

Procedure for the pulmonary management of non-ICU patients hospitalized in the context of the COVID-19 pandemic

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INTRODUCTION

The aim of this document is to develop guidance for the pulmonary management of patients in the context of the COVID-19 pandemic.

This guidance is complementary to the information published by the various bodies dependent on the Ministry of Health (<https://solidarites-sante.gouv.fr/soins-et-maladies/maladies/maladies-infectieuses/coronavirus/>), that is regularly updated, as well as the recommendations of other learned societies involved in the management of these patients, in particular regarding the management of patients with acute respiratory distress requiring invasive ventilatory support techniques in an intensive care unit (ICU) (https://www.srlf.org/wp-content/uploads/2020/03/RFE-COVID_V3_FINAL-1.pdf)

It should be noted that the guidance in this document is based on studies of other viral pandemics (influenza A, SARS, MERS) and the latest publications on the COVID-19 and on the already published recommendations, in particular those of the Italian Hospital Pulmonologists Association (AIPO, (1)). Therefore, the current level of evidence is low given the lack of methodological robustness and due to the recentness of the disease. This document will be updated according to the evolution of knowledge and changes.

COVID-2019 infection is an acute infection with a spontaneous resolution in most cases. The clinical presentation may vary from mild respiratory symptoms to severe pneumonia progressing to diffuse alveolar damage responsible for fulminant acute respiratory failure (2). Radiologically, COVID-2019 pneumonia is characterized by bilateral infiltrates that may progress to diffuse alveolar condensations. In less severe patients, computed tomography (CT) shows bilateral ground glass opacities predominantly in the subpleural region (45-62% of cases) (3) and in areas of subsegmental consolidation, while in more severe cases, lobar and subsegmental consolidations are found(4), with a peak of appearance of lesions 6-11 days after the onset of symptoms (3).

The prevalence of acute respiratory failure (ARF) in patients with COVID-19 infection has been estimated between 15 and 20% (2,5,6). Recent data from China has shown that 4-13% of patients have been treated with non-invasive ventilation (NIV) and 2.3-12% have been treated with invasive ventilation (2,5,7-9). Although the incidence of hypoxic ARF is unclear (due to the fact that the number of subjects actually affected is unknown), it appears that 14% of patients will develop a severe form requiring oxygen and 5% of patients will have to be admitted in an ICU and will require mechanical ventilation (2). Data from patients with severe ARF has shown that 67% of them had acute respiratory distress syndrome (ARDS) and 63%, 42% and 56% of patients had received high-flow nasal oxygen therapy (HFNOT), NIV and invasive ventilation, respectively. Finally, in more than 1,000 patients with COVID-19 infection, 41% of all hospitalized patients had received O₂ and 70% had severe forms.

In addition to mechanical ventilatory support in an ICU, various non-invasive ventilatory support techniques have been used in severe forms of ARF such as NIV, continuous positive airway pressure (CPAP) and humidified HFNOT. These techniques may be applied in conventional expert pneumology departments, but also in less specialized departments, given the exceedance of health capacities observed in some French regions.

The practical guidance described in this manuscript is intended to help clinicians in the pulmonary management of non-ICU patients in the context of the COVID19 pandemic. They cannot be considered as recommendations and only engage the responsibility of the authors, their experience of several weeks with patients

with COVID-19 infection, their expertise in the field of respiratory devices and their critical reading of the literature. The authors thank the SPLF for its confidence. This document will be updated on a regular basis.

AVAILABLE TOOLS

1) Oxygen therapy

Oxygen should be used in case of severe COVID-19 pulmonary disease probably as soon as the SpO₂ is <92% with a target SpO₂ ranging between 92 and 96%.

No randomized or non-randomized studies have assessed the use of O₂ in patients with COVID-19 infection. However, by extrapolating data from studies in patients with severe hypoxemic ARF, there is evidence to support the benefit of O₂ and the flow rate to be used. A meta-analysis of 25 controlled randomized studies has shown that a strategy without an upper limit of the O₂ flow rate (called "liberal arm") increased the risk of inpatient mortality (10). This has been confirmed in the LOCO₂ study that has shown an excess mortality at 28 days when a liberal oxygen therapy strategy was used (target SpO₂ >96%; PaO₂: 90-105 mmHg) compared to a conservative strategy (target SpO₂: 88-92%; PaO₂: 55-70 mmHg) (11). Thus, very pragmatically, all the recent recommendations propose a target SpO₂ considered reasonable between 92 and 96% (12).

The interface to be used has not been investigated. Comfort will be a priority while monitoring the efficacy (see the GAVO₂ procedure <http://splf.fr/gavo2/>). All pulmonologists who have managed patients with COVID-19 infection agree that monitoring the respiratory rate (RR) is very important in this disease.

2) Non-invasive ventilation (NIV)

In case of failure of oxygen therapy in all its available forms, NIV may be used if there is no urgent indication for intubation or as an interim solution when invasive ventilation is not available.

NIV should be used under close monitoring, the anaesthetist being present or at least informed.

The interface used should be a) that available and b) that in which the team is the most experienced. There is no benefit to use a helmet but it remains an option if the team is experienced in using it.

The interface should be adapted with a filter to prevent staff contamination.

No published study has assessed this technique in patients with COVID-19 infection. Only indirect evidence from studies in patients with ARF from other causes can be used. It should be noted that NIV is at high risk of aerosol dispersion of viral particles and both the equipment and staff should be protected (13–15) (see the GAVO₂ procedure <http://splf.fr/gavo2/>). Regarding hypoxemic ARF, meta-analyses of controlled randomized trials have shown reduced mortality and intubation rates with NIV. However, these meta-analyses have included patients with postoperative immunosuppression, acute heart failure and ARF, and their results are therefore poorly applicable to ARF due to COVID-19 infection where patients have bilateral hypoxemic pulmonary disease progressing to ARDS (7,16–18). In hypoxemic ARF resulting from causes other than acute heart failure, NIV has shown a high failure

rate (19), with sometimes a higher mortality (28%; 95% CI: 21-37%) than in patients treated with O₂ alone (23%; 95% CI: 16-33%) or with HFNOT (13%; 95% CI: 7-20%).

In a cohort of MERS patients, NIV has been associated with a better survival and a shorter length of hospital stay compared to the group of patients who were intubated without testing NIV before (20). However, NIV was associated with a high failure rate (92.4%) and intubation was needed in fine. Also, patients who underwent NIV before intubation required the use of NO and had a higher mortality rate (20). Data from other epidemics, including influenza, H1N1 and SARS shows failure rates of 10-70%.

In the COVID-19 pneumonia, it is also suggested that NIV could worsen severe forms of lung damage due to the high insufflation pressures and Vt (21,22) and could excessively delay intubation or make it more difficult (21). However, NIV should be considered in patients who will not be admitted to an ICU for intubation (23). If NIV is used, it should be noted that a Chinese study conducted in patients with viral ARDS has shown that when NIV was combined with prone positioning for 2 hours twice a day, intubation was more often avoided in patients with moderate ARDS (24).

Some patients with bilateral COVID-19 pneumonia could benefit de novo from NIV when they have a preexisting respiratory disorder related to this treatment (obesity hypoventilation syndrome, severe COPD, overlap syndrome, etc.). In any patient treated with long-term NIV or CPAP at home, the device, if it cannot be discontinued, should be adapted during hospitalization, possibly by temporarily lowering the pressure if excessive leaks are present and by following the previous recommendations concerning the mask and the circuit.

In these patients, monitoring should above all ensure early detection of hypoxemia worsening that generally occurs relatively early in patients with COVID-19 infection. Care should be taken to discharge patients with personal NIV and to contact the pulmonologist for further follow-up.

However, resources being limited and if there is no access to invasive ventilation, NIV should be considered as a possible tool.

If NIV is used in the emergency room or in a medicine department by a non-expert staff, a duty list with a healthcare professional expert in respiratory devices could be considered, by mobilizing all healthcare professionals who are experts in the field (physiotherapists, providers' technicians, providers' nurses). NIV should not be used in the emergency room in patients with confirmed or suspected COVID-19 infection before the assemblies suggested to prevent the airborne dispersion of the virus are implemented (see the GAVO2 procedure <http://splf.fr/gavo2/>).

Using a helmet may be an attractive solution because it is easy to use. A controlled randomized study has shown a decrease in intubation and mortality rates with NIV when it is delivered through a helmet in ARDS patients (25). It should be noted that the helmet allows reducing viral aerosol dispersion (26). However, the availability and cost of this device should be taken into account.

When a patient is treated with NIV, monitoring should be intensified. Hypoxemia worsening under NIV requires an assessment by anaesthetists for a potential transfer to an ICU for patients in whom management with intubation seems indicated and suitable. This decision will take into account not only the clinical severity, but also the context

of the underlying disorders and the wishes of the patient and their family. This requires a discussion on a case-by-case basis. In cases for which a transfer to an ICU is not indicated, NIV may be continued by trying to optimize it (while adding sufficient oxygen flow rates) if it is well tolerated and the symptoms improve. Otherwise, comfort measures and/or the addition of pharmacological actions or respiratory support (high-flow techniques) should be discussed in order to relieve dyspnea (27).

It is imperative not to insist with NIV or oxygen therapy in patients whose clinical condition or gas exchanges worsen since this could delay intubation and lead to a fatal outcome. Increased vigilance is necessary since muscle depletion appears late in patients with poor lung compliance, as is the case in patients with diffuse alveolar damage. This is falsely reassuring, and may lead to a sudden aggravation in a few minutes, with the constraint of an emergency intubation. In all cases, intubation should be anticipated, performed according to rigorous procedures and under conditions exposing a limited number of caregivers to droplets.

Technically, special attention should be given to the location where O₂ is added. The connector located at the back of the devices should be used first but, in case of failure or if high flow rates are needed, it is interesting to try to supply O₂ using a connector located near the mask. This is especially true in the presence of intentional leaks between the ventilator and the patient.

3) Continuous positive airway pressure (CPAP)

In case of failure of oxygen therapy in all its available forms, CPAP may be used if there is no urgent indication for intubation or as an interim solution when invasive ventilation is not available.

This solution is simpler, less expensive and possibly less harmful than NIV.

NIV should be used under close monitoring, the anaesthetist being present or at least informed.

The interface used should be a) that available and b) that in which the team is the most experienced.

There is no benefit to use a helmet but it remains an option if the team is experienced in using it.

The interface should be adapted with a filter to prevent staff contamination.

In ARDS, extrinsic positive end-expiratory pressure (PEEP) is used in case of invasive ventilation to prevent alveolar collapse. In addition, PEEP increases alveolar recruitment, improves oxygenation and reduces the need for O₂.

There is strong evidence to support the use of PEEP during invasive ventilation, but no article has investigated the use of PEEP during NIV in ARDS or in the context of the COVID-19 pandemic. Experiences from Italian and Chinese teams are shared but not published. Some teams have even proposed to combine prone positioning and non-invasive CPAP ventilation. It should be noted that this method has shown its benefit with NIV in ARDS (24).

Given the ease of use, the possibility of producing a PEEP with simpler tools than those necessary for NIV (Figure 2) and the least expertise to adjust the settings, this technique could be proposed with the same limits as those for NIV listed below but as a first line, before NIV.

It should be noted that these patients have very high inspiratory airflow needs and may depressurize a machine whose turbine is not powerful enough.

CPAP devices with a high O₂ flow rate (e.g., CPAP Boussignac) may also be used but caution should be taken because the flow rates necessary to achieve a pressure of 10 cm of H₂O are of about 30 L/min, and are thus rarely available in pneumology or medicine rooms because wall flowmeters for flow rates greater than 30 L/min are needed. These high flow rates are also associated with a high risk of viral aerosol dispersion. All the devices that can be used to deliver CPAP are summarized in Figure 2.

4) Humidified high-flow nasal oxygen therapy (HFNOT)

In case of severe hypoxemic COVID-19 pneumonia when conventional O₂ is ineffective, humidified HFNOT may be considered, but the risk of aerosol dispersion of viral particles and the technical limits of some devices needed in case of high FiO₂ should be taken into account.

No published study has assessed this technique in patients with COVID-19 infection. Only indirect evidence from studies in patients with ARF from other causes can be used.

HFNOT consists in using a high-flow gas mixture (up to 70 L/min) with variable proportions (FiO₂) of air and oxygen administered through a nasal cannula. Compared to conventional oxygen therapy, its advantages are the delivery of a constant and known FiO₂, a reduced dead space with a reduced work of breathing and the generation of a low positive pressure, which can lead to some degree of alveolar recruitment (28).

In a controlled randomized study of hypoxemic ARF, HFNOT has been compared to conventional oxygen therapy. It reduced the 90-day mortality but not the risk of intubation (19). But finally, a meta-analysis of 9 controlled randomized trials has shown a decreased number of intubations without improving the survival or length of hospital stay (29–31). Even if there is no difference in survival, the decrease in the number of intubations is an important result in the context of the COVID-19 pandemic where resources are insufficient.

On the other hand, some studies of SARS (mainly retrospective studies) have shown a significant increase in disease transmission to caregivers at the time of intubation in patients treated with HFNOT (OR: 6.6, 95% CI: 2.3-18,9) (13,14,32). However, outside this critical period of intubation, the caregivers in contact with SARS patients treated with HFNOT were not exposed to an increased risk of contamination. In technical studies assessing environmental bacterial dispersion, HFNOT did not exposed to an increased risk compared to conventional O₂ (33) and, caregivers in contact with SARS patients were not exposed to an increased risk of contamination (32). To limit the risk of contamination, it has been proposed to place a surgical mask on the face of HFNOT-treated patients but no study has supported this proposal to date.

Thus, its use should be limited to the established indications of hypoxemic ARF and is subjected to different procedures (19,31)

When it is used:

- Ensure maximum sealing of the interface.
- Limit the flow rate to the minimum necessary. Even at the risk of not being able to provide the set FiO₂ (in patients with a peak flow rate exceeding the set flow rate) (34), a FiO₂ should be preferred to a high flow rate in order to reduce the risk of aerosol contamination of caregivers (start at 30 L/min).

- Put a surgical mask on the patient with the O₂ cannula under the mask (NB: in this situation, the expiratory aerosol dispersion of particles is lateral) when another person is present in the room.
- For any care delivered within 1 meter of the patient, caregivers should wear strict protective clothing.

WARNING: Care should be taken to the fact that devices other than those dedicated to resuscitation may be too limited in FiO₂ and may be insufficient. The use of home devices may be considered but does not allow achieving significant FiO₂. The different tools available are summarized in Figure 3.

It is recommended to start with a setting of 30 L/min to achieve a target FiO₂ of at least 50%. If the flow rate exceeds 50 L/min or the FiO₂ exceeds 70%, the anaesthetist should be informed and assess the patient.

5) **Nebulized treatments.** Some key safety points for the staff are outlined here.

- Nebulized treatments should be limited as much as possible.
- Evaluate the possibility of administering beta-2-mimetics in another way (spray, powder). If there is no alternative, avoid staying within 1 m of the patient during nebulization and ventilate the room during aerosol inhalation.
- In tracheotomized patients, do not direct the circuit towards the staff during disconnections

6) **Insufflator/Exsufflator**

The insufflator/exsufflator should be limited to the established indications of assist cough, in particular in patients with neuromuscular disorders by protecting as much as possible caregivers.

No study has assessed the use of this device in the context of the COVID-19 epidemic. The patients are barely congested and the use of this device will be especially useful in case of pre-existing use.

This assisted cough technique consists in insufflating and exsufflating the patient's chest by applying positive inhalation and then negative exhalation pressures. Its use should be limited to the established indications.

It may be useful in patients with ineffective cough to improve the cleaning of proximal tracheobronchial secretions.

It is recommended to place an antibacterial filter at the inspiratory outlet of the device and to proceed to the usual assembly.

When this technique is indicated (see the GAVO₂ procedure <http://splf.fr/gavo2/>)

- In the presence of intentional leaks in the circuit, carry out the same assembly as with non-intentional leaks (see figure 3 of the GAVO₂ procedure).
- Try to maintain as much as possible the sealing of the mask on the face.
- Ask the patient, if possible, to do the session alone, by avoiding staying within 1 m of the patient during the sessions.
- If the patient needs help, wear strict protective clothing (gloves, FFP2 mask, goggle, overcoat).

7) **Tracheal suction**

In tracheotomized patients who cannot be disconnected from the ventilator, it is recommended, as long as patients are contagious, to systematically use a closed tracheal suction system that may be left in place for 7 days.

- Respiratory management strategy

Inpatient management outside of ICUs

The strategy to be used is based on that proposed by Scala for the management of ARF (35) (figure 1).

The first step is the triage of patients to avoid admitting a patient whose condition is too serious in an unsuitable department. A proposal for the triage of patients is shown in Appendix 1, to be adapted to local conditions. If a flowchart has already been considered locally, the local organization should obviously be preferred.

It is recommended to have an end-of-life sedation protocol available for patients if their condition worsens and an invasive approach is not possible. (Cf recommendations of palliative care societies: <http://www.sfap.org/actualite/outils-et-ressources-soins-palliatifs-et-covid-19>)

Procedure for treatment use:

- Check and treat comorbidities.
- Start with conventional oxygen therapy to achieve the target RR and SpO₂. It is suggested to start with a nasal cannula. In case of predominant oral breathing and/or failure of the nasal cannula and/or intolerance to high-flow nasal cannula, the use of the mask may be proposed. There is no limit to the use of the O₂ flow rate but beyond 6 L/min or when a high-concentration oxygen mask is used, the anaesthetist should be informed. Note that filtered oxygen masks are available (see the GAVO2 procedure <http://splf.fr/gavo2/>). Venturi masks are not recommended.
- Then, propose non-invasive ventilatory support (CPAP and HFNOT first and NIV as a last resort) if oxygen therapy is not sufficient. The criteria for proposing ventilatory support are detailed in Figure 1.

From this stage, the anaesthetist should be informed and if possible present, because a delayed intubation may increase the risk for the patient.

- An alternative before NIV is the administration of high-flow nasal oxygen. It should be noted that only devices accessible in ICUs (Optiflow[®], Vapotherm[®], some resuscitation ventilators with a high-flow mode) allow achieving high FiO₂ (Figure 3).
- Finally, intubation and invasive ventilation with the need for prone positioning techniques should be proposed in case of failure of the non-invasive approach. Chinese teams have reported clinical cases of prone positioning with non-invasive support but without any publication or validation during NIV. While waiting for the anaesthetist's intervention, this interim solution may be considered.

Monitoring

Close monitoring is recommended at least during the first 48-72 hours. It is recommended to monitor at least the SpO₂ and RR and the clinical parameters (dyspnea and ventilatory mechanics/use of accessory muscles) every 2-4 hours depending on the evolution. WARNING 1: Patients initially stable may suddenly become unstable (with refractory hypoxemia and high fever). WARNING 2: A late peak of new worsening has been noted in a significant percentage of patients (stability then rapid worsening after 48h, up to 7 days). WARNING 3: A neurological involvement is possible and may cause patients to not express correctly their respiratory failure (36).

Feeding of patients undergoing NIV

Some patients may require NIV/CPAP for 24 hours a day for several days. It is advised to propose enteral nutrition given via a nasogastric tube or parenteral feeding, either after 24 hours if the patient still undergoes NIV, or immediately if the device cannot be discontinued.

Patient discharge from the pneumology/acute medicine department.

Following the acute episode and after clinical improvement, the patient may be discharged from the pneumology or acute medicine department. The place of discharge will mainly depend on the respiratory devices and patient's sequelae.

- Discharge to home or to a non-pulmonary rehabilitation facility/nursing home for a short stay
 - In case of NIV/CPAP withdrawal (or for patients requiring long-term NIV/CPAP, clinical stability and pH normalization).
 - O₂ needs <2 L/min
- Discharge to a pulmonary rehabilitation facility/nursing home
 - In case of O₂ flow rate greater than 2 L/min
 - In case of tracheostomy with or without ventilation,
 - for patients requiring long-term NIV/CPAP, clinical stability and pH normalization.
- Discharge to a non-pulmonary rehabilitation facility/nursing home for a long stay
 - In case of ICU-acquired neuromyopathy and in the absence of respiratory device (to a pulmonary rehabilitation facility/nursing home in case of associated respiratory device except if O₂ <2 L/min)

The contagious period ranging from 8 to 15 days (9), it will ideally be necessary to check the negativity of samples before the patient is transferred. Otherwise, it is suggested to maintain the patient's isolation instructions and the prevention instructions for the breathing equipment.

Figure 1: Flowchart for the management of acute respiratory failure due to COVID-19 infection

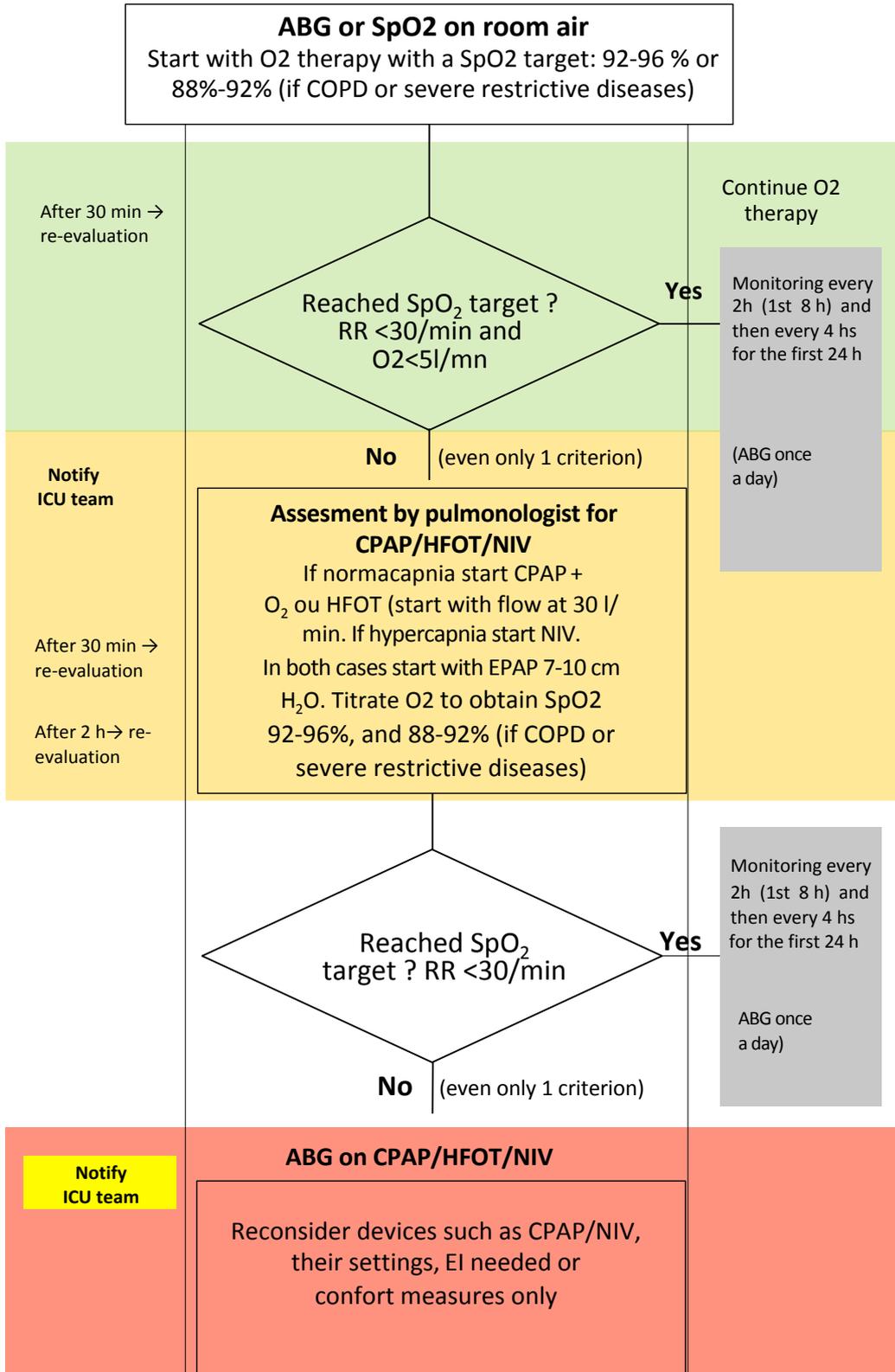


Figure 2: different devices to treat a patient with non-invasive positive end-expiratory pressure

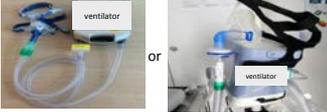
<p>ICU ventilator</p> 	<p>Life support ventilator, (single ou double limb circuit/expiratory valve)</p> 	<p>Bilevel ventilator (single limb circuit with intentional leak)</p> 	<p>Boussignac CPAP</p> 
<p>Avantages</p> <ul style="list-style-type: none"> - Possibility to ensure FiO_2 100% - Monitoring capabilities - Less viral spreading - Deliver EPAP even at low O_2 flow - Adjustable EPAP level - Powerful blower able to maintain EPAP level even with important leaks or high inspiratory effort 	<p>Avantages</p> <ul style="list-style-type: none"> - Less viral spreading - Deliver EPAP even at low O_2 flow - Adjustable EPAP level - Powerful blower able to maintain EPAP level even with important leaks or high inspiratory effort - Internal battery (transport possible) 	<p>Avantages</p> <ul style="list-style-type: none"> - Easier to use and easily available - Deliver EPAP even at low O_2 flow - Adjustable EPAP level - Powerful blower able to maintain EPAP level even with important leaks or high inspiratory effort 	<p>Avantages</p> <ul style="list-style-type: none"> - Easier to use - Doesn't need outlet power supply - Doesn't need settings - Disposable material
<p>Incoovenients</p> <ul style="list-style-type: none"> - Limited availability (only in ICU) - Burdensome for a non-trained physician - No internal battery, needs outlet power supply. Non-transportable 	<p>Incoovenients</p> <ul style="list-style-type: none"> - Limited availability - Burdensome for a non- trained physician 	<p>Incoovenients</p> <ul style="list-style-type: none"> - Should not be used with a vented mask with incorporated leak (viral spread) (see figure 2) - Need complex assembly 	<p>Incoovenients</p> <ul style="list-style-type: none"> - High risk spreading of viral particles (high flow) - Needs a flow of at least 30l/mn to provide a CPAP level of 10 cm H_2O - No available for transport - CPAP level not adjustable without manometer

Figure 3: different devices to treat a patient with humidified high-flow nasal oxygen therapy

In-hospital HFOT systems (Optiflow™, Vapotherm™)	Portable HFOT systems (Airvo™, My Airvo™)	ICU ventilators providing HFOT (Hamilton G5™, Monnal T60/75™, Servo U™, Evita Infinity V500™)	Home ventilators providing HFOT (Eove 150, Prisma 50)
			
<p>Avantages</p> <ul style="list-style-type: none"> - Possibility to ensure FiO₂ 100% at a flow higher than 60L/min - Easy to use and to set - Bubble heater- humidification system with dedicated circuit 	<p>Avantages</p> <ul style="list-style-type: none"> - Don't need neither wall air/ oxygen nor a blender - Display delivered FiO₂ - 3 level-preset temperature - Bubble heater- humidification system with dedicated circuit 	<p>Avantages</p> <ul style="list-style-type: none"> - Possibility to ensure FiO₂ 100% at a flow higher than 60L/min - Allow to switch to NIV or CPAP modes. Possibility of multiple programs - Bubble heater- humidification system with dedicated circuit 	<p>Avantages</p> <ul style="list-style-type: none"> - Don't need neither wall air/ oxygen nor a blender - Provide internal battery - Allow to switch to NIV or CPAP modes. Possibility of multiple programs
<p>Inconvenients</p> <ul style="list-style-type: none"> - Limited availability (mainly in ICU) - Need wall air/oxygen and a blender 	<p>Inconvenients</p> <ul style="list-style-type: none"> - Does not allow to ensure FiO₂ 100% (except if a 60L/min manometer is available) - No internal battery, needs outlet power supply. Non-transportable 	<p>Inconvenients</p> <ul style="list-style-type: none"> - Limited availability (only in ICU) - Burdensome for a non-trained physician - Need wall air/oxygen and a blender - No internal battery, needs outlet power supply. Non-transportable 	<p>Inconvenients</p> <ul style="list-style-type: none"> - Oxygen can be added up to a maximum flow of 20l/m (Eove 150) or 30 l/m (Prisma 50) - Maximal FiO₂ allowed: < 50% at 60l/min - Heater- humidification system without battery

References:

1. Managing the Respiratory care of patients with COVID-19 - English version [Internet]. AIPOnet News. [cited 2020 Apr 1]. Available from: <http://www.aiponet.it/news/speciale-covid-19/2426-managing-the-respiratory-care-of-patients-with-covid-19-english-version.html>
2. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA*. 2020 Feb 24;
3. Wang Y, Dong C, Hu Y, Li C, Ren Q, Zhang X, et al. Temporal Changes of CT Findings in 90 Patients with COVID-19 Pneumonia: A Longitudinal Study. *Radiology*. 2020 Mar 19;200843.
4. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. *Travel Med Infect Dis*. 2020 Mar 13;101623.
5. Guan W-J, Ni Z-Y, Hu Y, Liang W-H, Ou C-Q, He J-X, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020 Feb 28;
6. Shi Y, Yu X, Zhao H, Wang H, Zhao R, Sheng J. Host susceptibility to severe COVID-19 and establishment of a host risk score: findings of 487 cases outside Wuhan. *Crit Care*. 2020 18;24(1):108.
7. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020 Feb 24;
8. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. 2020 Feb 7;
9. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020 15;395(10223):507–13.
10. Chu DK, Kim LH-Y, Young PJ, Zamiri N, Almenawer SA, Jaeschke R, et al. Mortality and morbidity in acutely ill adults treated with liberal versus conservative oxygen therapy (IOTA): a systematic review and meta-analysis. *Lancet*. 2018 28;391(10131):1693–705.
11. Barrot L, Asfar P, Mauny F, Winiszewski H, Montini F, Badie J, et al. Liberal or Conservative Oxygen Therapy for Acute Respiratory Distress Syndrome. *N Engl J Med*. 2020 12;382(11):999–1008.
12. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). *Intensive Care Med*. 2020 Mar 28;
13. Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. *PLoS ONE*. 2012;7(4):e35797.
14. Fowler RA, Guest CB, Lapinsky SE, Sibbald WJ, Louie M, Tang P, et al. Transmission of severe acute respiratory syndrome during intubation and mechanical ventilation. *Am J Respir Crit Care Med*. 2004 Jun 1;169(11):1198–202.
15. Hui DSC, Zumla A. Severe Acute Respiratory Syndrome: Historical, Epidemiologic, and Clinical Features. *Infect Dis Clin North Am*. 2019;33(4):869–89.
16. Zayed Y, Banifadel M, Barbarawi M, Kheiri B, Chahine A, Rashdan L, et al. Noninvasive Oxygenation Strategies in Immunocompromised Patients With Acute Hypoxemic Respiratory Failure: A Pairwise and Network Meta-Analysis of Randomized Controlled Trials. *J Intensive Care Med*. 2019 May 2;885066619844713.

17. Xu X-P, Zhang X-C, Hu S-L, Xu J-Y, Xie J-F, Liu S-Q, et al. Noninvasive Ventilation in Acute Hypoxemic Nonhypercapnic Respiratory Failure: A Systematic Review and Meta-Analysis. *Crit Care Med*. 2017 Jul;45(7):e727–33.
18. Wang T, Zhang L, Luo K, He J, Ma Y, Li Z, et al. Noninvasive versus invasive mechanical ventilation for immunocompromised patients with acute respiratory failure: a systematic review and meta-analysis. *BMC Pulm Med*. 2016 27;16(1):129.
19. Frat J-P, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med*. 2015 Jun 4;372(23):2185–96.
20. Alraddadi BM, Qushmaq I, Al-Hameed FM, Mandourah Y, Almekhlafi GA, Jose J, et al. Noninvasive ventilation in critically ill patients with the Middle East respiratory syndrome. *Influenza Other Respir Viruses*. 2019;13(4):382–90.
21. Brochard L, Lefebvre J-C, Cordioli RL, Akoumianaki E, Richard J-CM. Noninvasive ventilation for patients with hypoxemic acute respiratory failure. *Semin Respir Crit Care Med*. 2014 Aug;35(4):492–500.
22. Slutsky AS, Ranieri VM. Ventilator-induced lung injury. *N Engl J Med*. 2013 Nov 28;369(22):2126–36.
23. Azoulay E, Kouatchet A, Jaber S, Lambert J, Meziani F, Schmidt M, et al. Noninvasive mechanical ventilation in patients having declined tracheal intubation. *Intensive Care Med*. 2013 Feb;39(2):292–301.
24. Ding L, Wang L, Ma W, He H. Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study. *Crit Care*. 2020 30;24(1):28.
25. Patel BK, Wolfe KS, Pohlman AS, Hall JB, Kress JP. Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial. *JAMA*. 2016 Jun 14;315(22):2435–41.
26. Hui DS, Chow BK, Lo T, Ng SS, Ko FW, Gin T, et al. Exhaled air dispersion during noninvasive ventilation via helmets and a total facemask. *Chest*. 2015 May;147(5):1336–43.
27. Tripodoro VA, Rabec CA, De Vito EL. Withdrawing noninvasive ventilation at end-of-life care: is there a right time? *Curr Opin Support Palliat Care*. 2019;13(4):344–50.
28. Drake MG. High-Flow Nasal Cannula Oxygen in Adults: An Evidence-based Assessment. *Ann Am Thorac Soc*. 2018;15(2):145–55.
29. Ni Y-N, Luo J, Yu H, Liu D, Liang B-M, Liang Z-A. The effect of high-flow nasal cannula in reducing the mortality and the rate of endotracheal intubation when used before mechanical ventilation compared with conventional oxygen therapy and noninvasive positive pressure ventilation. A systematic review and meta-analysis. *Am J Emerg Med*. 2018 Feb;36(2):226–33.
30. Ou X, Hua Y, Liu J, Gong C, Zhao W. Effect of high-flow nasal cannula oxygen therapy in adults with acute hypoxemic respiratory failure: a meta-analysis of randomized controlled trials. *CMAJ*. 2017 Feb 21;189(7):E260–7.
31. Rochweg B, Granton D, Wang DX, Helviz Y, Einav S, Frat JP, et al. High flow nasal cannula compared with conventional oxygen therapy for acute hypoxemic respiratory failure: a systematic review and meta-analysis. *Intensive Care Med*. 2019;45(5):563–72.
32. Raboud J, Shigayeva A, McGeer A, Bontovics E, Chapman M, Gravel D, et al. Risk factors for SARS transmission from patients requiring intubation: a multicentre investigation in Toronto, Canada. *PLoS ONE*. 2010 May 19;5(5):e10717.
33. Leung CCH, Joynt GM, Gomersall CD, Wong WT, Lee A, Ling L, et al. Comparison of high-flow nasal cannula versus oxygen face mask for environmental bacterial contamination in critically ill pneumonia patients: a randomized controlled crossover trial. *J Hosp Infect*. 2019 Jan;101(1):84–7.

34. Chikata Y, Oto J, Onodera M, Nishimura M. Humidification performance of humidifying devices for tracheostomized patients with spontaneous breathing: a bench study. *Respir Care*. 2013 Sep;58(9):1442–8.
35. Scala R, Pisani L. Noninvasive ventilation in acute respiratory failure: which recipe for success? *Eur Respir Rev*. 2018 Sep 30;27(149).
36. Li Y-C, Bai W-Z, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. *J Med Virol*. 2020 Feb 27;

APPENDIX 1

Proposal for the triage of patients with locally adaptable thresholds.

- *First contact: (emergency room or pneumology department airlock)*
 - o Triage of the patient according to the risk and area of origin in order to collect epidemiological and clinical information on the area of origin of the patient (red area or cluster area and/or exposure to a person known to be positive for SARS-CoV-2, and/or presence of persistent cough for more than 48-72 hours and dyspnea, SaO₂ <93% on room air)
 - o Collect a nasal swab or oropharyngeal swabs for PCR analysis, and perform chest CT scan (CT scan dedicated to COVID if possible) depending on its availability, the symptoms and the local patient care algorithm.
- Triage of patients into 4 categories according to the initial evaluation and evolution in the first hours as follows:
 - a) low risk (SaO₂ >94%, RR <20 breaths/min);
 - b) moderate risk (SaO₂ <94%, RR >20 breaths/min but response to oxygen at 10-15 L/min);
 - c) moderate-to-severe risk (SaO₂ <94%, RR >20 breaths/min but poor response to oxygen at 10-15 L/min and need for non-invasive ventilatory support with high FiO₂);
 - d) high risk (SaO₂ <94%, RR >24 breaths/min but poor response to oxygen at 10-15 L/min and to ventilatory support with high FiO₂ or with respiratory distress with PaO₂/FiO₂ <200
- *Transfer after triage*
 - o Transfer suspected or confirmed cases to dedicated COVID areas. Since a practical test performed too early can be a false negative, for patients with a strong suspicion, it is recommended to repeat the test on day 3 before considering it as COVID negative and to terminate isolation. In all cases, core samples (sputum) should be preferred in secreting patients due to a much higher sensitivity.
 - Patients classified into a) and b) can be monitored in the general pulmonology or medicine room with close monitoring of their evolution. Evaluation by the ICU before the onset of warning signs (see above)
 - Patients classified into c) should undergo a rapid assessment in the ICU.
 - Patients classified into d) should be transferred immediately to the ICU



GAVO₂

**Groupe assistance
ventilatoire et oxygène**

GAVO₂ PROCEDURES

TITLE: Home respiratory equipment of a patient with suspected or confirmed viral respiratory infection

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Ventilation or CPAP devices

The use of acute NIV should be limited to the established indications (respiratory acidosis, acute pulmonary edema and pre-oxygenation) and is subjected to other procedures.

In any long-term patient undergoing NIV or CPAP at home, the device, if it cannot be discontinued, should be adapted during hospitalization.

The use of ventilation or CPAP should be accompanied by the following precautions:

- Ensure the best sealing of the mask, for example by proposing a bucconasal mask, possibly by temporarily lowering the pressures if excessive leaks are present.
- Use an anti-infective filter at the ventilator outlet on the inspiratory circuit. CAUTION IN CASE OF LACK OF MATERIAL, THIS FILTER MAY BE REMOVED, ESPECIALLY IF THE VENTILATORS ARE ONLY USED TO TREAT COVID+ PATIENTS. (Figure 5)
- Use an anti-infective filter after the mask but with different positions depending on the exhalation site:
 - If the expiratory valve is offset, place an anti-infective filter at the expiratory valve outlet (figure 1);
 - If the expiratory valve is located in the ventilator, place an anti-infective filter just before the expiratory circuit input in the ventilator (Figure 2);
 - If it is a vented mask, switch to the same non-vented mask, add intentional leaks after an anti-infective filter (Figure 3 et 3 bis). If no similar non-vented model is available:
 - Propose an equivalent non-vented mask and add intentional leaks after an anti-infective filter (Figure 3 et 3 bis).
 - As a last resort: seal leaks from the patient's mask (adhesive tape, patafix™, glue, silicone, etc.) and add intentional leaks after an anti-infective filter (Figure 3 and 3 bis). Be careful not to block the anti-asphyxiation valve (Figure 4).
- The efficiency and tolerance of ventilation and the ventilator measurements should be verified when these filters are used.
- If the ventilator circuit can be calibrated, repeat it with this new assembly.
- Connect as follows: put on the mask, connect the circuit, start ventilation.
- Disconnect as follows: shutdown the ventilator and then remove the mask
- The use of filters contraindicates the use of heated humidifiers (risk of water saturation of the filters making them ineffective and increasing resistances). If humidification is needed, mixed antibacterial and heat and moisture exchanger (HME) (green filters) filters should thus be used. Note that to obtain a moistening effect, the HME filter must be placed both on the inspiratory and expiratory circuit (Figure 3 bis) which requires increased vigilance (see below).
- The antibacterial filters positioned on the inspiratory and expiratory branches of the ventilator are changed **once every 24 hours**. ATTENTION:, IN CASE OF FILTER SHORTAGE, IT HAS BEEN SHOWN THAT THE FILTERS CAN BE KEPT EFFICIENTLY FOR 48 HOURS AND SOME TEAMS KEEP THEM FOR 7 DAYS EXCEPT IN CASE OF VISUAL DETERIORATION
- HME filters also filter 99% of viruses but will have the disadvantage of soaking up moisture when the patient exhales and may need to be changed several times a day
- Discard all consumables after use and, if possible, ask the provider to disinfect the ventilator between two patients.

Nebulized treatments

Nebulized treatments should be limited as much as possible. Evaluate the possibility of administering beta-2-mimetics in another way (spray, powder). If there is no alternative, avoid staying within 1 m of the patient during

nebulization and ventilate the room during aerosol inhalation. In tracheotomized patients, do not direct the circuit towards the staff during disconnections.

Tracheal suction

Systematic use of a closed tracheal suction system, that may be left in place for 7 days.

Insufflator/Exsufflator

- Place an antibacterial filter at the inspiratory outlet of the device and proceed to the usual assembly.
- In the presence of intentional leaks in the circuit, carry out the same assembly as with non-intentional leaks (Figure 3).
- Try to maintain as much as possible the sealing of the mask on the face.
- Try to ask the patient to do the session alone, by avoiding staying within 1 m of the patient during the sessions.
- If the patient needs help, wear strict protective clothing (gloves, FFP2 mask, goggle, overcoat).

Humidified high-flow nasal oxygen therapy (HFNOT)

The use of acute HFNOT should be limited to the established indications and is subjected to different procedures. In any long-term patient treated with humidified HFNOT, in a patient who can be managed without it, it is recommended to discontinue its use.

When discontinuation is not possible:

- Ensure maximum sealing of the interface.
- Decrease the flow rate to the minimum necessary.
- Put a surgical mask on the patient with the O₂ cannula under the mask (NB: in this situation, the expiratory aerosol dispersion of particles is lateral) when a caregiver is present in the room.
- For any care delivered within 1 meter of the patient, caregivers should wear strict protective clothing.

Nasal oxygen (O₂)

The use of O₂ should be limited to the established indications in any long-term patient receiving O₂, if the patient can be managed without it, it is recommended to discontinue its use.

When discontinuation is not possible:

- Use oxygen masks and filtered exhalation if available (Figure 6).
- If there is no specific mask available, put the O₂ cannula under a surgical mask (NB: in this situation, the expiratory aerosol dispersion of particles is lateral) when a caregiver is present in the room.
- Decrease the flow rate to the minimum necessary (<6 L/min).
- For any care delivered within 1 meter of the patient, caregivers should wear strict protective clothing.

Material management

- For any intervention on the patient, it is recommended to discontinue oxygen therapy, NIV and aerosols before removing the O2 cannula or the mask if necessary in order to avoid the exposure of caregiver to aerosol dispersion.
- Properly clean and disinfect the outside of the ventilator through a surface cleaning according to your department protocol.
- All material from a positive patient should be disposed of immediately after use by the DASRI. However, in the context of a potentially significant demand for material and the risk of rapid stock shortage, masks and circuits may be decontaminated and reused for other COVID+ patients.
- Complete decontamination must be performed when the ventilator must be used thereafter for a non-COVID+ patient through spraying of disinfectant product with dedicated devices, generally found at the providers.
- The electrostatic antibacterial/antiviral filters should theoretically be changed every day but, in case of shortage, they can be kept for up to 7 days if their macroscopic appearance is correct. Please note, HME filters get wet faster and must be changed more regularly, sometimes several times a day, especially if the patient breathes in and out through them.

Figure 1: Offset exhalation valve



Figure 2: Internal exhalation valve

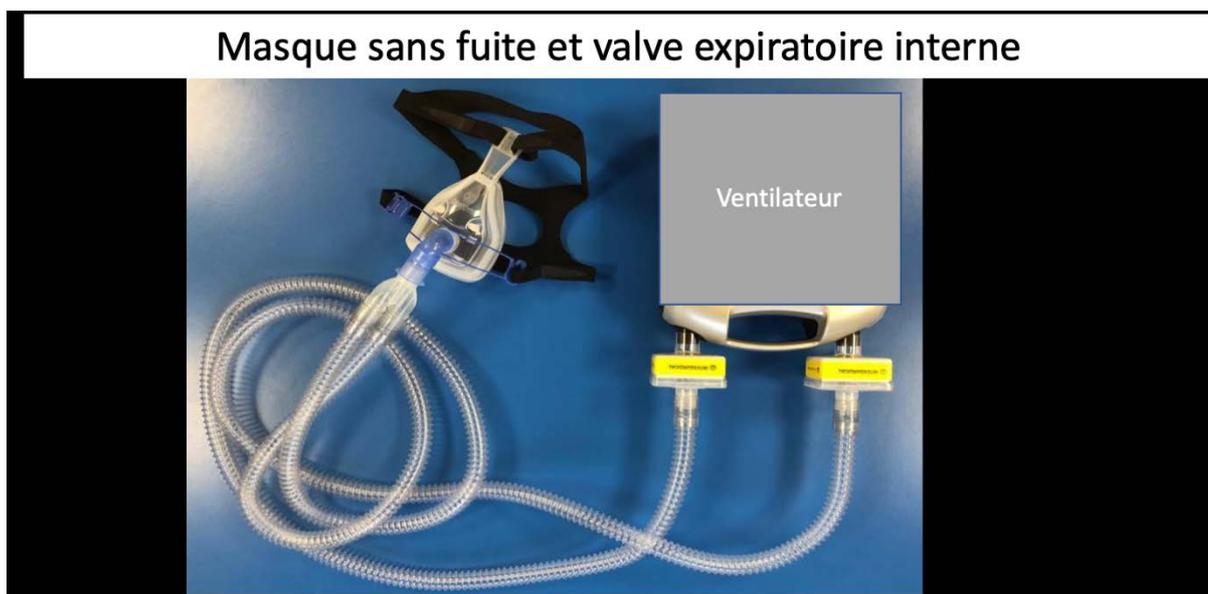


Figure 3: Assemblies to obtain a filter with offset intentional leaks

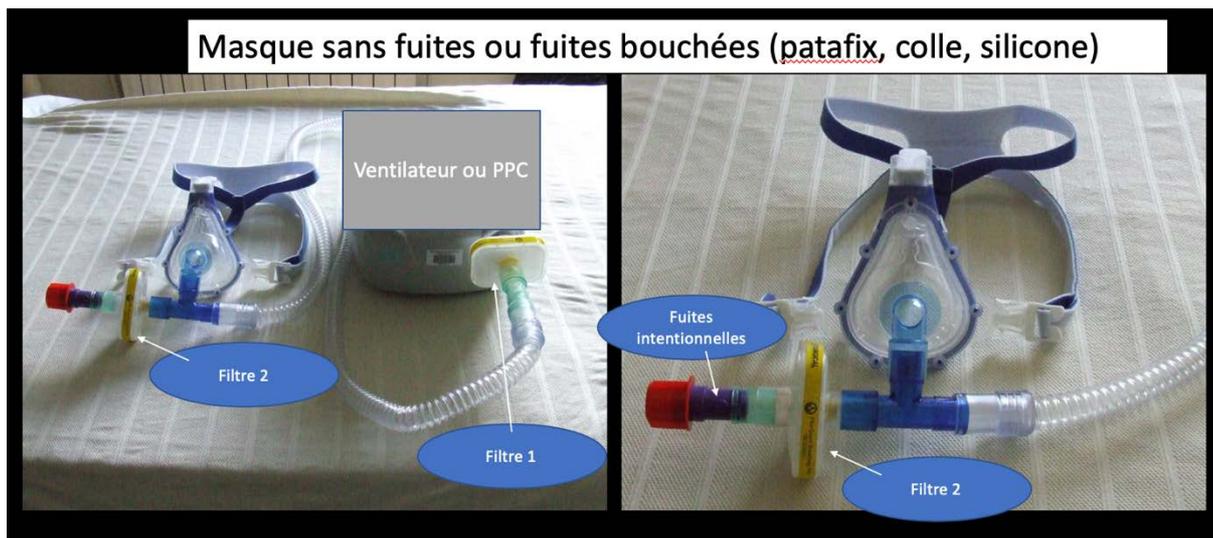


Figure 3 bis: Assembly without offsetting intentional leaks

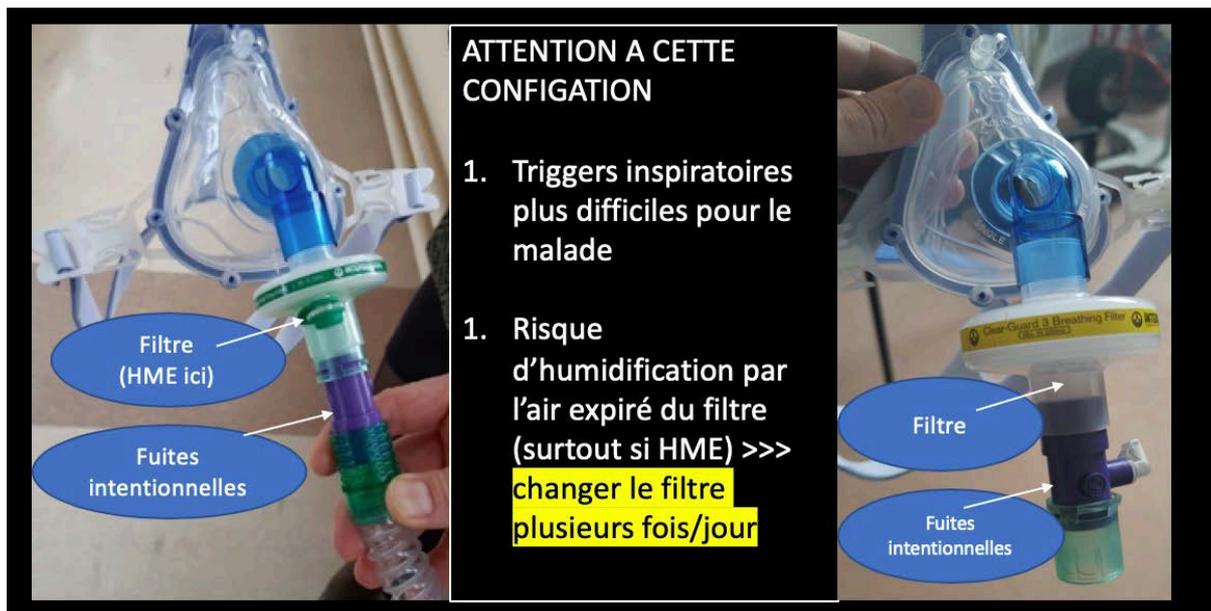


Figure 4: example of sealing of leaks without blocking the anti-axphyxiation valve ports



Figure 5: Alternative assembly if antibacterial/antiviral filters are lacking: only 1 filter on the expiratory circuit

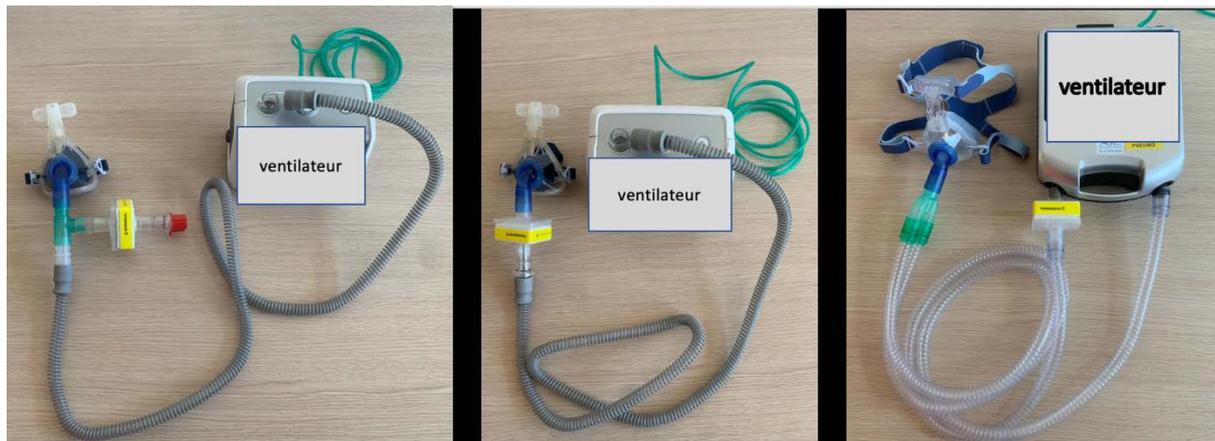


Figure 6: O₂ mask with filtered expiration (Fitamask™ from Intersurgical)



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Useful references:

1: Hui DS, Chow BK, Lo T, Ng SS, Ko FW, Gin T, Chan MTV. Exhaled air dispersion during noninvasive ventilation via helmets and a total facemask. *Chest*. 2015 May;147(5):1336-1343. doi: 10.1378/chest.14-1934. PubMed PMID: 25392954.

2: Hui DS, Chow BK, Chu L, Ng SS, Lee N, Gin T, Chan MT. Exhaled air dispersion during coughing with and without wearing a surgical or N95 mask. *PLoS One*. 2012;7(12):e50845. doi: 10.1371/journal.pone.0050845. Epub 2012 Dec 5. PubMed PMID: 23239991; PubMed Central PMCID: PMC3516468.

3: Hui DS, Chow BK, Chu L, Ng SS, Lai ST, Gin T, Chan MT. Exhaled air dispersion and removal is influenced by isolation room size and ventilation settings during oxygen delivery via nasal cannula. *Respirology*. 2011 Aug;16(6):1005-13. doi: 10.1111/j.1440-1843.2011.01995.x. PubMed PMID: 21605275.

4: Hui DS, Chow BK, Ng SS, Chu LCY, Hall SD, Gin T, Sung JJY, Chan MTV. Exhaled air dispersion distances during noninvasive ventilation via different Respironics face masks. *Chest*. 2009 Oct;136(4):998-1005. doi: 10.1378/chest.09-0434. Epub 2009 May 1. PubMed PMID: 19411297.

5: Hui DS, Chow BK, Chu LCY, Ng SS, Hall SD, Gin T, Chan MTV. Exhaled air and aerosolized droplet dispersion during application of a jet nebulizer. *Chest*. 2009 Mar;135(3):648-654. doi: 10.1378/chest.08-1998. PubMed PMID: 19265085.

6: Hui DS, Chan MT, Chow B. Aerosol dispersion during various respiratory therapies: a risk assessment model of nosocomial infection to health care workers. *Hong Kong Med J*. 2014 Aug;20 Suppl 4:9-13. PubMed PMID: 25224111.

7: Hui DS, Chow BK, Lo T, Tsang OTY, Ko FW, Ng SS, Gin T, Chan MTV. Exhaled air dispersion during high-flow nasal cannula therapy versus CPAP via different masks. *Eur Respir J*. 2019 Apr 11;53(4). pii: 1802339. doi: 10.1183/13993003.02339-2018. Print 2019 Apr. PubMed PMID: 30705129.

8. Simonds AK, Hanak A, Chatwin M, Morrell M, Hall A, Parker KH, et al. Evaluation of droplet dispersion during non-invasive ventilation, oxygen therapy, nebuliser treatment and chest physiotherapy in clinical practice: implications for management of pandemic influenza and other airborne infections. *Health technology assessment (Winchester, England)*. 2010;14(46):131-72.