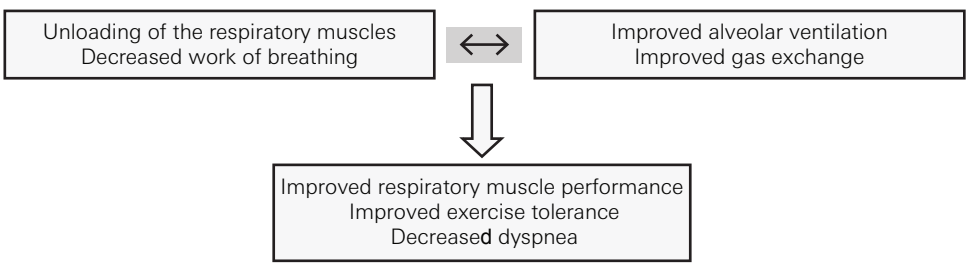
4.10 Oxygen therapy and non-invasive ventilation (NIV)

Authors: Maura Prella, Angela Koutsokera, Sarosh Irani, Cédric **Dumans**

1. INTRODUCTION

- Despite the continuous improvement of CF care, respiratory care remains the main cause of morbidity and mortality.
- Oxygen therapy is the standard of care for CF patients with hypoxemia. To timely identify patients who may need short-term or long-term oxygen therapy (LTOT):
  - $SatO_2$ should be evaluated at every visit.
  - $SatO_2$ should be evaluated during standardized exercise (e.g. 6 min walk test) routinely.
  - Nocturnal capnography and/or oximetry are recommended in symptomatic patients (e.g. abnormal saturation at rest, decreased sleep quality, frequent awakenings or morning headaches). During exacerbations, oximetry may help adapt short-term oxygen therapy **(see also Chapter "*Clinical Evaluation*")**.
- Non-invasive ventilation (NIV) in CF is most commonly used during acute respiratory failure, chronic hypercapnic respiratory failure or exercise. The use of NIV in this context has increased exponentially over the past 2 decades.
  - The main physiological effects of NIV are depicted in **Figure 1**.
  - In addition, NIV is associated with less traumatic and infectious complications compared to invasive ventilation. NIV allows the patient to eat, move and communicate. This improves patient comfort and prevents the use of sedation.

Figure 1: Main physiological effects of NIV



2. OXYGEN THERAPY

2.1 Indications for oxygen therapy in CF

- **So far, there are no standard criteria to guide prescription of oxygen in CF** but classic recommendations used for chronic obstructive pulmonary disease provide guidance. Therefore, oxygen therapy in CF should be considered in the following situations :
  - $PaO_2 < 7.3$ kPa (55 mmHg) or $SatO_2 \leq 88\%$ at rest
  - $PaO_2 < 7.9$ kPa (59 mmHg) or $SatO_2 \leq 89\%$ at rest with evidence of cor pulmonale

- PaO_2 < 7.3kPa (55 mmHg) or $SatO_2$ ≤ 88% during exercise if oxygen therapy improves exercise capacity
- Desaturation during sleep (<88%) with signs or symptoms of nocturnal hypoxemia (e.g. impaired cognitive function, morning headaches, restlessness, or insomnia)

- In CF, oxygen therapy is usually prescribed in the following situations:
  - **During respiratory exacerbations** associated with hypoxemia to allow a $SatO_2$ between 90 and 92% (for hypercapnic patients a lower $SatO_2$ target of 89-90% may be considered if not treated with NIV).
  - **During chronic respiratory failure:** LTOT is the standard of care for hypoxemic CF patients to allow a $SatO_2$ between 90 and 92% (for hypercapnic patients NIV should also be considered).
  - **During physiotherapy or exercise:** patients with normal $SatO_2$ at rest but desaturation during exercise are eligible for ambulatory oxygen therapy if exercise capacity is improved with oxygen. Oxygen should be titrated to limit exercise desaturation (target $SatO_2$ > 90%).
  - **For nocturnal desaturation:**
    - For patients who desaturate during sleep, evaluation with a sleep study (to assess for sleep-disordered breathing) should be considered.
    - Nocturnal hypoventilation typically precedes daytime hypoventilation. It is considered to be due to a significant fall in tidal volume which is more pronounced during REM sleep. **Table 1** presents potential causes of hypoventilation in CF.
    - No standard criteria are currently available to define the cut-off level of nocturnal hypoxemia which is clinically significant and merits nocturnal oxygen initiation. In general terms,
      - a $SatO_2$ < 90% for ≥ 10% of the total sleep or
      - a $SatO_2$ drop of ≥ 4% below baseline for ≥ 5 min are considered significant.
    - In case of nocturnal hypoventilation, **concomitant hypercapnia** must be assessed and treated if necessary (see below).
  - **At altitude/air travelling:** CF patients may become hypoxemic at altitude but are usually asymptomatic. Resting sea-level $SatO_2$ is not reliable to predict hypoxemia at altitude. For patients whose eligibility to be at altitude is in doubt, hypoxia inhalation tests are recommended before travelling. For more information on this subject **(see Chapter "*Travelling, altitude and diving*")**.

Table 1: Potential causes of hypoventilation in CF (adapted from[1])

Respiratory muscle weakness	due to muscle waisting and dysfunction
Poor chest wall elasticity	due to kyphosis
Central nervous system depression	due to opioids administered for chronic pain
Sleep disordered breathing	due to decreased tidal volume

Note: Nocturnal desaturations are common during exacerbations and usually improve with treatment

2.2 Practical aspects of long-term oxygen therapy (LTOT)

- There are three types of oxygen delivery systems available: concentrators (stationary or portable), liquid oxygen (backup unit and portable liquid oxygen flask) and compressed gas cylinders. Concentrators or liquid oxygen are the systems used most frequently in CF.
- The general recommendations of oxygen prescription in Switzerland can be found in the site of the Swiss Association of Pulmonology (www.pneumo.ch).
- Some considerations to guide prescription of LTOT are shown in **Table 2**.

Table 2: Considerations for prescribing LTOT

The indication and titration of oxygen therapy should be evaluated regularly
Oxygen needs should be assessed at rest, during exercise and during sleep
The choice of the equipment should be individualized to meet patients' needs at a sustainable cost
Encouraging an active lifestyle should be a central point. For that reason – portable systems should be offered in addition to static systems – oxygen conserving systems, such as reservoir cannulas or on-demand oxygen pulse devices, should be considered to prolong oxygen supply of portable systems and improve mobility
Regular controls of $SatO_2$ measurement need to be performed at rest as well as during exercise because open mouth respiration during effort may affect the intake of O_2 and positional variations may alter its efficacy.
Psychological aspects (e.g. embarrassment or depression) should be addressed
All patients using oxygen therapy should be informed on oxygen safety issues and material maintenance

3. NIV

3.1 Indications for NIV in CF

- **So far, no standard criteria for NIV initiation are available in CF**. Classic recommendations used for chronic obstructive pulmonary disease or neuromuscular disorders may provide guidance but are not always pertinent in CF. Taking into account these limitations, NIV may be considered when the following criteria are met :
  1. Symptoms (fatigue, dyspnea, morning headache etc.)
     and
  2. Physiological criteria (one of the following):
     a) $PaCO_2 \geq 55$ mmHg.
     b) $PaCO_2$ 50–54 mmHg and nocturnal desaturation (i.e. oxygen saturation measured by pulse oximeter ≤ 88% for 5 continuous minutes while receiving oxygen therapy ≥ 2 L/min).
     c) $PaCO_2$ 50–54 mmHg and hospitalization related to recurrent episodes of hypercapnic respiratory failure (≥ 2 episodes in a 12-month period).

- In CF NIV may be indicated in the following situations:
  - **During an acute severe respiratory exacerbation**: in case of hypoxemia with or without hypercapnia in severy ill patients. Because of the extremely poor outcomes of CF patients with invasive ventilation, NIV is preferred when possible and is used as a first line treatment to prevent worsening.
  - **During chronic hypercapnic respiratory failure**: NIV should be considered in case of documented significant and symptomatic nocturnal or diurnal hypercapnia. Sleep quality is often improved with NIV.
  - **During palliative care**: in this context, quality of life and also control of dyspnea and anxiety are a priority. The goal of NIV (palliation of symptoms) should be explicit and NIV can be discontinued at any time if the burden of treatment outweights the benefit **(see also Chapter "*Palliative and end-of-life care*")**.
  - **During physiotherapy**: NIV has been used as an adjunct to airway clearance techniques in patients with moderate to severe disease **(see also Chapter "*Physiotherapy*")**.
  - **During exercise**: NIV may be justified to decrease dyspnea, increase oxygenation and improve exercise tolerance in patients in whom dyspnea and fatigue limit effective training.
  - **In pregnancy**: there is limited information on the safety and efficacy of NIV in pregnant CF patients both in an acute and chronic setting. NIV may be considered during pregnancy (to avoid intubation and to allow an acceptable length of gestation) or intrapartum**.**

3.2 Contraindications for NIV in CF

- Most contraindications are relative and have been used as exclusion criteria in clinical studies.
- Even in the presence of these contraindications **(Table 3)**, decision of NIV should be individualized. If invasive ventilation is not considered appropriate (e.g. in severe cases where transplantation is not considered), NIV may be attempted.

3.3 Practical aspects of NIV

- NIV may be initiated outside the ICU (emergency room, intermediate care, controlled ward environment) if caregivers are used to this technique.
- NIV can be used just during the night, for a part of the day or for 24h as indicated by the clinical status.
- At patient discharge with NIV, some points to consider are:
  - Support system: service and maintenance 365 days a year.
  - Requirement for battery backup if dependence increases (to use for transport or in case of power failure).
  - Requirement of a backup machine if regular NIV use approaches ≥ 16 hours per day.
  - For material maintenance and cleaning refer to the specific manufacturer requirements.

3.4 Ventilators, interfaces and humidification

- NIV can be delivered using either a pressure or a volume preset ventilator. The setting of the ventilator seems to be more important than the ventilator mode.

Table 3: Contraindications of NIV (adapted from[2])

Absolute	Uncontrolled hemodynamic instability
	Life threatening hypoxemia (except if rapidly controlled by NIV)
	Impossibility to protect the airways • Coma, confusion or agitation (except if they occur due to hypercapnia) • Risk of bronchoaspiration (e.g. vomiting)
	Mechanical problems • Cranio-facial trauma or burn • Recent facial, upper airway or gastro-oesophageal surgery • Upper airway obstruction
	Gastrointestinal bleeding
	Undrained pneumothorax
Relative	Hypercapnic coma
	Controlled hemodynamic instability
	Abundant secretions
	Anxiety

- Ventilatory modes: Pressure targeted modes are preferred (better leak compensation, avoidance of high peak pressures). Among pressure targeted modes, bi-level positive airway pressure (Bi-PAP) is used by the majority of patients mainly because of better comfort.
- Ventilatory settings: the ventilator settings are adjusted to relieve symptoms associated with alveolar hypoventilation. They are adapted according to the SpO2, blood gases, tidal volume and respiratory rate.
  - EPAP: in cases of Bi-PAP with expiratory ports, a minimum level of 4 cmH_2O is recommended to prevent CO_2 rebreathing. Various benefits are associated with EPAP: stabilization of the upper airway during sleep, recruitment of the alveoli as well as increase in functional residual capacity, decreased atelectasis and reduction of the inspiratory work required to trigger inspiration in patients with intrinsic PEEP.
  - IPAP: is titrated to achieve sufficient volume ventilation and normalization of $PaCO_2$.
  - Cycling criteria: expiratory cycling is titrated above 35% of inspiratory peak flow to improve patient-ventilator synchrony and to reduce dynamic hyperinflation.
- Interfaces: many different interface types are currently available and each is associated with different advantages and disadvantages **(Table 4)**. Nasal masks are the most appropriate for CF patients allowing to cough and expectorate, but also for being less associated with gastric distension. Nasal obstruction or mouth leaks may limit their use and full face-masks are then preferred.
- Humidification: NIV can lead to excess loss of water vapor → oral/nasal dryness → more copious secretions. To alleviate these effects, adequate fluid intake and heated humidification are required.

Table 4: Commonly used types of interfaces, advantages and disadvantages (adapted from[2])

Interface	Advantages	Disadvantages
Nasal mask	Good for long-term use	Problems with mouth leaks or nasal pathology
Oronasal mask	Can solve problems with mouth leaks	Can be claustrophobic Theoretical risk of aspiration after vomiting
Nasal plugs	No pressure over nasal bridge Useful for claustrophobic patients Can be used by patients wearing spectacles	Can slip off face, problems with mouth leaks or nasal pathology
Full-face mask	Useful for claustrophobic patients Useful in case of nasal and facial pressure sores	Short-term use in acute care settings

3.5 Nutrition during NIV

- Excessive dyspnea and NIV dependency make eating difficult. Adequate fluid and nutrient intake to meet patients' nutritional requirements is important.
- If long term NIV is expected, Percutaneous Endoscopic Gastrostomy (PEG) feeding should be considered.
- When nasogastric tubes are used they can cause problems with mask fitting and air leaks. Small bore tubes are preferable in this situation.
- Simple measures may improve tolerance and decrease the risk of bronchoaspiration:
  - When possible, smaller, more regular meals are recommended rather than large meals.
  - During enteral feeding, patients should not be in a supine but rather in a semi-sitting position.

3.6 Administration of inhaled drugs during NIV

- Data on aerosol delivery during NIV are very limited.
- Whenever possible nebulized drugs should be administered off NIV.
- In NIV-depended patients, inhaled drugs can be administered
  - By using a metered dose inhaler and a spacer: the drug is administered into the ventilator circuit or
  - By adding a nebulizer to the circuit: a T-piece is placed, preferably between the exhalation valve and the patient (to decrease loss of drug in the circuit although this increases dead space ventilation).

3.7 Troubleshooting during NIV (Table 5)

Table 5: Potential practical problems during NIV and suggested solutions (adapted from[2])

Complications due to	Associated symptom/sign	Potential solutions
Interface	Discomfort Skin erythema Skin pressure sores or ulcers	Repositioning, change the tightness of the straps, change the size and/or type of the interface
		Use of a skin protection dressing Consider allergy to mask material or cleaning product
	Claustrophobia	Discussion of specific concerns and reassurance, relaxation techniques, anxiolysis
	Difficulty wearing spectacles	Some masks have straps to allow wearing glasses
Air flow	Air leaks	Repositioning, change the tightness of the straps, change the size and/or type of the interface.
		Be sure that the straps or cushioned parts of the mask are not worn
	Oral or nasal dryness	Use a humidifier
		Adequate fluid intake to avoid dehydration
	Nasal congestion	Nasal decongestant
	Gastric distension	Lowering inspiratory pressure, use of nasal mask
	Corneal irritation	Measures to decrease air leaks Eye lubricants

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