



Use of high flow nasal cannula for preoxygenation and apneic oxygenation during intubation

Jean-Damien Ricard^{1,2}, Baptiste Gaborieau^{1,2}, Juliette Bernier¹, Camille Le Breton¹, Jonathan Messika³

¹Intensive Care Unit, Louis-Mourier Hospital, Colombes, France; ²University of Paris, Paris, France; ³University of Paris, Physiopathology and Epidemiology of Respiratory Diseases, Paris, France

Correspondence to: Prof. Jean-Damien Ricard, MD, PhD. Medical-Surgical Intensive Care Unit, Louis-Mourier Hospital, F-92700, Colombes, France. Email: jean-damien.ricard@aphp.fr.

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Need for intubation in patients with acute respiratory failure remains important when respiratory condition deteriorates and places these severely hypoxemic patients at higher risks of desaturation than patients without respiratory failure (1). Between 30 to 40% of patients with acute respiratory failure will require intubation despite initial management with high flow nasal cannula (HFNC) oxygen (2-4).

This figure is higher in patients initially treated with non-invasive ventilation or with standard conventional oxygen, in particular in those with a PaO₂/FIO₂ below 200 (4,5). These patients are obviously at high risk of desaturation during the procedure.

Timing and decision of intubation

In addition to initial level of hypoxemia, timing of intubation is a key feature to consider when discussing hazards of intubation and how to avoid them (6). Interestingly, data in the literature suggests that optimal timing may differ depending on the patient's primary diagnosis. In the case of acute hypoxemic respiratory failure, studies have found that unduly delaying intubation worsens patients' outcome (7). Conversely, in septic shock, a post-hoc analysis of the Sepsispam study found that practices regarding intubation affected patient outcome (8). Those ICUs with the highest rate of early intubation had a greater proportion of mortality in comparison to ICUs with middle rate of early intubation. Those ICUs with

the lowest rate of early intubation had a non-significant increased mortality. Because intubation of septic patients may be prompted by either hemodynamic, respiratory or neurologic reasons, and because sepsis often originates from pneumonia, it is difficult to draw any firm conclusion from this post-hoc analysis, but taken together, data clearly indicates that late is not desirable, but early may also be associated with worse outcome. Hence, appropriate timing of intubation during high flow therapy is a daily challenge. Predicting which patients will fail and require intubation is hazardous and determining optimal time to intubate not always easy. Recently, we developed an index to help predict outcome of patients receiving HFNC. The ROX index (which is defined by the ratio of SpO₂ over FiO₂, divided by respiratory rate) has its best accuracy to identify which patients will succeed and which will fail under HFNC when it is calculated at 12 h after the start of HFNC therapy (2,3). Importantly, the dynamics of changes of the ROX are also discriminative, hence the index can be calculated over time, and an increasing ROX is associated with a better outcome than a decreasing one (3).

Preoxygenation in the ICU with HFNC or standard oxygen: analysis of the available data

Because an increasing number of patients with acute hypoxemic respiratory failure are treated with HFNC, those that ultimately require intubation will already have

the device in place to perform preoxygenation.

To date, preoxygenation and apneic oxygenation during the intubation process of critically patients with HFNC was evaluated in one before-after study (9) and four RCTs (10–13) (*Table 1*). Very similar outcomes (lowest SpO₂ and number of SpO₂ below 80%), similar HFNC settings (50–60 L/min and 100% FiO₂) were used in these five studies. Similarly, the comparator was mostly standard bag-valve mask oxygenation in these studies with the exception of one for which the comparator was NIV.

In patients with mild to moderate hypoxemia, the before-after study found that use of HFT improved preoxygenation and prevented occurrence of profound desaturation compared to conventional preoxygenation (9). In similar patients, one multicenter RCT found a significant reduction in intubation-related severe adverse events with HFNC but no difference in lowest SpO₂ value in comparison with conventional preoxygenation (12) and another a significant increase in SpO₂ after preoxygenation with HFNC in those previously receiving low-flow oxygen (11). During the 1 min of apnea after anesthesia induction, SpO₂ dropped significantly in the control group, whereas there was no significant decrease in the HFNC group. In more severely hypoxemic patients, a multicenter RCT reported similar lower SpO₂ and number of episodes of profound desaturation between conventional preoxygenation and HFNC (10). The fourth multicenter RCT (13) compared HFT to NIV and will be discussed below.

Taken together, none of these studies found a worse outcome with HFNC and some a significant improvement.

Despite these results, some are still reluctant to use high flow instead of standard oxygen (14).

This may seem intriguing.

No study ever demonstrated a better outcome of ARDS patients ventilated with a Dräger V500 ventilator compared to a Siemens Servo C. Had one the choice however, I am confident no one would hesitate today between the two when choosing a ventilator to manage an ARDS patient.

A significant technological gap separates the two, with better performances and new features in favour of the most recent one.

Isn't the situation similar between standard oxygen and HFNC?

If so, why do we require HFNC to demonstrate better outcomes?

The same analogy applies to administration of vasopressors in septic shock. Who would nowadays administer vasopressors diluted in a pouch of saline and

adjusting the flow with a simple manual flow regulator rather than via a precision syringe pump? Teams readily accepted this technological improvement without requiring a study demonstrating a survival difference between the two devices used in septic shock patients.

Preoxygenation in the ICU with HFNC or standard oxygen: what this new study adds

Intubation of hypoxemic patients is a hazardous procedure and complications may be fatal (15). Should our concern not be the patients' utmost safety? Most studies have focused on desaturation as primary outcome, because severer hypoxemia is frequent and may lead to cardiac arrest during intubation; however, other complications need also to be addressed.

Recently, Guitton and colleagues compared HFNC to standard bag-valve mask to preoxygenate patients with mild to moderate hypoxemia requiring tracheal intubation (12). The study was a multicentre, open-label, randomized controlled trial. HFNC was set at 60 L/min and preoxygenation oxygen flow was 15 L/min in the standard group. One hundred and eighty-four patients were enrolled.

The median lowest SpO₂ during intubation was not significantly different between the two groups, despite a greater incidence of difficult intubations in the HFNC group.

Similarly, fewer patients in the HFNC group experienced drops in SpO₂: 12% vs. 23% in the standard oxygen group. Overall, a significant higher incidence of severe adverse events was observed in the standard oxygen group compared to the HFNC group. This was also the case for the moderate complications. This was coherent with the results of the multivariate analysis that evidenced an association between HFNC and less episodes of desaturation below 90% and less intubation-related complications.

Hence, in mild to moderate hypoxemic patients requiring tracheal intubation in the ICU, two independent studies, using different trial designs, come to the same conclusion: HFNC is superior to standard oxygen to prevent intubation-related complications.

Preoxygenation in the ICU: does NIV perform better?

In patients with more severe hypoxemia, several studies have compared HFNC to non-invasive ventilation (*Table 1*).

A landmark study by Baillard and colleagues indicated

Table 1 Mains characteristics and results of studies assessing preoxygenation with HFNC and NIV in the ICU

Study first author, year of publication	Study design, setting, total N of patients	Comparators (number of patients per group)	Main outcome measure	Number of patients with desaturation <80% (or % of pts)	Other outcomes/analysis	Comments
Miguel-Montanes, 2015	<ul style="list-style-type: none"> Quasi-experimental sequential study Non-severely hypoxemic ICU patients requiring intubation 101 patients 	<ul style="list-style-type: none"> HFNC (51) NRB Facemask (50) 	Lowest SpO ₂ : <ul style="list-style-type: none"> High flow: 99% Facemask: 94% P=0.007	<ul style="list-style-type: none"> HFNC: 1 NRB Facemask: 7 P=0.03	Multivariate analysis found HFNC as protective factor against SpO ₂ <80	<ul style="list-style-type: none"> Not randomized Severe hypoxemic patients not included
Vourc'h, 2015	<ul style="list-style-type: none"> Prospective, multicenter open label RCT Hypoxaemic acute respiratory failure requiring intubation 6 ICUs, 119 patients 	<ul style="list-style-type: none"> HFNC (62) NRB Facemask (57) 	Lowest SpO ₂ : <ul style="list-style-type: none"> HFNC: 91.5 NRB Facemask: 89.5 P=0.44	<ul style="list-style-type: none"> HFNC: 16 NRB Facemask: 13 P=0.46		<ul style="list-style-type: none"> No evidence for upper airway patency (no mention of jaw thrust)
Simon, 2016	<ul style="list-style-type: none"> Open label, prospective, single center RCT Patients with respiratory failure (PaO₂/FiO₂ <300 mmHg) requiring intubation 40 patients 	<ul style="list-style-type: none"> HFNC (20) Bag-valve (20) 	Lowest SpO ₂ : <ul style="list-style-type: none"> HFNC: 89% Bag-valve: 86% P=0.56	<ul style="list-style-type: none"> HFNC: 5 (25%) Bag-valve: 5 (25%) P>0.99	<ul style="list-style-type: none"> HFNC: significant increase in SpO₂ in patients previously receiving low-flow oxygen (P=0.007) Bag-valve: significant decrease in SpO₂ during the 1 min of apnea after RSI 	<ul style="list-style-type: none"> Small sample No evidence for upper airway patency (no mention of jaw thrust)
Baillard, 2005	<ul style="list-style-type: none"> Open label, prospective RCT Acute respiratory failure requiring intubation 2 ICUs, 53 patients 	<ul style="list-style-type: none"> NIV (26) Bag-valve (27) 	Lowest SpO ₂ : <ul style="list-style-type: none"> NIV: 93% Bag-valve: 81% P<0.001	<ul style="list-style-type: none"> NIV: 2 Bag-valve: 12 P<0.01		<ul style="list-style-type: none"> Only patients with no contraindications to NIV were included No oxygen supply during laryngoscopy
Baillard, 2018	<ul style="list-style-type: none"> Open label, multicenter RCT Hypoxaemic acute respiratory failure requiring intubation 6 ICUs, 201 patients 	<ul style="list-style-type: none"> NIV (99) Facemask (102) 	Maximal SOFA value at Day 7: <ul style="list-style-type: none"> NIV: 9 Facemask: 10 P=0.65	<ul style="list-style-type: none"> NIV: 18 (18.4%) Facemask: 28 (27.7%) 		<ul style="list-style-type: none"> Results do not confirm the same team's first original study
Guitton, 2019	<ul style="list-style-type: none"> Open label, multicenter, randomized trial Non-severely hypoxemic patients ICU requiring intubation 7 ICUs, 184 patients 	<ul style="list-style-type: none"> HFNC (95) Bag-valve mask (89) 	Lowest SpO ₂ : <ul style="list-style-type: none"> HFNC: 100% Bag-valve mask: 99% P=0.30	<ul style="list-style-type: none"> HFNC: 2 (2%) Bag-valve mask: 7 (8%) P=0.06	Intubation-related adverse events: <ul style="list-style-type: none"> HFNC 6 (6%); Bag-valve mask 17 (19%) P=0.007	<ul style="list-style-type: none"> Severe hypoxemic patients not included Jaw-thrust maneuver: HFNC: 13% Bag-valve mask: 33% P=0.0009

Table 1 (continued)

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Study first author, year of publication	Study design, setting, total N of patients	Comparators (number of patients per group)	Main outcome measure	Number of patients with desaturation <80% (or % of pts)	Other outcomes/analysis	Comments
Besnier, 2016	<ul style="list-style-type: none"> Retrospective, single center Patients intubated for acute respiratory failure after pre-oxygenation with HFNC or NIV 52 patients 	<ul style="list-style-type: none"> NIV (39) HFNC (13) 	Lowest SpO ₂ : no difference P=0.82	<ul style="list-style-type: none"> HFNC: 3 with SpO₂ between 70% and 80% NIV: 1 with SpO₂ between 70% and 80% and 5 with SpO₂ <70% P=0.31		<ul style="list-style-type: none"> Retrospective study Single center Small sample size
Frat, 2019	<ul style="list-style-type: none"> Multicentre, open-label, parallel-group RCT Acute hypoxaemic respiratory failure (PaO₂/FIO₂ <300) 28 ICUs, 313 patients 	<ul style="list-style-type: none"> NIV (142) HFNC (171) 	SpO ₂ <80% • NIV: 33 (23%) • HFNC 47 (27%) P=0.39	SpO ₂ <80%: • P/F ≤200: NIV: 28 (24%); HFNC: 44 (35%) P=0.0459 • P/F >200: NIV: 5 (20%); HFNC: 3 (7%) P=0.10	Lowest SpO ₂ in: • All patients: NIV: 87%; HFNC: 84% P=0.13 • P/F ≤200: NIV 86%; HFNC 81% P=0.02 • P/F >200: NIV: 90%; HFNC: 93% P=0.31	<ul style="list-style-type: none"> Largest RCT to date

HFNC, high flow nasal cannula; NRB, non-rebreathing; RCT, randomized controlled trial; ICU, intensive care unit; P/F, PaO₂/FIO₂.

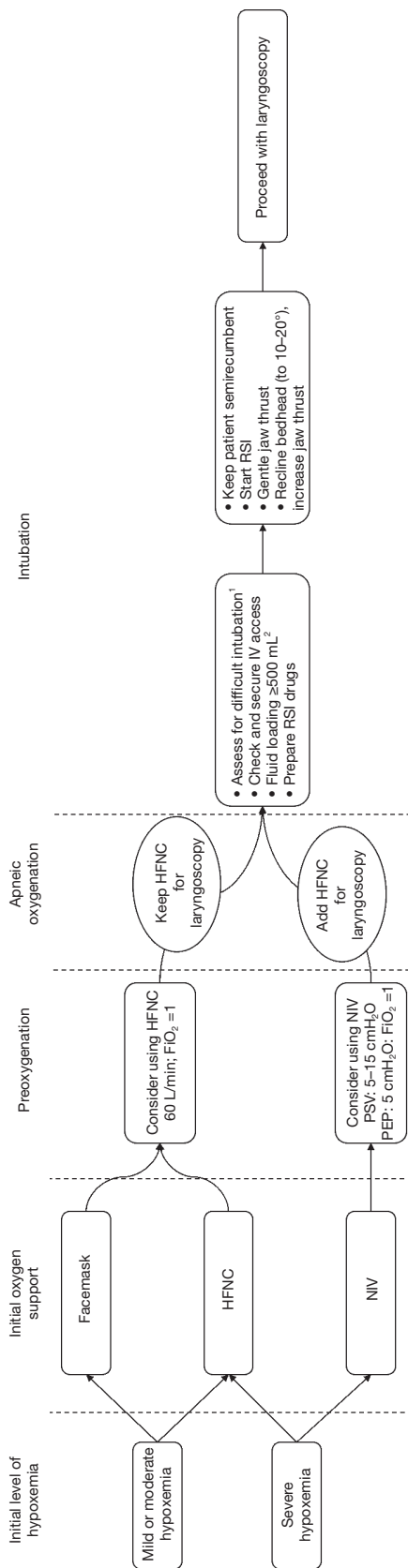


Figure 1 Algorithm of intubation in ICU. The choice of the preoxygenation method is based on the device the patient is supported with at the time of intubation decision. 1, using the MACOCHA scale; ², except in case of left heart failure or cardiogenic pulmonary. NIV, noninvasive ventilation; HFNC, high-flow nasal cannula oxygen support; RSI, rapid sequence induction.

the superiority of NIV over standard oxygen to prevent severe desaturation episodes ($SpO_2 < 80\%$) (16). However, in a subsequent study, the same authors failed to show any benefits of NIV as a preoxygenation method to reduce organ dysfunction compared with usual preoxygenation in hypoxemic, critically ill patients requiring tracheal intubation (17).

We recently conducted a randomized multicentre control trial that compared NIV to HFNC to ensure preoxygenation of patients with acute hypoxemic respiratory failure requiring tracheal intubation in the ICU (13). If there was no difference in the incidence of severe hypoxaemia (23% with NIV *vs.* 27% with HFNC) in the overall study patients, we found that patients with moderate-to-severe hypoxaemia ($PaO_2/FiO_2 \leq 200$ mmHg), severe hypoxaemia occurred less frequently after preoxygenation with NIV than with nasal high-flow (24% *vs.* 35% respectively, $P=0.0459$). Importantly, serious adverse events did not differ between the two groups.

Hence, although there does seem to exist a benefit in using NIV in the more severe patients, this benefit is small, and is not found for serious adverse events other than desaturation.

Concluding remarks: our patients’ safety above all

Regarding desaturation, it is insightful to look at individual patient data. A quick look at Figure 2 of Guitton and colleagues’ study shows that 4 patients in the standard oxygen group experienced desaturation below 50% (versus none in the HFNC group)! Obviously, figures are much too small for any valid statistical analysis, but in an individual patient safety perspective, these four patients were at great risk for potentially fatal cardiac arrest. Interestingly, similar very profound desaturations were observed by Besnier *et al.* in patients preoxygenated with NIV but none with HFNC, despite the absence of difference in median lowest SpO_2 values between the two devices (18).

Based on these results, we suggest in *Figure 1*, our practical approach on preoxygenation and apneic oxygenation during intubation of ICU patients.

It is our responsibility as intensivist we take all the necessary precautions so that none of our patients ever experience such desaturations. Data, including the important study by Guitton *et al.* (12), shows this is better achieved with HFNC than with conventional preoxygenation.

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Footnote

Conflicts of Interest: JD Ricard declares travel and accommodation expenses covered by Fisher & Paykel to attend scientific meetings. J Messika declares travel and accommodation expenses covered by Fisher & Paykel and CSL Behring to attend scientific meetings. The other 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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