannula for HFNO does not interfere with application of a facemask when additional mask ventilation is needed.

In adults

In 48 neurosurgical adult patients [10], the efficacy of HFNO with oxygen flow of 50 L/min was compared with oxygen 10 L/min through a facemask, in increasing arterial partial pressure of oxygen (PaO₂). After 5 min of preoxygenation, the median PaO₂ was significantly higher for HFNO (471 mmHg) than for facemask oxygenation (357 mmHg). However, after induction of anesthesia, PaO₂ decreased significantly in the HFNO group, but not in the facemask group in which bag-mask ventilation was performed. This suggests that HFNO is more efficient than facemask oxygenation to ensure high PaO₂ before induction of anesthesia, but HFNO is less effective than facemask ventilation in maintaining high PaO₂. Nevertheless, seven patients in the facemask group required the use of airway adjuncts such as oropharyngeal airways, but none of the patients in the HFNO group did, suggesting that HFNO is easily incorporated.

In a male patient who had acute epiglottitis requiring emergency tracheal intubation [45], his airway assessment showed Mallampati score 2, the thyromental distance > 6 cm, poor dentition, good mouth opening and neck range of movement, and an easily palpable cricothyroid membrane. Despite intravenous antibiotics and steroids, airway obstruction was progressed rapidly and required airway intervention. HFNO 70 L/min was used combined with target-controlled infusion (TCI) of propofol allowing spontaneous breathing. The minimum oxygen saturation was 96% after tracheal intubation.
Oxygenation can be more difficult in obese patients, because the incidence of difficult mask ventilation and tracheal intubation may increase with obesity. The head-up position is helpful to maximize the efficacy of apneic oxygenation by reducing atelectasis and subsequent pulmonary shunting [12,30]. One study of obese patients has shown that HFNO of 50 L/min had the highest PaO\textsubscript{2} value after 3–5 min of preoxygenation in morbidly obese patients, and PaO\textsubscript{2} decreased as preoxygenation time was extended up to 7 min [40]. Therefore, the appropriate duration of preoxygenation using HFNO remains to be determined.

In children

Compared to adults, children are more prone to exposure to rapid desaturation in the order of seconds after cessation of ventilation, due to decreased functional residual capacity, higher oxygen consumption, increased closing capacity, and higher airway collapse [17,46]. One study has shown that the mean desaturation time until SpO\textsubscript{2} reached 90% was significantly shorter in children (160 sec) than in adolescents (382 sec), and substantially shorter in infants (97 sec). In fact, the incidence of desaturation is common in children (4–10% during induction of anesthesia and 20% during tracheal intubation) [18]. Therefore, in children, optimal oxygenation strategies are crucial to extend the duration of safe apnea.

HFNO may extend safe apnea time in children. In one study of 48 children under 10 years with normal airways [47], in the facemask group, bag-valve ventilation was ceased and jaw thrust was maintained, whereas in the HFNO group, the flow rates of 2 L/kg/min, 35, 40, and 50 L/min were applied according to body weight, and jaw thrust was performed during apnea. The main hypothesis was that safe apnea time (time to become SpO\textsubscript{2} 92%) for HFNO would be more than the double length of the apnea time for the facemask group, and the results confirm that this hypothesis was true.
In another study of 60 children, aged 1–6 years, weighing 10–20 kg, HFNO 2 L/kg/min with
FiO₂ 1.0, HFNO 2 L/kg/min with FiO₂ 0.3, and low-flow nasal oxygenation 0.2 L/kg/min with FiO₂
1.0, were compared [48]. Bag-valve mask ventilation was ceased when the target of EtO₂ > 90%
was reached. Apnea was terminated when SpO₂ was less than 95%, transcutaneous CO₂ (tcCO₂)
reached 65 mmHg, or apnea duration reached 10 min. SpO₂ had decreased < 95% within 10 min
in all the patients with HFNO (FiO₂ 0.3), in three patients (17%) with low-flow nasal oxygenation,
but in none with HFNO (FiO₂ 1.0), indicating that HFNO 2 L/kg/min with FiO₂ 0.3 is not effective.
The tcCO₂ had exceeded > 65 mmHg within 10 min, in 16 patients (80%) for HFNO with FiO₂ 1.0,
and in 13 patients (72%) for low-flow nasal oxygenation group. For HFNO 2 L/kg/min with FiO₂
1.0, the median safe apnea time was 7.6 min, with the range of 5.2–10 min. Therefore, in children,
HFNO 2 L/kg/min with FiO₂ 1.0 can maintain SpO₂ for 10 min, but there is a higher risk of
hypercapnea, and that this method may be useful for surgery lasing 5–6 min. It is not known
whether or not a higher flow (e.g. 4 L/kg/min) with a FiO₂ less than 1.0 can be effective.

HFNO for rapid-sequence induction of anesthesia

In the operating rooms

HFNO may also have a potential role during rapid-sequence induction of anesthesia in the
operating room. In one study of 80 adults receiving rapid-sequence induction of anesthesia, the
efficacy of oxygenation was compared between HFNO of 70 L/min and facemask oxygenation of
10 L/min [37]. The lowest SpO₂ up to 1 min after tracheal intubation was similar, but SpO₂
decreased < 96% in seven patients (18%) in the facemask group, whereas none in the HFNO group.
None of the patients had complications such as regurgitation of gastric contents, and there was no
significant difference in the safe apnea time, between HFNO (median: 116 sec) and facemask
(median: 109 sec).
In another study of 40 adult patients receiving rapid-sequence induction of anesthesia for emergency surgery, the efficacy between HFNO 70 L/min and facemask oxygenation 12 L/min were compared [49]. In the HFNO group, HFNO was maintained throughout the induction period, whereas in the facemask group, the jaw was kept threated without bag-mask ventilation. In all the patients, the trachea was intubated successfully, and there was no significant difference in PaO₂ between the groups. Nevertheless, the time taken to intubate the trachea took significantly longer for the HFNO group (the mean of 248 sec) than for the facemask group (123 sec). The authors of the report state that this difference was not due to apparent difference in procedural difficulty, but the difference is quite marked. It might be that the presence of a nasal cannula mechanically or psychologically enabled more careful time-consuming laryngoscopy and tracheal intubation.

These results indicate that HFNO with jaw thrust is an efficient method to prevent desaturation during 3–4 min of apnea during rapid-sequence induction of anesthesia in adults, even if cricoid pressure is being performed.

Outside the operating rooms

Securing the airway is frequently more difficult outside the operating rooms than inside [50,51]. This is because outside the operating room, unstable physiological status of patients such as cardiopulmonary disease, low cardiac output, or hypermetabolic states, limit the efficiency of preoxygenation and peroxygenation. In addition, emergency procedures, poor planning, less skilled staff, and inadequate availability of equipment increase the incidence of difficult intubation up to approximately 12% [44,52,53]. Therefore, tracheal intubation is associated with a high incidence of hypoxemia, which is the most commonly associated complication (approximately 19–26%) [52,54], and is linked to hemodynamic deterioration, cardiac arrest, and death [12,55]. The incidence of death related to airway management has been reported to be 38-fold higher in
emergency department, and 58-fold higher in the ICU, than the incident in the operating rooms [12].

Meta-analyses have shown that oxygenation through a nasal cannula with various flow rates is
effective in preventing desaturation in patients who received emergency tracheal intubation [21,44].

In a study of 101 adult patients requiring rapid-sequence induction of anesthesia and intubation in
the ICU [53], the efficacy of HFNO was compared with non-rebreathing bag reservoir facemask
combined with nasopharyngeal catheter. For HFNO group, HFNO 60 L/min with FiO₂ 1.0 was
used for 3 min before induction of anesthesia (preoxygenation) and continued to use after induction
of anesthesia and during tracheal intubation. For the facemask group, oxygen 15 L/min was given
for at least 3 min before induction of anesthesia, and after induction, a facemask was removed and a
nasal cannula was placed and oxygen 6 L/min was insufflated. The median of the lowest SpO₂
was significantly higher in the HFNO group (100%, range: 95–100%) than in facemask group (94%;
83–99%). Episodes of severe hypoxemia (SpO₂ < 80%) was significantly lower in the HFNO
group (2%) than in facemask group (14%), and 1 cardiac arrest due to hypoxemia occurred in the
facemask group. Multivariate analysis indicated that HFNO was an independent factor preventing
severe hypoxemia.

Nevertheless, the HNFO may not be effective in improving oxygenation when tracheal intubation
is required in hypoxemic patients. In one study of 119 patients, who had acute hypoxemic
respiratory failure that required rapid-sequence induction and intubation (respiratory rate > 30
breaths/min, FiO₂ requirement > 50%, PaO₂/FiO₂ < 300 mmHg) [56], either HFNO of 60 L/min of
FiO₂ 1.0 or facemask oxygenation of 15 L/min was used. There was no significant difference in
the lowest SpO₂ (92% in HFNO group and 90% in facemask group) and severe hypoxemia of SpO₂
< 80% during tracheal intubation (16 [26%] in HFNO group and 13 [22%] in facemask group).

Similarly, another study comparing the efficacy of HFNO 50 L/min and bag-valve-mask
ventilation 10 L/min, in 40 critically ill patients, who had hypoxemic respiratory failure (PaO₂/FiO₂
< 300 mmHg) [35], the lowest mean SpO$_2$ during tracheal intubation and the occurrence of severe hypoxemia (SpO$_2$ < 80%) were similar between the groups.

In a report of 49 adult patients requiring rapid-sequence induction due to severe acute hypoxemic respiratory failure in the ICU (respiratory rate > 30 breaths/min, FiO$_2$ requirement ≥ 50%, PaO$_2$/FiO$_2$ < 300 mmHg) [57], the efficacy of preoxygenation with HFNO of 60 L/min with FiO$_2$ 1.0 plus non-invasive ventilation, and non-invasive ventilation was compared. HFNO plus non-invasive ventilation resulted in improved oxygenation and less frequent episodes of desaturation (SpO$_2$ < 80%). Therefore, HFNO combined with non-invasive ventilation reduce the incidence of severe hypoxemia during rapid-sequence induction of anesthesia in patients with severe acute hypoxemic respiratory failure.

In a prospective observational study, investigating the efficacy of HFNO 60 L/min during emergency tracheal intubation in 71 adult patients in the ICU, in the operating room, or in the emergency department, the median (range) apnea time was 80 (30–480) sec [38]. Significant desaturation (reduction in SpO$_2$ > 10% after induction of anesthesia) occurred in five patients (7%), who had acute respiratory failure (two patients) or who had difficulty maintaining airway patency during apnea (three patients). There were no complications from the use of HFNO.

In the ICU, patients’ conditions regarding respiratory disease and techniques used in control and intervention groups are varied. The intubation protocol including intubation equipment, patient positioning, preoxygenation approach, operators, and medications have not been standardized [58]. This may be a reason for the discrepancy of out-of-hospital studies. Moreover, the definitions of clinical outcomes vary between studies. For example, the standard of definition of hypoxemia is usually the SpO$_2$ value, which is the starting point of the steep slope on the oxygen dissociation curve of hemoglobin [59]. Nevertheless, desaturation can be defined differently, which may be another reason for the conflicting results. Therefore, the efficacy of apneic HFNO compared to
low-flow nasal apneic oxygenation is still unclear in emergency airway management in the ICU [3,21]. At least it is now apparent that HFNO alone may not be beneficial in patients who have severe respiratory failure [35,56]. This may be because pulmonary shunting or easily collapsed airways precludes the benefits of HFNO. To overcome this limitation, other techniques providing high positive airway pressure may be required [59].

Complications

Hypercapnea

One major possible problem with apneic oxygenation using HFNO is excessive hypercapnia. One study has shown that PaCO₂ increased with the speed of 3 mmHg/min, during apneic oxygenation with HFNO 50 L/min [10]. PaCO₂ was significantly higher during apnea with HFNO than in bag-mask ventilation, but the resultant rise in PaCO₂ in HFNO seemed tolerable, because the highest PaCO₂ value was approximately 65 mmHg after the completion of tracheal intubation. Flow rates up to 70 L/min may be required to achieve the maximum clearance of CO₂. In contrast, CO₂ accumulation was similar between HFNO and facemask preoxygenation in rapid-sequence induction in emergency surgery [37,49], potentially due to short observation period and more rapid increase in CO₂ during the first minute after the start of apnea. Clearance of carbon dioxide during HFNO may be superior to low-flow oxygen delivery system [60].

In children aged up to 10 years [47], the mean tcCO₂, which was measured at the end of apnea, was 62 mmHg (range 49–79 mmHg), and the mean rate of CO₂ increase was 2.4 mmHg/min (range 0.2–3.9 mmHg/min). However, the rate of CO₂ increase was not significantly lower when HFNO was combined with jaw thrust compared to jaw thrust in isolation during apnea. In a study of children aged up to 6 years [48], tcCO₂ increased at a rate of median (range) of 4.1 (2.2–5.3) kPa/min with HFNO with FiO₂ 1.0, and the rate of tcCO₂ increase was similar to that of the low-
flow nasal oxygenation group. It has also been shown that smaller the children, the faster the increase in tcCO$_2$ during apnea. These results imply that the efficiency of CO$_2$ clearance by HFNO is not prominent in children. This may be because the CO$_2$ increase is larger in children than in adults, and in smaller children than in larger children, due to their higher metabolic demands.

The application of HFNO interrupts the earlier detection of CO$_2$ rise and airway obstruction compared to bag-mask ventilation. Therefore, transcutaneous monitoring of CO$_2$ [10,47] and use of oxygen reserve index sensors may help to minimize this risk and optimize utilization of HFNO.

Gastric insufflation

Gastric insufflation is a theoretical complication of HFNO, because HFNO generates a positive airway pressure. The increase in nasal flow rate of 10 L/min is known to cause 1.2 cmH$_2$O increase in nasopharyngeal airway pressure when healthy volunteers breathed with their mouths closed using HFNO [4], and thus the airway pressure would increase to around 3 cmH$_2$O at 30 L/min, and around 12 cmH$_2$O at 100 L/min.

No serious complications, such as gastric insufflation, regurgitation, or pulmonary aspiration of gastric contents, so far have been reported, even in morbidly obese patients [37,40]. The number of studies are still limited, and thus true risk of gastric insufflation associated with the use of HFNO during anesthesia remains to be elucidated.

Settings of HFNO for induction of anesthesia

Flow rate

Reports of the use of HFNO indicated various high-flow rates such as 50 L/min [10,35,36,40], 60 L/min [33,38,53,56,57], or 70 L/min [34,37,49]. One study has shown that the median intratracheal FiO$_2$ was significantly increased from 67% to 93% as the flow rate increased from 15
L/min to 45 L/min [61]. Similarly, another study has shown that the increase in flow rate of HFNO from 10 L/min to 50 L/min can achieve higher FiO$_2$ [62]. Therefore, applying a higher flow rate, greater than 50 L/min is advisable to achieve maximal effects of oxygenation.

Generally, HFNO is well tolerated by awake patients [36,37], but some may experience moderate or severe discomfort, when flow is 50–70 L/min [10,34]. Therefore, it may be prudent to start HFNO with a relatively low flow rate (30–40 L/min) when the patient is awake, and to increase the flow rate (50–70 L/min). When the patient cannot tolerate a high flow, the flow should immediately be reduced to 30–40 L/min, and once the patient has lost consciousness, the flow should be increased back to 50–70 L/min [10,36,37,49]. In children, adequate flow rate has been indicated as 2 L/kg/min for children weighing 0–15 (or 20) kg, 35 L/min for those weighing 15 (or 20)–30 kg, 40 L/min for those weighing 30–50 kg, and 50 L/min for those weighing > 50 kg [47,48].

**FiO$_2$**

As the FiO$_2$ increases, the safe apnea time is extended. In addition, one study has shown that an increase in FiO$_2$ from 0.9 to 1.0 achieved a greater increase in safe apnea time than did an increase of FiO$_2$ from 0.21 to 0.9 [63]. Therefore, FiO$_2$ should usually be set to 1.0 for maximizing safe apnea time in adults, including morbidly obese patients [40] and those requiring rapid-sequence induction of anesthesia [37,53].

In children, HFNO with FiO$_2$ 0.3 may not be as efficient for extending safe apnea time when compared to HFNO with FiO$_2$ 1.0 [48]; therefore, when the HFNO is used, FiO$_2$ should be kept high.

**Breathing method**

There is still little evidence as to which breathing method is the best. In some studies, the patient
was asked to maintain normal breathing [33,34], whereas in other studies, deep breathing [36].

One clear feature is that the efficacy of HFNO in oxygenation is reduced when the patient’s mouth is open [2]. In one study [64], when HFNO 35 L/min was applied in postoperative cardiac surgery adult patients, the mean nasopharyngeal positive airway pressure was 2.7 cmH\textsubscript{2}O when the patient’s mouth was closed, whereas only 1.2 cmH\textsubscript{2}O when the mouth was open. Similarly, in another study [65], the increase in flow rates of HFNO resulted in increased mean airway pressures as 0.7 cmH\textsubscript{2}O per every 10 L/min when the mouth was closed, and the increased rate of airway pressure was significantly reduced as 0.4 cmH\textsubscript{2}O when the mouth was open. Further [61], the median of mean airway pressure significantly increased from 0.4 cmH\textsubscript{2}O to 2 cmH\textsubscript{2}O as the oxygen flow was increased from 15 L/min to 45 L/min, but significantly decreased from 2 cmH\textsubscript{2}O to 0.6 cmH\textsubscript{2}O when the mouth was open. However, FiO\textsubscript{2} was not significantly different between closed and open mouth with HFNO of 45 L/min [61]. In a study in which the EtO\textsubscript{2} was measured during HFNO of 60 L/min [33], HFNO increased the EtO\textsubscript{2} when the patient’s mouth was closed (86 kPa), whereas it failed to increase EtO\textsubscript{2} (49 kPa).

Another crucial point during HFNO is that the patency of the upper airway is essential to provide adequate oxygenation [17]. The patency of the upper airway needs to be maintained using head tilt [38], jaw thrust [37,38,47–49], chin lift [37,38], and insertion of a pharyngeal airway [48].

Theoretically, deep breathing through the nose, with the mouth shut would be the best for preoxygenation [33,34,36,40].
**HFNO for awake intubation**

Awake tracheal intubation is another situation of securing the airway for which HFNO may be valuable. Patients undergoing awake fiberoptic intubation are at risk of desaturation due to underlying airway diseases, obesity, or sudden complete airway obstruction which can be caused by oversedation or topicalization [66]. The use of HFNO is a theoretical advantage of oxygenation during awake fiberoptic intubation. This has been confirmed by an observational study of 50 adult patients [67], in which HFNO 50–70 L/min was used during awake fiberoptic intubation. HFNO increased the median (range) of SpO₂ from the baseline values of 98 (83–100)% to 100 (93–100)%, and none of the patients exhibited desaturation below baseline SpO₂ during the procedure. Median (range) of EtCO₂ was 4.8 (3.5–6.7) kPa after securing the airway. HFNO was also successfully used during surgical tracheostomy in a sedated patient with upper airway obstruction secondary to an infective acute leukemic mass [68].
**HFNO for airway surgery**

Upper airway surgery often requires repetitive tracheal intubation and extubation during the procedure to obtain the surgical field and allow the manipulation. It is therefore necessary to use specialized methods to reduce stressful conditions, by extending safe apnea time and preventing hypoxemia [69]. There are several oxygenation techniques for airway surgery, such as transtracheal or transglottic jet ventilation, controlled mechanical ventilation using a small sized tracheal tube, and intermittent apneic ventilation [70]. Among these techniques, jet ventilation is least preferred due to a higher risk of barotrauma compared to the other techniques. The ideal method may be the tubeless technique which enables an optimal view of the surgical field and prevents tracheal tube-related injuries to the airways. The use of HFNO is a revolutionary oxygenation technique for airway surgery, and may replace the use of a tracheal tube during laryngomicrosurgery (Table 2).

**Reported use**

Patel and Nouraei [60] are the first to report the use of HFNO during airway surgery. They used the technique in 25 adult patients undergoing hypopharyngeal or laryngotraacheal surgery, such as for benign laryngeal conditions, for obstructive sleep apnea, and for benign or malignant head and neck conditions. There were 12 obese patients and 9 patients with stridor. Median BMI (range) was 30 (18–52) kg/m$^2$. Median apnea time was 14 min, with the longest 65 min. None of the patients exhibited desaturation of SpO$_2$ < 90% when HFNO 70 L/min was used. Further, none of the patients experienced complications such as cardiac arrhythmia due to CO$_2$ increase during apnea.

Booth et al. [71] used a “traditional” use of HFNO during airway surgery, by maintaining spontaneous breathing. In 30 adult patients who underwent laryngotracheal surgery due to laryngotracheal stenosis or papilloma, HFNO 70 L/min was applied, while anesthesia was
maintained with TCI propofol, maintaining spontaneous breathing. Median duration of spontaneous breathing (range) was 44 (18–100) min. Only one patient experienced desaturation, due to miscalculated remifentanil overdose and tracheal intubation during surgery was required. In another three patients, SpO\textsubscript{2} decreased less than 90% during laser surgery, while FiO\textsubscript{2} had been reduced to 0.3. Nevertheless, SpO\textsubscript{2} increased rapidly when FiO\textsubscript{2} was increased back to 1.0.

In another report of 28 adult patients undergoing airway surgery, apnea oxygenation was provided by a unique system called Perioperative Insufflatory Nasal Therapy system, with the flow rate of 80 L/min [72]. In four patients, SpO\textsubscript{2} decreased to 85–90% lasting less than 2 min at several timings, after injection of rocuronium. Oxygen saturation was increased by jaw thrust and increasing flow rate to 120 L/min after removal of suspension laryngoscope or insertion of a supraglottic airway. A different HFNO equipment (Optiflow) has a maximal flow rate of only 70 L/min; therefore, the rescue technique of increasing flow rate up to 120 L/min is not feasible.

HFNO has also been successfully used in patients with difficult airways. For example, in a 55-year-old male who had severe supraglottic-pharyngeal stenosis, HFNO 70 L/min of FiO\textsubscript{2} 1.0 was applied, and the patient remained apneic for 26 min using propofol, remifentanil, and rocuronium [73]. After transecting the scar tissue along the lateral epiglottic border resulting in partial release of the stenotic lesion, laser-safe tracheal tube was placed through the opening. Until the tracheal tube was inserted, SpO\textsubscript{2} was maintained at greater than 90%. In another report of a male patient, who was morbidly obese with BMI 40 kg/m\textsuperscript{2}, had neck circumference of 45 cm, mouth opening of two finger breaths, and Mallampati 4, HFNO 60 L/min enabled surgery of 14 min, without desaturation [74].

HFNO may also be used in children, including premature babies, undergoing airway surgery. For example, one report describes successful use of HFNO (at the flow rate of 2 L/kg/min) in more than 30 children (aged 6 days to 13 years) undergoing airway surgery (e.g. aryepiglottoplasty,
subglottic cyst excision, tracheal dilatations, and endoscopic cricoid splints) [75]. FiO₂ was titrated to maintain SpO₂ at 95–99%, and spontaneous breathing was successfully preserved during surgery.

A premature male baby who had subglottic web after repeated tracheal intubations. He had severe inspiratory stridor requiring laser resection and dilatation under general anesthesia [69]. Anesthesia was induced with sevoflurane and maintained with infusion of propofol and remifentanil. Rocuronium was used to obtain full neuromuscular blockade and an uncuffed tube was inserted. The surgeon placed the Parsons laryngoscope with the suspension apparatus. For resection of the subglottic web, the trachea was extubated until SpO₂ fell to 80%, and then re-intubated. The apnea time was 39 and 41 sec; however, it could be increased to 95 and 160 sec when HFNO 4L/kg/min of FiO₂ 0.3 was applied. When HFNO with FiO₂ 1.0 was used, the apnea time extended over 4 min. After 2–4 min of apnea under HFNO, EtCO₂ was measured as 48–66 mmHg. This case report indicates that HFNO is efficient at extending safe apnea time in an infant undergoing laryngeal repair, even with low FiO₂ of 0.3.

Complications

Several complications associated with the use of HFNO during airway surgery have been reported.

Hypoxemia

One major complication associated with the use of HFNO during airway surgery is failure to maintain oxygenation. For example, in one report of the use of HFNO 50 L/min during laryngomicrosurgery [76], SpO₂ decreased to 72% in one of 23 patients, and tracheal intubation was temporarily required. In this case, HFNO was restarted and surgery could be finished without further complications.
In 20 infants and children (aged between 5 days to 15 years) undergoing upper airway surgery or dynamic airway assessment lasting 3–61 min, oxygenation was maintained by HFNO, but one neonate required rescue tracheal intubation at 3 min after apnea due to desaturation of 77% [77]. In a 35-year-old man with parapharyngeal mass and a narrowing of the trachea to 4 mm, emergency surgical tracheostomy under sedation was performed, while HFNO of 30 L/min was applied with the patient in a head-up position of 40° [78]. When sedation level was deepened, the respiratory rate decreased and complete airway obstruction occurred. SpO₂ rapidly decreased to 89%, and immediate tracheostomy was required. This case indicates that, if the airway is obstructed, HFNO could delay, but would not be able to prevent, hypoxemia.

Excessive hypercapnea

Hypercapnea is another major complication during airway surgery, because unlike short periods of apneic oxygenation before tracheal intubation, apneic oxygenation during airway surgery can be as long as 40–60 min. There have been some reports in which excessive hypercapnia required tracheal intubation or jet ventilation [79]. For example, in a case series of 30 non-obese patients who underwent elective short laryngeal procedures, HFNO 70 L/min was applied under apnea during surgery and the surgeon inserted a rigid tubular laryngoscope [80]. In one patient, HFNO needed to be stopped and supraglottic jet ventilation was required, because PaCO₂ exceeded a predetermined threshold of 11 kPa.

Compared with low-flow oxygenation, HFNO enables greater clearance of CO₂ [72]. When HFNO (70–80 L/min) is used in adults for apneic oxygenation, the EtCO₂ increases at a rate of 0.12–0.17 kPa/min [60,72,80]. By maintaining spontaneous breathing, the increase in EtCO₂ can be reduced further (e.g. 0.03 kPa/min) [71].

The increase in EtCO₂ is much faster in children than in adults. For example, in children
weighing 10–20 kg, the mean rate of transcutaneous CO\textsubscript{2} increase was 0.55 kPa/min [48]. Smaller children presented a more rapid CO\textsubscript{2} increase [48]. In a case report of infants weighing 4 kg, EtCO\textsubscript{2} was increased from 35 mmHg to 51–52 mmHg after 250–251 sec of apnea with HFNO of 4 L/kg/min [69].

One feature of the increase in the CO\textsubscript{2} during apnea is that, for an initial 1–2 min, CO\textsubscript{2} increases rapidly, and then slows down [81]. For example, in one study [81], apnea increased PaCO\textsubscript{2} at a rate of 12 mmHg/min in the first minute, followed by a slow rise of 3.4 mmHg/min.

The exact mechanism of CO\textsubscript{2} clearance during HFNO is unclear, although cardiogenic oscillations, dead space gas mixing, and micro-ventilation induced by pharyngeal pressure variations appear to be important factors [82].

Airway fire

Airway fire is a well-known complication which can happen during head and neck surgery using lasers. Ignition sources such as diathermy or laser may have accidental contact with fuel such as a tracheal tube or surgical drapes in an oxygen rich environment, and surgical fire can occur [83]. If HFNO is used during laser airway surgery, a high concentration of oxygen flows down the surgical field of the airway and is easier to ignite when electrosurgical devices meet the fuel. A case report of a 65-year-old female patient has been presented [84]. She was scheduled to receive palatal biopsy. She had titanium dental implants for clipping a palatal obturator after a previous surgery. HFNO 30 L/min of FiO\textsubscript{2} 1.0 was used under spontaneous breathing after administering propofol and fentanyl. A burn occurred on the diathermy shaft when the surgeon used a diathermy to achieve hemostasis at the biopsy site. Fortunately, the tissue of the patient was not harmed. It is recommended that during the use of HFNO, FiO\textsubscript{2} should be lowered to the minimum [72]. One possible method is to titrate FiO\textsubscript{2} into 0.3 using a gas blender [71]. It is recommended for
clinicians to have constant vigilance about the risk of airway fires with laser or diathermy.

Settings of HFNO in surgery

When HFNO is planned to use for oxygenation during airway surgery, special care needs to be considered for anesthesia method, airway patency, breathing mode, oxygen concentration, the flow rate, and topicalization of the airway, to maximize the margin of safety.

Anesthesia needs to be maintained with intravenous anesthesia, such as TCI of propofol [45,71,73,74,76,80] or its continuous infusion [60,69,72,77,79], because inhalational anesthetics cannot be administered through the HFNO and will be washed out with high flow of gases not attaining adequate depth of anesthesia [85].

Reported flow rates of HFNO vary from 50 L/min [76] to 80 L/min [45,60,71–74,79,80] in adults, and the flow rate ≥ 50 L/min seems adequate. In children, the flow rate should be adjusted according to body weight [69,77]. FiO₂ may be adjusted, but it would be safer to start with 1.0.

When performing apneic oxygenation, it is necessary to make sure that the airway is not obstructed during airway surgery. Jaw thrust may frequently be required to maintain airway patency [60,71,72,79,80]. In the case of microlaryngeal surgery, the surgeon usually inserts a suspension laryngoscope around the glottis, and this device may help to maintain airway patency during surgery [69,71–73]. It may be useful to insert a tubular laryngoscope by surgeons to ensure that the dorsal part of the laryngeal inlet is open to allow oxygen flow [80]. It should be kept in mind, however, that suspension laryngoscopy is accompanied with opened mouth, and this may limit the generation of positive airway pressure by HFNO [72].

HFNO may be used both in patients who are apnea [60,69,72–74,76,79,80] and in those breathing spontaneously [45,71,75,77,78]. Preservation of spontaneous breathing may permit better control of CO₂ increase, airway patency, and oxygenation [45]. Additionally, spontaneous
breathing may help surgeons to locate the glottis, by confirming bubbling or movement of vocal
cords, even if there is a severe laryngeal edema obscuring the anatomy.  Spontaneous breathing
could reduce the risk of neuromuscular blockade-induced complete airway obstruction.

To maintain spontaneous breathing, adequate titration of sedative or anesthetic agents to maintain
deep sedation, and adequate topicalization of the upper airway, are needed to make sure that the
patient can tolerate surgery to the airway [71,75,77].  One method is to perform laryngoscopy and
spray a local anesthetic to the airway, before airway surgery [71].  The risk of airway reactivity
will increase, when neuromuscular blockade is not sufficient, topicalization of the airway is not
adequate, and repeated attempts at insertion of surgical instruments are required.  In a case report
of an infant undergoing laryngeal repair, the surgical procedure may need multiple attempts at
intubation and extubation alongside a full neuromuscular blockade [69].  In addition, surgical
stimulation is changed constantly during surgery, and sedative agents have to be titrated
continuously in response to patient and surgical conditions; this may result in too deep sedation,
associated with accidental and sudden apnea [71].

Acute respiratory acidosis due to CO₂ increase during apnea does not pose a significant risk [80].
In addition, moderate CO₂ accumulation up to 100 mmHg is not associated with cardiac arrhythmia
or sympathetic stimulation [60,86], whereas severe CO₂ retention more than 100 mmHg is
associated with delayed recovery, ICU admission, and complications such as postoperative
congestive heart failure [86].  Patients who had a risk of CO₂ increase such as pulmonary
hypertension, obstructive airway diseases, raised intracranial pressure, and cardiac dysrhythmia
may be excluded for HFNO use.  As there is a good agreement between tcCO₂ and arterial PaCO₂,
the tcCO₂ monitoring should be useful to detect hypercapnia [79,80].

Backup plan
Clinicians should be aware of possible desaturation during surgery and must have a backup plan to perform other oxygenation techniques. One plan is the use of jet ventilation. In one report of one patient who had tracheobronchomalacia with BMI of 34 kg/m² and another patient who had spasmodic dysphonia with BMI of 52 kg/m², desaturation occurred during surgery, but jet ventilation was successfully established to increase saturation [60]. In another report [74], infraglottic jet insufflation via cannula cricothyroidotomy was considered to rescue desaturation, as this method does not interfere with ongoing surgery. In emergencies such as acute epiglottitis [45] or supraglottic-pharyngeal stenosis [73], clinicians should always consider the possible failure of HFNO and a priori prepare emergency tracheostomy. The front of the neck should be evaluated thoroughly preoperatively, and the surgeon should be immediately available in the event of complete airway obstruction. In a case series [79], tracheal intubation of a smaller tube or supraglottic jet ventilation was considered before apneic oxygenation, and was performed when transcutaneous CO₂ reached 70 mmHg.
Summary of efficacy of HFNO

HFNO for induction of anesthesia

It seems reasonable to conclude that HFNO is superior to conventional oxygenation techniques in adults and children requiring tracheal intubation in the operating room (Fig. 2). Regarding specific populations such as those with obesity, pregnancy, or rapid-sequence induction of anesthesia, HFNO may be a feasible technique for delaying hypoxemia. In contrast, the efficacy of HFNO in critically ill patients remains unclear. Because the number of reported clinical trials and conflicting results is still insufficient, the most adequate format and indication of HFNO should be explored and standardized in larger clinical trials.

When the first attempt of tracheal intubation has failed, immediate decision should be made, such as whether and when bag-mask ventilation should be commenced. If a facemask is used during preoxygenation and a nasal cannula is used only during apneic periods of laryngoscopy until tracheal tube insertion is completed, the nasal cannula may impair efficient preoxygenation via a facemask, by introducing oxygen leaks and entrainment of room air [87]. When a nasal cannula is used together with a facemask oxygen, oxygen insufflation at 10 L/min or greater is recommended [87].

HFNO may be most relevant in patients who will undergo rapid-sequence induction of anesthesia in which apneic period is relatively short (i.e., 1 min), compared to a usual induction of anesthesia, and in which bag-mask ventilation can be avoided [37,40]. If it takes more than 3-4 min to secure the airway and bag-mask ventilation is allowed, then the usefulness of HFNO may be less, because oxygen saturation may decrease more with passive apneic oxygenation compared to that with active bag-mask ventilation [10]. Nevertheless, the majority of cases of difficult oxygenation after induction of anesthesia cannot be predicted preoperatively [88], and thus some suggest that HFNO should be carried out in all the patients receiving anesthesia [23]. At the same time, clinicians...
should be aware that HFNO is not a tool for rescuing SpO₂ when significant desaturation occurs. Therefore, preoperative airway assessment should be performed meticulously, and should build an airway strategy with a backup plan, before induction of anesthesia.

The addition of HFNO to difficult airway guidelines and expanding areas of application into special populations such as those with reduced cardiopulmonary reserve, children, obesity, and pregnancy should be considered [89].

**HFNO for airway surgery**

Close communication, understanding, and teamwork are essential to establish intraoperative oxygenation using HFNO during airway surgery. HFNO should not preclude an alternate oxygenation plan, which should be made preoperatively, to resolve significant desaturation, hypercarbia, and acidosis. Therefore, good planning and preparation should be enacted prior to preoxygenation. For short-duration surgery, CO₂ increase and not oxygenation may be the factor determining the duration of apnea. Transcutaneous CO₂ monitoring is recommended for long procedures lasting more than 30 min [90].
Conclusions

HFNO is a promising new technique that keeps patients safer during anesthesia. Despite mounting evidence for its use, more research and clinical trials are needed to establish the ideal use of this technique in various populations. We hope that this review will help readers understand the relevant techniques and facilitate an introduction to Airway Management Guidelines in the future.
References


42. Quinn AC, Milne D, Columb M, Gorton H, Knight M. Failed tracheal intubation in obstetric anaesthesia: 2 yr national case-control study in the UK. Br J Anaesth 2013; 110:
74–80.


67. Badiger S, John M, Fearnley RA, Ahmad I. Optimizing oxygenation and intubation conditions during awake fibre-optic intubation using a high-flow nasal oxygen-delivery


84. Onwochei D, El-Boghdadly K, Oakley R, Ahmad I. Intra-oral ignition of monopolar diathermy during transnasal humidified rapid-insufflation ventilatory exchange


Table 1. Characteristics of Clinical Studies of High-flow Nasal Oxygenation (HFNO) during Induction of Anesthesia

<table>
<thead>
<tr>
<th>Year, author, design</th>
<th>Number of patients, location, inclusion (I), exclusion (E)</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Outcome and results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pillai et al. (2016), prospective study [33]</td>
<td>(n = 10) I: adult healthy volunteers, E: Respiratory or cardiac disease</td>
<td>OIA: HFNO 60 L/min for 3 min (with mouth closed and open)</td>
<td>OIA: FM 10 L/min for 3 min</td>
<td>1) EtO(_2), mean (SD) (P = 0.001): I (mouth closed): 85.6 (6.4) kPa I (mouth open): 48.7 (26.4) kPa C: 88.5 (6.2) kPa 2) Transcutaneous oxygen partial pressures, mean (SD) (P = 0.03): I (mouth closed): 36.4 (6.5) kPa I (mouth open): 25.5 (15.7) kPa</td>
</tr>
<tr>
<td>Ang et al. (2017), prospective pilot study [34]</td>
<td>(n = 21) I: adult healthy volunteers</td>
<td>OIA: HFNO 70 L/min for 30, 60, 90, 120, 150, 180 sec</td>
<td>No control</td>
<td>1) EtO(_2), median (IQR) [range]: I (30 seconds): 72% (66–79%) [45–82%] I (60 seconds): 79% (71–86%) [65–89%] I (90 seconds): 84% (77–88%) [64–91%] I (120 seconds): 87% (80–91%) [72–93%] I (150 seconds): 88% (83–90%) [75–94%] I (180 seconds): 86% (84–90%) [78–92%]</td>
</tr>
<tr>
<td>Heinrich et al. (2014), prospective RCT [40]</td>
<td>(n = 33) OR I: morbidly obese adult patients scheduled for laparoscopic bariatric surgery. (BMI ≥ 35 kg/m(^2)) E: severe pulmonary disorder, known or anticipated difficult airway</td>
<td>OIA: HFNO 50 L/min of FiO(_2) 1.0 for 7 min (mouth closed)</td>
<td>OIA: FM 12 L/min of FiO(_2) 1.0 for 7 min</td>
<td>1) PaO(_2), median (IQR): I: 380 (339–443) mmHg C: 337 (295–390) mmHg</td>
</tr>
<tr>
<td>Study (Year, Reference)</td>
<td>Study Type</td>
<td>I: Age/Gender</td>
<td>E: Inclusion Criteria</td>
<td>OIA</td>
</tr>
<tr>
<td>------------------------</td>
<td>------------</td>
<td>---------------</td>
<td>----------------------</td>
<td>-----</td>
</tr>
<tr>
<td>Tan et al. (2019), prospective observational study [36]</td>
<td>(n = 73)</td>
<td>ASA 2 Pregnant women</td>
<td>Significant nasal pathology, severe cardiac or respiratory disease, pre-eclampsia, sepsis</td>
<td>OIA: HFNO 30 L/min for 30 sec, then 50 L/min for 150 sec. (deep breathing, with mouth closed)</td>
</tr>
<tr>
<td>Ng et al. (2018), prospective RCT [10]</td>
<td>(n = 48)</td>
<td>ASA 1-3 adult patients</td>
<td>BMI &gt; 35 kg/m(^2), known or anticipated difficult airway, rapid sequence induction, significant raised intracranial pressure, active nasal bleeding, base of skull fracture</td>
<td>OIA: HFNO 30 L/min for 30 sec, then 50 L/min for 270 sec</td>
</tr>
<tr>
<td>Lee et al. (2018), case report</td>
<td>(n = 1)</td>
<td>Adult</td>
<td>Emergent endotracheal intubation for acute epiglottitis</td>
<td>OIA: HFNO 50 L/min with FiO(_2) 1.0 OIS, OIL: HFNO 70 L/min with FiO(_2) 1.0 (Spontaneous respiration, no neuromuscular relaxation)</td>
</tr>
<tr>
<td>Humphreys et al. (2017), prospective RCT [47]</td>
<td>(n = 48)</td>
<td>Healthy children (age: 0–6 months, 7–24 months, 2–5 yr and 6–10 yr old)</td>
<td>Known or anticipated difficult airway, congenital heart or lung disease, obesity (BMI &gt; 30 kg/m(^2)), risk of aspiration</td>
<td>OIS: bag-mask ventilation for 3 min. OIL: HFNO 0–15 kg, 2 L/kg/min; 15–30 kg, 35 L/min; 30–50 kg, 40 L/min; and &gt; 50 kg, 50 L/min</td>
</tr>
<tr>
<td>Riva et al. (2018), prospective RCT [48]</td>
<td>(n = 60)</td>
<td>ASA 1-2 children (age: 1-6 yr, weight: 10-20 kg)</td>
<td>Known or anticipated difficult airway, congenital heart or lung disease, obesity (BMI &gt; 30 kg/m(^2)), risk of aspiration</td>
<td>OIS: bag-mask ventilation OIL: HFNO 2 L/kg/min of FiO(_2) 1.0 (n = 20, FiO(_2) 1.0) OIS: bag-mask ventilation OIL: HFNO 0.2 L/kg/min of FiO(_2) 1.0 (n = 20, FiO(_2) 0.3)</td>
</tr>
<tr>
<td>Study</td>
<td>Sample Size</td>
<td>Intervention</td>
<td>Outcome 1</td>
<td>Outcome 2</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>-------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Lodenius et al. (2018), prospective RCT</td>
<td>(n = 80)</td>
<td>OR</td>
<td>I: Adult patients who required rapid sequence induction</td>
<td>E: BMI &gt; 35 kg/m²</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OIA: HFNO 40 L/min, then 70 L/min of FiO2 1.0 for 3 min.</td>
<td>OIS, OIL: HFNO 70 L/min of FiO2 1.0 for 3 min.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>OIS: FM 10 L/min, no bag-mask ventilation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>OIL: no oxygenation.</td>
</tr>
<tr>
<td>Mir et al. (2017), prospective RCT</td>
<td>(n = 40)</td>
<td>OR</td>
<td>I: Adult Patients who required rapid sequence induction</td>
<td>E: severe respiratory disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OIA: HFNO 30 L/min, then 70 L/min for 3 min.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>OIS, OIL: HFNO 70 L/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>OIS: FM 12 L/min, no bag-mask ventilation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>OIL: no oxygenation.</td>
</tr>
<tr>
<td>Miguel-Martinez et al. (2015), prospective</td>
<td>(n = 101)</td>
<td>ICU</td>
<td>I: Adult patients who required rapid sequence induction</td>
<td>E: cardiac arrest, severe hypoxemia (defined as SpO2 &lt; 95% under a NRM with an oxygen flow of 15 L/min), patients already receiving HFNO, and patients under NIV</td>
</tr>
<tr>
<td>before-after study</td>
<td></td>
<td></td>
<td>OIA: HFNO 60 L/min of FiO2 1.0 for 3 min.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>OIS, OIL: HFNO 60 L/min of FiO2 1.0 for 3 min.</td>
</tr>
<tr>
<td>Vourc’h et al. (2015), prospective RCT</td>
<td>(n = 119)</td>
<td>ICU</td>
<td>I: Adult patients who required rapid sequence induction with acute hypoxemic respiratory failure</td>
<td>E: cardiac arrest, asphyxia, nasopharyngeal obstacle, Grade 4 glottis exposure on the Cormack-Lehane scale</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OIA: HFNO 60 L/min of FiO2 1.0 for 4 min.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>OIS, OIL: HFNO 60 L/min of FiO2 1.0 for 4 min.</td>
</tr>
<tr>
<td>Simon et al. (2016), prospective RCT</td>
<td>(n = 40)</td>
<td>ICU</td>
<td>I: Adult patients who required rapid sequence induction with hypoxemic respiratory failure</td>
<td>E: nasopharyngeal obstruction or blockage, suspected or known</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OIA: HFNO 50 L/min of FiO2 1.0</td>
<td></td>
</tr>
</tbody>
</table>

This article is protected by copyright of Korean Journal of Anesthesiology. All rights reserved.
Jabor et al. (2016), prospective RCT [57]

**ICU**
- I: Adult patients who required rapid sequence induction with acute hypoxemic respiratory failure
- E: cardiac arrest, nasopharyngeal obstruction, usual contraindications to NIV

**N** = 49

**OIA:** HFNO 60 L/min of FiO$_2$ 1.0 with NIV for 4 min
**OIS:** HFNO 60 L/min of FiO$_2$ 1.0 with NIV
**OIL:** HFNO 60 L/min of FiO$_2$ 1.0

1) **lowest SpO$_2$, median (IQR) (P = 0.029):**
- I: 100% (95–100%)
- C: 96% (92–99%)

Doyle et al. (2016), prospective observational study [38]

**ICU, OR, ED**
- I: Adult patients requiring intubation
- **N** = 71

**OIA:** HFNO 60 L/min for 3 min.
**OIS, OIL:** HFNO 60 L/min

No control

1) **Incidence of desaturation (reduction of SpO$_2$ > 10%):**
- I: 5 patients (7%)


This article is protected by copyright of Korean Journal of Anesthesiology. All rights reserved.
Table 2. Characteristics of Clinical Studies of High-flow Nasal Oxygenation (HFNO) for Airway Surgery

<table>
<thead>
<tr>
<th>Year, author, design</th>
<th>Number of patients</th>
<th>Inclusion</th>
<th>Apnea or spontaneous relaxation, neuromuscular relaxation</th>
<th>Oxygenation</th>
<th>Time of apnea or spontaneous respiration</th>
<th>SpO(_2) and EtCO(_2) or PaCO(_2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patel et al. (2015), case series [60]</td>
<td>25</td>
<td>Adult Surgery for laryngotracheal stenosis, vocal fold pathology and obstructive sleep apnea, and benign and malignant hypopharyngeal obstruction</td>
<td>Apnea. Rocuronium 0.5 mg/kg</td>
<td>Preoxygenation: HFNO 70 L/min with FiO(_2) 1.0 for 10 min</td>
<td>Median (IQR) [range]: 14 (9–19) [5–65] minutes</td>
<td>SpO(_2) ≥ 90% EtCO(_2), mean (SD) [range]: 7.8 (2.4) [4.9–15.3] kPa.</td>
</tr>
<tr>
<td>Booth et al. (2017), case series [71]</td>
<td>30</td>
<td>Adult Elective microlaryngoscopic surgery</td>
<td>Spontaneous respiration</td>
<td>Preoxygenation: HFNO 30 L/min with FiO(_2) 1.0 for 1 min, then 50 L/min for 2 min. Peroxygenation: HFNO 70 L/min with FiO(_2) 1.0.</td>
<td>Median (IQR) [range]: 44 (40–49.5) [18–100] minutes</td>
<td></td>
</tr>
<tr>
<td>Lyon et al. (2017), case series [72]</td>
<td>28</td>
<td>Adult Laryngeal or tracheal surgeries</td>
<td>Apnea Rocuronium</td>
<td>Preoxygenation: HFNO 80 L/min with FiO(_2) 1.0 for 3 min. Peroxygenation: HFNO 80 L/min with FiO(_2) 1.0.</td>
<td>Median (IQR) [range]: 19 (15-24) [9-37] minutes</td>
<td>SpO(_2) ≥ 85% EtCO(_2), median (IQR) [range]: 8.2 (7.2–9.4) [5.8–11.8] kPa.</td>
</tr>
<tr>
<td>Tam et al. (2017), case report [73]</td>
<td>1</td>
<td>Adult CO(_2) laser release of supraglottic pharyngeal stenosis</td>
<td>Apnea Rocuronium and succinylcholine</td>
<td>Preoxygenation: HFNO 35 L/min with FiO(_2) 1.0 for 3 min. Peroxygenation: HFNO 70 L/min with FiO(_2) 1.0.</td>
<td>26 minutes</td>
<td>SpO(_2) ≥ 90%</td>
</tr>
<tr>
<td>Lee et al. (2018), case report [74]</td>
<td>1</td>
<td>Adult Morbid obesity Elective panendoscopy and biopsy of vocal cord lesion</td>
<td>Apnea Rocuronium 0.3 mg/kg</td>
<td>Preoxygenation: HFNO 20 L/min, then 60 L/min with FiO(_2) 1.0 for 15 min. Peroxygenation: HFNO 60 L/min with FiO(_2) 1.0.</td>
<td>14 minutes</td>
<td>SpO(_2) ≥ 98% PaCO(_2): 60 mmHg</td>
</tr>
<tr>
<td>McCormack et al. (2017), &gt; 30 Children</td>
<td></td>
<td>Spontaneous respiration</td>
<td>Preoxygenation and peroxygenation: HFNO 2</td>
<td>30–40 minutes</td>
<td>teCO(_2) 6.5-7 kPa</td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>Type</td>
<td>Participant Characteristics</td>
<td>Procedure/Procedure Details</td>
<td>Preoxygenation</td>
<td>Peroxygenation</td>
<td>SpO₂ ≥ 80%</td>
</tr>
<tr>
<td>----------------------</td>
<td>----------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td>----------------</td>
<td>----------------</td>
<td>------------</td>
</tr>
<tr>
<td>Riva et al. (2016),</td>
<td>1</td>
<td>Premature baby boy, weighed 4 kg with a corrected age between 43 and 46 weeks Laser resection</td>
<td>Apnea. Rocuronium Peroxygention: HFNO 4 L/kg/min with FiO₂ 0.3 or 1.0.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang et al. (2018),</td>
<td>23</td>
<td>Adult Elective laryngomicrosurgery for vocal cord polyp, cyst, and laryngeal tumor biopsy.</td>
<td>Apnea. Succinylcholine 1.5 mg/kg Preoxygention: HFNO 20 L/min with FiO₂ 1.0 for 5 min. Peroxygention: HFNO 50 L/min with FiO₂ 1.0.</td>
<td>Mean (SD): 24.1 (6.4) minutes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humphreys et al. (2017), case series</td>
<td>20</td>
<td>Children, age 5 days to 15 years Upper airway surgery or dynamic airway assessment</td>
<td>Spontaneous respiration No neuromuscular relaxation Preoxygention and peroxygention: HFNO (0-12 kg) 2 L/kg/min (13-15 kg) 30 L/min (15-30 kg) 35 L/min (30-50 kg) 40 L/min (&gt; 50 kg) 50 L/min</td>
<td>Median [range]: 32 [3–61] minutes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desai et al. (2017), case report</td>
<td>1</td>
<td>Adult Emergent surgical tracheostomy due to parapharyngeal abscess</td>
<td>Spontaneous respiration No neuromuscular relaxation Preoxygention: HFNO 30 L/min with FiO₂ 1.0 for 15 min. Peroxygention: HFNO 30 L/min with FiO₂ 1.0.</td>
<td>40 minutes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ebeling et al. (2018), case series</td>
<td>3</td>
<td>Adult (1) microdebridement of bilateral true vocal cord polyps and Reinke’s edema (2) tracheal balloon dilation of subglottis stenosis (3) biopsy of vocal cord lesion</td>
<td>Apnea. Rocuronium Preoxygention: HFNO 60 L/min with FiO₂ 1.0 for 5 min. (1) 15 minutes (2) 15 minutes (3) 40 minutes Peroxygention: HFNO 60 L/min with FiO₂ 1.0.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gustafsson et al. (2017),</td>
<td>31</td>
<td>Adult Elective short laryngeal</td>
<td>Apnea. Rocuronium Preoxygention: HFNO 40 L/min with FiO₂ 1.0 for 3 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case series</td>
<td>Procedures, such as mg/kg</td>
<td>min.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------</td>
<td>---------------------------</td>
<td>------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[80]</td>
<td>Microlaryngoscopy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Peroxygenation: HFNO 70 L/min with FiO2 1.0.

Fig. 1. Recent areas of use for high-flow nasal oxygenation, including at the anesthetic induction period and intraoperative period.
**Fig. 2.** Equipment for high-flow nasal oxygenation (Optiflow™, Fisher & Paykel Healthcare, New Zealand). (A) Optiflow™ consists of a flow meter, humidifier, and heating system, heated non-condensing circuit, nasal cannula, head strap, and oxygen connector for gas supply. (B) Nasal cannula. (C) Humidifier and heating system (© Fisher & Paykel Healthcare 2018. Used with permission).
Fig. 3. High-flow nasal oxygenation for tracheal intubation in the operating room. (A) Preoxygenation. (B) Apneic oxygenation (© Fisher & Paykel Healthcare 2018. Used with permission).