Nasal high flow application for perioperative support of respiratory system in adult patients

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Abstract: Perioperative respiratory support is by far the most significant goal of anesthesiologists. Maintenance of oxygenation within safe limits is achieved using conventional oxygen devices and pressure support ventilation in order to reduce adverse respiratory and non-respiratory events. Over the past decade, nasal high flow (NHF) has been introduced for oxygen therapy in adults with hypoxemic respiratory failure. In the present review, we present the physiologic effects of NHF that make it suitable for respiratory support during the perioperative period of adult patients, its clinical implications and compare it to current clinical practice.

Keywords: Apneic oxygenation; nasal high flow (NHF); perioperative; post-extubation; preoxygenation

Introduction

Maintenance of oxygenation within safe limits, i.e., peripheral arterial oxygen saturation (SpO_2) ≥90%, during the perioperative management of airway is by far the most significant goal of anesthesiologists. Especially, during intubation and until the artificial airway is established, there is a sufficient time without ventilation during which significant desaturation may occur with deleterious effects on the patient such as dysrhythmias, hemodynamic decompensation and ultimately death (1,2). The rate of desaturation is determined by various factors, such as patient's underlying condition and body habitus (3). For example, among healthy individuals, the time to desaturation is much shorter in obese adults and in children. Moreover, among critically ill patients, situations that affect

cardiac output or pulmonary gas exchange ability make the desaturation time even shorter (3).

On the other hand, extubation after major surgery poses the patient at risk for respiratory complications with hypoxemia being the most common one (up to 30–50%) (4,5). Even a brief episode of oxygen desaturation after tracheal extubation in the operating theatre is associated with a higher risk of acute respiratory failure (ARF) and re-intubation (4) as well as discharge to a skilled nursing facility or long-term care facility (6). This effect is dose-dependent: longer periods and greater degrees of desaturation (SpO_2 <80%) are associated with increased morbidity (6).

With the goal of reducing adverse respiratory events in the perioperative period, oxygen supplementation with conventional devices (i.e., nasal prongs, Venturi mask) with or without non-invasive positive pressure ventilation has

been used so far (7,8). Over the past decade, nasal high flow (NHF) has been introduced for oxygen therapy in adults with hypoxemic ARF. The device consists of an air/oxygen blender connected via an active heated humidifier to a nasal cannula, through a single limb, heated inspiratory circuit. It delivers a fraction of inspired oxygen (FiO_2) from 21% to 100% with a flow rate up to 60 L/min. FiO_2 adjustments are independent of the flow rate settings so that the patient is administered heated, humidified high-flow oxygen, with flow that can be set above the patient's maximum inspiratory flow rate (9). Currently, the evidence of the use of NHF in the perioperative management is growing (10-12). In the present review, we present the physiologic effects of NHF that make it suitable for respiratory support during intubation and after extubation in post-anesthetic care unit, its clinical implications in the perioperative management of adult patients and compare it to current clinical practice.

Materials and methods

We performed a computerized database search to identify randomized and nonrandomized trials and case series using NHF in perioperative patients. We searched for published and accepted ahead of print articles in bibliographic databases, including ISI Web of Science, PubMed, Science Direct Scopus, Wiley online library, Google Scholar and other international databases and websites. In addition, the literature research also involved a manual search of bibliographies of the identified papers and relevant information to meet the objectives of this study. Keywords used in the search were: "high flow nasal cannula", "nasal high flow" and "preoxygenation", "apneic oxygenation", "postoperative", "extubation", "intubation". The literature was limited to journal articles written in English. Two reviewers screened all potential references for inclusion. The last update of the search was performed in August 2019.

Preoxygenation

Pathophysiology

Safe apnea time is defined as the time from cessation of breathing or ventilation until the SpO_2 declines to 90%, after which it falls precipitously (13). Preoxygenation before intubation (pre-intubation) is used to increase oxygen reserves in order to prolong safe apnea time and allow more time to secure the airway (14). The importance of preoxygenation before intubation has been emphasized in

guidelines by the American Society of Anesthesiologists and other international anesthesia organizations, and it has become a minimum standard of care during induction of anesthesia (14,15). Different preoxygenation techniques are used (spontaneous breathing through a facemask at FiO_2 100% for at least 3 minutes, vital capacity maneuvers for 8 breaths, etc.) with or without application of positive pressure ventilation in order to preserve oxygenation (14,16).

Pre-oxygenation denitrogenises the lungs and creates an alveolar oxygen reservoir (17). Denitrogenation of lungs is based on breathing at high FiO_2 (FiO_2 =100%) virtually replacing nitrogen in functional residual capacity (FRC), increasing oxygen stores from 450 up to 3,000 mL which is many times above oxygen consumption of an adult patient (18). The size of this reservoir can be further increased by reducing dependent atelectasis which is a well-described complication of general anesthesia, caused primarily by a reduction of FRC and to a lesser degree by compression of thoracic cavity (19) driven by changes in the shape of chest wall, diaphragm and abdominal pressure.

NHF has a favorable profile for preoxygenation (*Table 1*). NHF generates a modest level of positive airway pressure because of the imposed expiratory resistance to the patient's exhalation against the continuous high flow of incoming gas (20). Studies on NHF have demonstrated an effect comparable with that of continuous positive airway pressure (CPAP) which is extremely important since the application of CPAP of 5 cmH_2O for 5 min during preoxygenation clearly provides a longer duration of apnea before clinically significant arterial desaturation occurs (21,22). An average positive end-expiratory pressure (PEEP) of 1.5–7 cmH_2O can be achieved with the use of NHF which is flow dependent (20) and could increase the size of oxygen reservoir by reducing dependent atelectasis (23). As it has been demonstrated, NHF increases end-expiratory lung volume (EELV) by 25% which may be explained by the recruitment of alveoli, and prevention of alveolar collapse (24). This effect is more pronounced in subjects with higher body mass index (BMI), regardless of body position (24,25) which may be significantly important in obese people whose management during preoxygenation is a great daily challenge.

Furthermore, NHF provides a more stable and higher FiO_2 by delivering high flow rates that can match or even exceed the patient's inspiratory flow demand. By this mechanism, entrainment of room air and thus dilution of administered oxygen is reduced which is in contrast to conventional oxygen devices where oxygen is administered

Table 1 Main mechanisms of action in each stage of perioperative setting

Mechanisms of action	Preoxygenation	Apneic oxygenation	Post-extubation
PEEP effect	X	–	X
Mechanical splinting of the nasopharynx	–	X	X
CO_2 washout & reduction of nasopharyngeal dead space	–	X	X
Enhanced lung mucociliary clearance	–	–	X
Reduction of work of breathing	–	–	X
Consistent and higher FiO_2	X	X	X

X, indicates the responsible mechanism of action. PEEP, positive end-expiratory pressure; CO_2, carbon dioxide; FiO_2, fraction of inspired oxygen.

with flows up to 15 L/min independent of the patient's respiratory rate or inspiratory flow, leading to a greater mixture of room air with the administered oxygen, lowering thus the actual inspired FiO_2 (26,27). Vargas *et al.* reported that even in hypoxemic patients, NHF can increase the partial pressure of arterial oxygen (PaO_2)/FiO_2 ratio making it ideal for preoxygenation in this group of patients who are characterized by a reduced safe apnea time (28).

Clinical evidence

The ability of NHF to combine moderate PEEP effect and more constant FiO_2 levels along with the growing use in patients with hypoxemic respiratory failure led a number of investigators to examine its role as a preoxygenation method. Two recent randomized studies compared the efficacy of transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) technique (flow rate up to 70 L/min, FiO_2 =100%) versus facemask (flow rate 10–12 L/min, FiO_2 =100%) as a preoxygenation method in patients undergoing rapid sequence induction (RSI) of anesthesia for emergency surgery (29,30). None of them showed any differences in oxygenation indices (PaO_2, SpO_2) between study groups. However, NHF mechanisms of action take a few minutes to evolve and thus RSI is not an optimal setting to investigate NHF efficacy. Nonetheless, unexpected problems might arise during RSI, i.e., prolongation of apnea time, and a device that maintains oxygen within safer limits for a longer period of time such as NHF, is likely to be beneficial. Indeed, apnea time was significantly longer with NHF (29), while no patient suffered from desaturation (29,30).

Considerable studies have been performed to date in order to investigate the specific role of NHF as a preoxygenation device in different types of surgery. In

neurosurgical patients undergoing elective endotracheal intubation (ETI), NHF was compared to standard facemask from the time of anesthetic induction until successful intubation (31). Preoxygenation was commenced with a standard facemask and THRIVE technique in the facemask group and NHF group respectively. As soon as the patient lost consciousness after administration of anesthetic drugs and muscle relaxants, bag-mask ventilation (BMV) was applied in the facemask group while in the NHF the THRIVE technique was continued as a method of apneic oxygenation. Although PaO_2 was higher with NHF at the end of preoxygenation, it decreased after the apneic oxygenation period, and was significantly lower when compared to patients who received BMV in the facemask group. A concomitant greater rise in $PaCO_2$ was also observed in the NHF group which could be deleterious to patients with known raised intracranial pressure (31).

Preoxygenation of pregnant women is really challenging since the incidence of difficult airway together with reduced respiratory reserves (decreased FRC) makes this group of patients vulnerable to catastrophic complications if intubation procedure fails. An observational prospective study on pregnant women using NHF as preoxygenation method (32), estimated the percentage of women who would achieve end-tidal expired fraction of O_2 (E_TO_2) above 90% after 3 minutes, which is the recommended target by the Obstetric Anaesthetists' Association and the Difficult Airway Society (33). Only 60% of patients reached this cut-off criterion without any changes in fetal heart rate. A linear negative association between E_TO_2 value and BMI was also observed. Similar results were recorded by Shippam *et al.* when standard facemask was compared to NHF for preoxygenation in healthy term pregnant women. Significantly fewer patients in the NHF group achieved the E_TO_2 >90% target (34). Authors in both

studies hypothesized that air entrainment may have partially contributed to the inadequacy of NHF since only a part of NHF group kept their mouth closed during the 3-minute process of preoxygenation which could have led to dilution of administered oxygen and lower airway pressures. Also, anatomical and physiological changes in the upper airway of a pregnant woman may change the *in vivo* aerodynamics of NHF by decreasing the delivered inspired concentration of oxygen and the level of positive airway pressure compared with its use in the nonpregnant individual (35).

Obese patients also represent a distinct group in terms of physiology through the anesthetic perspective. Such patients have a greater risk for intubation related complications for a number of reasons related to body habitus such as atelectasis, loss of FRC, difficulties in BMV and difficult airway management (36,37). NHF has been examined for preoxygenation of morbidly obese patients (BMI $\geq$35 kg/m^2) undergoing bariatric surgery. Patients were equally separated in three groups: standard preoxygenation via facemask (standard group), CPAP 7 cmH$_2$O (CPAP group) and NHF group. Preoxygenation with NHF provided significantly increased PaO$_2$ levels compared to standard group and comparable to that of CPAP group. A possible explanation could be the decrease of dead space ventilation with NHF (38). In contrast, in PREOPTIPOP trial, where non-invasive ventilation (NIV) and NHF were compared as preoxygenation techniques in obese patients (BMI >35 kg/m^2), median E$_T$O$_2$ within 2 minutes of post-intubation was significantly higher in the NIV group. NHF brought lower E$_T$O$_2$, lower SpO$_2$ and more oxygen desaturation than NIV (39). However, these discrepancies could be explained by methodological issues between these two studies. Nevertheless, NHF is an acceptable alternative device in obese patients when NIV is not available or contraindicated.

Although data on the preoxygenation efficacy of NHF in patients with established ARF who underwent any type of surgery are scarce, valuable conclusions can be drawn from studies in critically ill patients. NHF has been directly compared to NIV as a means of preoxygenation in non-surgical patients requiring intubation for ARF in two studies. (40,41). No significant differences were reported between groups regarding the lowest SpO$_2$. However, amongst patients with moderate to severe hypoxemia (PaO$_2$/FiO$_2$ <200 mmHg), risk of desaturation was lower with NIV. The combination of NHF with NIV as a novel preoxygenation strategy could offer some obvious advantages over conventional NIV alone in hypoxemic patients. Application of NHF after NIV removal at the end of preoxygenation in order to allow the passage of the orotracheal tube through the mouth could prevent alveolar derecruitment and ensure apnoeic oxygenation. Indeed, in OPTINIV trial, the combination of NHF and NIV in patients with severe hypoxemia resulted in higher minimal SpO$_2$ values during intubation compared to NIV alone. There was a clinically meaningful but statistical non-significant reduction in intubation related complications between groups, since the study was underpowered to address this outcome (42).

Studies evaluating NHF as an alternative preoxygenation technique have provided conflicting results. Such discrepancies can be explained on the basis of some key differences between studies such as severity of hypoxemia at baseline, indications for intubation, numerous comparators [NIV, facemask, bag-valve-mask (BVM)] and methodology (maintenance of airway patency, avoidance of breathing through open mouth). Surprisingly the majority of these studies measured SpO$_2$ as a primary endpoint for NHF preoxygenation instead of E$_T$O$_2$, a more accurate marker of effective lung denitrogenation. We can assume that we are still far from establishing NHF as an equally effective preoxygenation method in different categories of surgical patients, although in patients with mild to moderate hypoxemia, NHF seems to be at least as effective as standard oxygen therapy and may even lead in reduction of severe desaturation events in the peri-intubation period. NIV on the other hand, is beneficial in comparison to NHF in severely hypoxemic patients, either as a stand-alone preoxygenation mode or in conjunction with NHF. Current data preclude the use of NHF in specific populations such as pregnant and neurosurgical patients.

Apneic oxygenation

Pathophysiology

Whatever technique or device is used for preoxygenation, it must be interrupted during intubation in order to allow laryngoscopy, resulting thus in desaturation (3). A strategy to extend the safe apnea time, during the peri-intubation period is continuous nasopharyngeal oxygen supply without ventilation which is called apneic oxygenation or aventilatory mass flow (43).

During apneic state, average oxygen uptake is 250 mL/min while only 8–20 mL/min of carbon dioxide (CO$_2$) are eliminated from bloodstream to the alveoli

creating a negative pressure gradient of up to 20 cmH_2O that drives oxygen into the lungs (44,45). Provided that a patent air passageway exists between the lungs and the exterior, gas is drawn down from the nasopharynx to the distal airway. By increasing the pharyngeal oxygen content with supplemental oxygen via different apneic oxygenation techniques (i.e., nasopharyngeal catheter, standard nasal cannula), we achieve to prolong the safe apnea time and delay desaturation (46-49).

Currently, apneic oxygenation during ETI is endorsed by guidelines for the management of anticipated difficult airway management (14,33,50). NHF, as an apneic oxygenation technique, has a theoretical advantageous profile combined with the ability to be continuously applied throughout the procedure of ETI (*Table 1*). Using NHF, pressurization of the upper airway above atmospheric pressure during inspiration, provides mechanical splinting of the nasopharynx preventing thus supraglottic collapse and keeping the passage between the lungs and the exterior patent (51). Moreover, high flow rates of air into the nasopharynx via NHF produces a continuous flushing effect, forcing respiratory gases rich in CO_2 out of the airway. Nasopharyngeal dead space washout reduces the rate of increase in end-tidal CO_2 ($ETCO_2$) which is a major issue during apneic oxygenation and at the same time provides a fresh reservoir of oxygen (52,53).

Clinical evidence

Patel *et al.* (53) applied NHF at 70 L/min for apneic oxygenation (referred to as THRIVE technique) in patients with reduced cardiorespiratory reserves and known or expected difficult airway. NHF accomplished median apnea time of 14 min and eliminated desaturation (SpO_2 <90%) events. Interestingly, there was not any unexpected interruption of the procedure because of any desaturation or other CO_2-related complications. Rate of $ETCO_2$ rise was 0.15 kPa/min which is significantly lower than the expected rise of $ETCO_2$ (0.35–0.45 kPa/min) based on previous literature (53).

In agreement with the abovementioned results, two subsequent studies using NHF for apneic oxygenation throughout anesthesia in patients undergoing laryngeal and tracheal surgery, reported increased apnea time, while maintaining SpO_2 above 91% (54,55). Only four desaturation events were recorded. One of these episodes subsided with airway maneuvers and increment in NHF flow (from 80 to 120 L/min) while the others took place at the end of surgery and were managed with positive pressure ventilation. Mean

$ETCO_2$ increment rate (0.17 kPa/min) was in agreement with previously reported values by Patel *et al.* (53). The above studies suggest a possible "apneic ventilation" effect for NHF besides oxygenation, accounting for CO_2 clearance. Hermez *et al.* hypothesized that an interplay between THRIVE mediated cascade of vortices in the upper airway (oropharynx to glottis) and cardiac oscillations might be responsible for gas exchange. Using *in vitro* airway models, they were able to visualize flow pattern and measure turbulence levels as well CO_2 clearance rate, simulating cardiac oscillations. THRIVE was able to create a series of interlocking vortices to the glottis being pulled downward the trachea during cardiac diastole while the opposite fluid movement took place during cardiac systole providing a flushing mechanism for CO_2 from the carina to pharynx (56).

On the contrary with previously mentioned studies, FELLOW trial showed no benefit for NHF in terms of oxygen saturation during apnea time. This single-center randomized controlled trial divided 150 critically ill patients to receive preoxygenation with NHF set to 15 L/min flow of 100% FiO_2 (intervention group) or usual care (control group). NHF was continued throughout the apnea time in the intervention group patients while the patients in the control group were intubated without supplemental oxygen during laryngoscopy. Median lowest SpO_2 values and number of severe desaturation events were not significantly different between groups. These findings could be attributed to both NHF application at low flow rates, given that NHF effects are mainly flow depended as well as to the absence of true apnea in approximately 70% of patients in both groups, potentially masking any benefit from apneic oxygenation (57).

NHF appears to provide extended apnea times and a CO_2 washout effect without compromising oxygenation. Nevertheless, routine use of NHF as a standard preoxygenation method prior to ETI cannot be recommended on the basis of existing data, though its safety profile and theoretical advantages compared to standard preoxygenation strategies make NHF appealing as first-line choice. Substantial heterogeneity among existing studies, methodological issues and lack of power limit the generalizability of their findings.

Postoperative

Pathophysiology

General anesthesia, muscle relaxants, surgery duration and

postoperative pain may contribute to significant alterations of respiratory system's mechanical properties mainly the reduction of FRC due to the cranial shift of the diaphragm with the reduction being higher as the surgical site approaches the diaphragm (58), resulting in postintubation atelectasis and hypoxemia persisting for up to 48 hours postoperatively (4-6,59). Conventional oxygen therapy (COT) with nasal prongs, cannula or masks is the main supportive treatment administered to patients after planned extubation (60). However, the maximum oxygen flow rate delivered by COT cannot exceed 15 L/min, which is often by far lower than the patients' own inspiratory flow rate.

NIV in the postoperative setting, could decrease the reintubation rate in high-risk patients when compared to COT (61,62). However, the routine use of NIV in those patients is still inconclusive. Air leaks, patient discomfort and claustrophobia, gastric distension and pulmonary aspiration are some of the issues encountered when applying NIV (63). Additionally, NIV should be applied in a monitored setting, requiring a high degree of health-care resources (63).

Theoretically, NHF advantageous mechanisms of action could prove over standard respiratory support systems in the postoperative setting (*Table 1*). As it has already been mentioned, NHF significantly increases the PaO_2/FiO_2 ratio compared to low flow oxygen devices either because of provision of higher and more constant FiO_2 values (27) or the generation of positive airway pressures that can recruit atelectatic areas (20,26). Its tolerance has repeatedly been shown to be excellent (64). Furthermore, the continuous heating and humidification of the administered gas (65), reduces the required metabolic cost of warming, increases the relative humidity of the inspired gas mixture especially in high flow rates (66) and facilitates clearance of airway secretions as demonstrated in patients with chronic obstructive pulmonary disease and bronchiectasis (67). Efficient clearance of airway secretion may be of vital importance in surgical patients in order to prevent post-extubation respiratory failure.

Clinical evidence

Few studies have been published to date on the use of NHF after extubation and even fewer on its use in the postoperative setting. Maggiore *et al.* studied the role of NHF versus COT in patients after extubation (68). Although NHF improved oxygenation, decreased respiratory rate, $PaCO_2$ and the need for re-intubation,

only half of the patients included in the study were post-surgery patients. In addition, only patients mechanically ventilated for more than 24 hours were included in the study, excluding thus patients undergoing elective or urgent surgery that were extubated immediately postoperatively. It is therefore difficult to extract any conclusions for a protentional role of NHF in the postoperative setting.

A large randomized controlled trial involving patients in intensive care unit (ICU) with high-risk for extubation failure showed that NHF was not inferior to NIV in prevention of re-intubation (10). Another significant finding of this study was that post-extubation respiratory failure rate was higher in the NIV group than in the NHF group that was attributed to intolerance of NIV. Same authors compared NHF with COT in ICU patients at low-risk for re-intubation after planned extubation (11). In accordance with previous findings, NHF further reduced the re-intubation rates in low-risk patients because of more efficient respiratory support and lower rates of post-extubation respiratory failure. However, it should be noticed that both studies (10,11) included mixed populations (medical and surgical patients) and thus the results cannot be generalized for the specific postoperative time.

In patients after major abdominal surgery, NHF has been studied as prophylactic treatment in the perioperative setting (69). In a randomized controlled trial, NHF was directly compared to usual care with COT in patients with moderate to high-risk for developing postoperative pulmonary complications according to the ARISKAT risk score. Direct extubation onto NHF after surgery did not result in a clinical advantage in terms of oxygenation and respiratory function over standard oxygen therapy. However, the rate of hypoxemia in the usual care group was lower than anticipated and thus it was unlikely that patients in the NHF group would have a further reduction of this risk which limits the value of the present work. There were also no significant differences in other postoperative outcomes, especially pulmonary complications and length of hospital stay.

The results of studies on NHF in patients after cardiothoracic surgery are more encouraging. Postoperative pulmonary complications have a high incidence in these patients and complications may increase morbidity and mortality, leading to a prolonged ICU and hospital length of stay (70). In a study by Parke *et al.* (71) not-intubated post-cardiac surgery patients with moderate hypoxemia treated with NHF had a lower incidence of escalation therapy to NIV compared to patients treated with high flow face mask.

In a similar group, Corley et al. using electrical impedance tomography, showed that NHF application at high flow rates compared to low flow oxygen devices significantly increased EELV (by 25%) and decreased respiratory rate, implying recruitment of atelectatic areas and improvement of lung compliance due to positive airway pressure generation by NHF (24). Interestingly, the benefits were more profound in the subgroup of patients with BMI ≥30 kg/m². However, this result was not confirmed by the same authors a few years later (72), who reported that preventive application of NHF immediately after extubation of post-cardiac surgery patients with a BMI ≥30 kg/m did not lead to improvements in respiratory function compared to COT. Oxygenation indices, dyspnea score and radiological atelectasis score were not different between NHF group and the COT group (72). Although, in their first study (24) a significant correlation was found between positive airway pressure generation and EELV, further work is required to determine whether these increases in airway pressure and EELV translate to improvements in clinically important patient outcomes.

In a non-inferiority study by Stephan et al. (73) NHF was compared to intermittent bilevel positive airway pressure (BiPAP) in cardiothoracic patients with ARF or at risk for developing ARF after extubation. NHF did not result in a worse rate of treatment failure when compared with BiPAP. Effects on respiratory variables were rapid with both methods. BiPAP was associated with a higher PaO_2/FiO_2 ratio while NHF with lower values of $PaCO_2$ and respiratory rate. Zochios et al. tried to clarify the role of NHF either as prophylactic therapy after extubation or as treatment for post-extubation respiratory failure (74). Oxygenation, respiratory rate, PaO_2/FiO_2 ratio, atelectasis, dyspnea and ICU length of stay did not differ significantly between patients treated with NHF and those treated with COT. However, the population heterogeneity in the involved studies, the different primary outcomes and the small number of subjects could have a significant impact on the results.

The role of NHF in postoperative setting remains questionable. Most evidence on NHF was collected from studies in post-extubated ICU patients (12,75-77) which is somehow a distinct group of patients given their increased morbidity as well as their exposure to invasive mechanical ventilation. The incidence of unanticipated early postoperative reintubations is very low (0–3.5%) making difficult for a respiratory device such as NHF to further decrease reintubation rate (78). A meta-analysis by Huang

et al. (77), showed that NHF compared to COT may reduce reintubation (or reintubation plus NIV) rates in critically ill patients but not in postoperative patients. On the contrary, a more recent meta-analysis of 10 studies comparing NHF with COT in postoperative patients reported that NHF significantly reduced the reintubation rate and rate of escalation of respiratory support without any effect on postoperative pulmonary complications or mortality (79). Nevertheless, as it is stated by the authors, the limitations of this meta-analysis (single-center studies, small number of patients, different primary outcomes of the studies included, different timing and duration of NHF) do not allow for robust conclusions.

Another obvious advantage of NHF in the postoperative care is that it does not require patient cooperation, is better tolerated by patients, its equipment is easier to use and reduces nursing workload (80). However, its inappropriate use may lead to adverse outcomes. Patient's vital signs and respiratory parameters (SpO_2, respiratory rate, thoraco-abdominal asynchrony and auxiliary respiratory muscle use) (81) must be monitored regularly in order to avoid undesired respiratory and cardiac complications. Kang et al. suggested that intubating a patient who had failed on NHF therapy within 48 h of starting NHF is associated with lower overall mortality compared to those who were intubated after 48 h (82). NHF is well tolerated by most of the patients and this can mask any objective signs of deterioration that indicate an uncontrolled disease resulting in prolonged intubation delays and poor hospital outcomes.

Conclusions

NHF mechanisms of actions exert various effects in the respiratory system, including improved gas exchange, lower respiratory rate and effort, improved lung volume, dynamic compliance, transpulmonary pressures and homogeneity of ventilation (83) leading to the assumption that this respiratory device will perfectly fit in the peri-operative setting. Although the mechanisms of NHF have been rigorously studied and its advantages over COT have been stated in several studies, randomized controlled trials have failed to establish a significant role either as a preoxygenation tool, or after extubation in the postoperative care. As far as it concerns its role for apneic oxygenation, it seems that high flow rates (50–60 L/min) can maintain oxygen saturation after commencement of apnoea to safer levels allowing more time until the artificial airway is established. The discrepancies in the

results from studies published so far do not allow to make specific recommendations. Larger and carefully designed randomized controlled trials are needed to define its role in perioperative medicine.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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