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# Long-term mechanical ventilation and nutrition

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**Summary** Mechanical ventilation (MV) in chronic situations is commonly used, either delivered invasively or by means of non-invasive interfaces, to control hypoventilation in patients with chest wall, neuromuscular or obstructive lung diseases (either in adulthood or childhood). The global prevalence of ventilator-assisted individuals (VAI) in Europe ranges from 2 to 30 per 100 000 population according to different countries.

Nutrition is a common problem to face with in patients with chronic respiratory diseases: nonetheless, it is a key component in the long-term management of underweight COPD patients whose muscular disfunction may rapidly turn to peripheral muscle waste. Since long-term mechanical ventilation (LTMV) is usually prescribed in end-stage respiratory diseases with poor nutritional status, nutrition and dietary intake related problems need to be carefully assessed and corrected in these patients.

This paper aims to review the most recent innovations in the field of nutritional status and food intake-related problems of VAI (both in adulthood and in childhood).
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## Long-term mechanical ventilation

Mechanical ventilation is used to augment or take over an individual's spontaneous respiration. This intervention may be required to address acute oxygenation difficulties or compensate for ventilatory pump failure. Mechanical ventilation is usually continued until the acute lung injury and/or pump failure recovers. Less commonly mechanical ventilation is used as a treatment in its own right to control chronic hypoventilation in patients with chest wall, neuromuscular or obstructive lung disease (see Table 1).

Most recent data suggest that the global prevalence of ventilator-assisted individuals (VAI) in Europe ranges from 2 to 30 per 100 000 population according to different countries.[1,2] Long-term mechanical ventilation (LTMV) may be used continuously or for shorter periods e.g. during sleep. Artificial ventilation is achieved by delivering positive pressure to the airway (either invasively via tracheotomy, or non-invasively via nasal/oral interface) or applying negative pressure to the chest wall.

The predominant mode is now nasal intermittent positive pressure ventilation (NIPPV) which is superceding tracheostomy intermittent positive pressure ventilation (T-IPPV) in most cases where bulbar reflexes are intact and ventilatory dependence is not complete.[3] The widespread application of NIPPV has been made possible by

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**Table 1** Aims of mechanical ventilation.

The goals of mechanical ventilation are to:
- Control respiratory acidosis
- Improve gas exchange
- Reduce or take over the work of breathing
- Reverse atelectasis
- Reduce cardiac workload
- Minimise the complications related to ventilatory support

improvements in ventilators' technology and mask design. Pioneering use of NIPPV in Duchenne muscular dystrophy (DMD)[4] has been followed by work in other restrictive groups,[5] and more recently also in patients with chronic obstructive pulmonary disease (COPD), although with less level of evidence.[6,7]

Nasal, oral and full face mask interfaces are available; nasal plugs which sit in the nares are useful alternatives. In addition to commercial masks, customised interfaces can be individually constructed and are favoured by some centres.[8] Intermittent positive pressure ventilation via mouthpiece is used only in some centres in the USA and France; its most well-documented role is in patients with post-polio respiratory muscle weakness.[9] Mouthpieces may be purchased commercially or custom-made; they can cause orthodontic deformity and are therefore unsuitable in children.

A wide range of ventilators has been designed for primarily domiciliary use.[8] These may offer advantages in terms of performance over ventilators intended for intensive care application and are more easy to use in the home. They are mainly classified into volume pre-set and pressure pre-set devices or, according to the way to assist patient, into assist, assist-control or control modes; in the last 5–10 years pressure pre-set machines, particularly bi-level pressure support equipment has become more prominent.[8]

Since the 1960s LTMV through tracheostomy has been an option in the management of subjects suffering from chronic respiratory insufficiency in stabilised neuromuscular disorders, kyphoscoliosis or other restrictive conditions, central hypoventilation and COPD.[10] Usually, in the latter cases, the choice of mechanical ventilation is long-term: to reduce episodes of acute respiratory failure caused by the progression of the disease, to enhance the quality of life and to improve survival. Prolonged invasive ventilatory life support is mandatory for patients completely unable to breathe on their own: this is the condition of the subject defined as unweanable. Typically, these patients have high level quadriplegia, but we can also include the advanced steps of progressive neurological disorders (i.e. amiotrophic lateral sclerosis).

Some patients who develop ventilatory failure may start with NIPPV and then progress to T-IPPV as bulbar weakness and increased ventilatory dependence occur. Clearly a careful evaluation of swallowing function, ability to cough, and ventilatory capacity are essential. The timing of the initiation of ventilatory support is important: there is no evidence to suggest that prophylactic NIPPV is beneficial before the development of hypercapnia, and it may even be detrimental in causing a delay in seeking medical advice during acute exacerbations.

Intermittent negative pressure ventilation (INPV) is less commonly used in progressive neuromuscular diseases;[11] it may provoke or exacerbate upper airway collapse. Advantages and contraindications of INPV are shown in Table 2. Nevertheless when treating patients with INPV several limitations should be considered: (i) the lack of upper airway protection, especially in unconscious and/or neurological patients may result in aspiration, given the reported effect of INPV on the lower oesophageal sphincter,[12] an effect to be prevented by premedication with metoclopramide;(ii) upper airway obstruction may occur[13] or be enhanced in unconscious patients, in patients with neurological disorders with bulbar dysfunction and in those with sleep apnoea syndrome. However, it has been reported[14] that in unconscious patients with normal bulbar function, the placement of a naso-gastric tube and the positioning of an oro-pharyngeal airway can minimise the risk of aspiration and/or airway collapsibility.

Long-term mechanical ventilation has been proposed in addition to long-term oxygen therapy (LTOT)[15] in chronically hypercapnic COPD patients with the theoretical rationale: to improve gas

**Table 2** Side effects reported with INPV.

- Tiredness
- Depression
- Musculo-skeletal pain or tightness
- Oesophagitis
- Rib fractures and pneumothorax
- Impaired sleep quality
- Upper airway obstruction
- Poor compliance

exchange;[16] to unload the ventilatory muscles;[16–18] to reset the central respiratory drive.[19] Physiological studies have shown that non-invasive mechanical ventilation may unload the diaphragm in stable COPD[16–18] while some clinical studies suggested that non-invasive nocturnal ventilation could be associated with day-time arterial blood gas improvement, reduced hospitalisation and need of tracheotomy.[6,20,21]

While NIPPV has been gaining increasing popularity in the management of chronic respiratory failure resulting from neuromuscular and restrictive chest wall diseases,[5,7] controlled trials in stable COPD patients reported conflicting results on short-term, clinical and functional outcome.[22–25] Even fewer data are reported on the long-term effects.[6,19,21] More recently, a 2-year multicentre controlled and randomised study has shown that the addition of nocturnal NIPPV to usual oxygen in hypercapnic COPD patients may result in better outcomes (stabilisation of $PaCO_2$ decrease of chronic dyspnoea, improvement in quality of life and reduction in ICU admissions) as compared with patients continuing on LTOT alone.[26]

## Nutrition

### Size of the problem

A compromised nutrition has been associated with a poor prognosis in stable COPD patients with and without respiratory failure.[27–29] Nutritional status has been recently studied in 744 patients on long-term respiratory treatments (LTOT or LTMV);[30] authors have found that fat-free mass (FFM), body mass index (BMI) below 20 and low serum albumin were the most sensitive parameters detecting malnutrition. Indeed, FFM appeared to be the most sensitive and relevant nutritional parameter according to patient's impairment and disability as assessed by $FEV_1$ and 6-min walked distance.[30]

Therefore, nutritional assessment and management is an important therapeutic option in patients with chronic respiratory diseases[31] also when dealing with prolonged/difficult weaning from mechanical ventilation.[32] In the study by Sivasothy et al.,[33] chronically ventilated hypercapnic COPD patients with body mass index (BMI) value lower than 20 showed a worse survival. Since 1990, only 19 (56%) out of 37 papers on LTMV (Source MEDLINE, Key words: LTMV + Nutrition, excluding ventilatory support due to sleep apnoea), reported BMI of the studied patients. Long-term mechanical ventilation is usually prescribed in patients with end-stage respiratory disease. Indeed in all 19 studies mean BMI was lower than 25, being more compromised in COPD than in restrictive thoracic diseases.[21,23–25,34,35] In chronically ventilated patients with cystic fibrosis BMI was lower than 20.[36] Especially in COPD patients, respiratory muscle dysfunction may be due also to conditions other than impaired nutrition and/or metabolism (e.g. hyperinflation, change in diaphragm configuration).[37] Indeed an impaired nutritional status associated with respiratory muscle dysfunction was described in six out of 37 papers (three in COPD and three in restrictive thoracic diseases).[21,33,34,38–40]

**Table 3** Adverse effects of malnutrition on thoraco-pulmonary functions.

- Altered ventilatory drive
- Reduction in the ventilatory response to hypoxia
- Decreased mass, force, contractility and endurace of the diaphragm
- Decreased respiratory muscle strength
- Hypercapnia
- Reduced synthesis of alveolar surfactant
- Altered humoral and cellular immunity
- Increased bacterial adhesion in the lower respiratory tract

Table 3 emphasises the effects of malnutrition in patients with respiratory diseases. Nevertheless, specific nutritional deficiency like hypophosphatemia, can also have consequences on respiratory function, otherwise causing acute respiratory failure.[41] Moreover, abnormally high lipid synthesis from glucose and decreased triglyceride mobilisation, due to the lack of physical exercise, may contribute to an increase in the fat mass of patients.[42]

### Assessment and solutions

In the last decade, nutritional screening and therapy has been considered as an essential component in the long-term management of pulmonary rehabilitation dealing, in particular, with systemic manifestations such as weight loss, muscle wasting and altered muscle metabolism which are typical in advanced stages of COPD patients.

The association between underweight per se and increased mortality risk has been well established in numerous retrospective studies ranging from selected COPD patients to population-based

samples.[27,43,44] Two prospective studies even showed in COPD patients with a BMI $< 25\,kg/m^2$ that weight gain was associated with decreased mortality risk.[27,45] Therefore, it can be concluded that not only underweight COPD should be considered for caloric supplementation but also patients with a BMI $< 25\,kg/m^2$ and involuntary weight loss. This implies that COPD patients who suffer from weight loss, and even weight stable patients at risk, should be encouraged to increase their apparently normal energy intake.

Treatment of weight loss may be achieved by increasing dietary intake or preventing weight loss by means of protein synthesis stimulation. However, in the home setting it is more difficult for patients to balance their energy expenditure.

When oral nutritional supplements are considered, it is important to realise that there are limitations to the caloric amount of supplements that can be given daily; also the portion size and distribution of supplements during the day is important to consider.[46] Substrate oxidation and ventilation are intrinsically related and theoretically meal related dyspnoea and impaired ventilatory reserves might restrict the carbohydrate content of nutritional support in respiratory disease. Earlier studies indeed showed adverse effects of a carbohydrate-rich energy overload (970 kcal)[47] but not using a normal energy load (500 kcal) [48] on carbon dioxide production. Recent studies show that carbohydrate-rich supplements may even have positive effects. A fat-rich supplement, but not an equicaloric carbohydrate-rich supplement, has been shown to cause an acute increase in dyspnoea.[46]

Sometimes increasing energy intake among severe COPD cases is difficult to accomplish. Therefore, interventions should also be extended to prevention and early treatment of weight loss, that is, before patients are extremely wasted. This means expanding the target group to include primary care patients before they have become underweight, and putting more emphasis on dietary change than on medically prescribed supplementation.

From a nutritional point of view, wasting of muscle mass is due to an impaired balance between protein synthesis (anabolism) and protein breakdown (catabolism). However, other non-nutritive factors including physical inactivity (which is quite a typical attitude in patients undergoing LTMV), alterations in the neuro-endocrine response and presence of a systemic inflammatory response may contribute to a negative protein balance. Several studies have therefore investigated in underweight COPD patients the effects of pharmacological anabolic stimuli to promote protein synthesis including anabolic steroids and growth hormone. These studies were indeed able to document a significant gain in muscle mass after intervention[49] illustrating that there is room for specific stimulation of protein synthesis in these patients. This may also be achieved by increasing protein intake and optimisation of essential amino acid intake. It has been clearly shown in other wasting conditions that adequate intake of protein is also a prerequisite for optimal efficacy of anabolic drugs.[50] Of interest are the consistently reduced plasma levels of branched chain amino acids (BCAAs) in underweight COPD patients and in those with low muscle mass.[51,52] Leucine is an interesting nutritional substrate since it serves as precursor and enhances activity and synthesis of proteins in skeletal muscle.[53] Current insight into the molecular mechanisms of cachexia indicates a complex interaction between inflammatory mediators, oxidative stress and growth factors involved in processes that govern skeletal muscle fibre degeneration, apoptosis and regeneration.[54] At present from a nutritional and metabolic perspective, specific interest has recently been focused on fatty acid modulation, like the n-3 polyunsaturated fatty acids (PUFA), since fatty acid composition of inflammatory and immune cells is sensitive to change according to the fatty acid composition of the diet. Fish oil (containing PUFA) supplementation has beneficial effects on the systemic inflammatory response and disease activity in conditions as rheumatoid arthritis and inflammatory bowel disease.[51] Clearly more clinical trials are required to investigate the potential role of fatty acids enriched supplements in cachexia or other chronic wasting conditions like advanced COPD or chronic respiratory failure.

## Food intake-related problems in LTMV patients

Since the 1960s long-term T-IPPV has been performed in neuromuscular disorders, kyphoscoliosis or other restrictive conditions, central hypoventilation and COPD.[10] Prolonged invasive mechanical ventilation is mandatory in patients completely unable to breathe on their own[55] and it is still considered the gold standard against which other more recent techniques are compared. Nevertheless, one of the most important problems occurring in patients needing prolonged T-IPPV is swallowing dysfunction. Although a swallowing dysfunction is usually induced by an underlying neuromuscular disease, many factors may contribute including:

acute illness and medications used to treat these conditions (steroids, neuromuscular blocking agents, general sedatives), prolonged inactivity of swallowing muscles, injury due to endotracheal intubation, tracheostomy tube.[56] Tracheostomy per se has been described to limit swallowing function by either compressing the oesophagus or decreasing larynx elevation and anterior displacement.[57] When T-IPPV is used, an inflated tracheostomy tube cuff anchors the strap muscles in the neck, hampering laryngeal elevation and neck rotation. This results in reduced glottic closure and increased laryngeal penetration, increasing the chances of aspiration.[58]

Recent studies both in acute and chronic setting[58–60] suggested that swallowing dysfunction and pulmonary aspiration occur in patients receiving ventilatory support through a cuffed tracheostomy tube. Nevertheless, the real incidence of aspiration is difficult to determine, since investigators often use different criteria for its presence.[56,58] Therefore, dietary intake through the mouth should be carefully evaluated. Recognition of swallowing dysfunction in these patients may identify patients at high risk of aspiration, and thereby help to avoid related complications such as recurrent pneumonia[61] and atelectasis. In a recent study[60] of patients receiving MV via artificial airways for more than 15 days, swallowing abnormality detected at bedside examination was found in 34% of cases without any significant difference according to the presence or absence of an underlying neuromuscular disease. In these patients, barium swallow with video-fluoroscopy (BS/VF) was abnormal in 83% of patients. In 50% of patients who underwent direct laryngoscopy important abnormalities were found that contributed to swallowing dysfunction. Results of early ($<$1 month) repeated BS/VF examination in patients were unchanged; however in a small group of patients, later studies ($>$1 month) revealed significant improvement. These authors[60] concluded that patients requiring prolonged mechanical ventilation present a high incidence of swallowing abnormalities, regardless the presence or absence of neuromuscular disorders; BS/VF and direct laryngoscopy can provide useful information about laryngeal action and swallowing, and can facilitate the implementation of corrective actions (selected food, head postures, coached cough reflex) to prevent respiratory complications.

In a study by Schoenhofer et al.[59] aspiration was found in 16% of patients independent of whether documented clinically on the basis of cough, distress after swallowing, expectoration or suctioning at bronchoscopy of enteral nutrition or by means of scintigraphic method after $^{99m}$Tc-labelled meal. Clinical assessment was able to discover swallowing dysfunction in 6.5% of patients negative to scintigraphy. On the other hand, scintigraphy was positive in 6.5% of patients with negative clinical assessment. Overall presence of swallowing dysfunction was therefore found in 29% of these patients with need of prolonged invasive MV.

Independent on the need of NIPPV or T-IPPV, when dysphagia is present, VAI are commonly referred to a multidisciplinary team (including neurologist, nutritionist, gastro-enterologist) since the decision for either corrective actions preventing respiratory complications (such as use of higher consistency food or specific head postures)[62,63] or long-term enteral nutrition cannot be usually delayed. Patient's ventilatory insufficiency is rarely recognised and treated before tachypnoea and dyspnoea hamper swallowing efforts. Since weight loss correlates with swallowing impairment,[64] body weight almost invariably increases once adequate ventilatory assistance and dietary intake are provided.[65] The use of NIPPV facilitates swallowing efforts, but the patients must be trained to coordinate the assisted breathing with swallowing.

In general, non-invasive respiratory aid alternatives to tracheostomy are effective until severe bulbar muscle dysfunction results in ongoing aspiration of food and saliva. When aspiration causes an arterial oxygen desaturation below 95%, despite optimal use of assisted ventilation and coughing methods, bronchial mucus and food pooling may result in episodes of pneumonia.[64]

Dysphagia-associated nutritional deficiencies are very common but rarely diagnosed early, and their management especially for patients with neuromuscular disorders is often considered to be of secondary importance. The consequences can be severe on locomotion and respiratory function as well as on other bodily systems.

Percutaneous endoscopic gastrostomy (PEG) as a measure of enteral tube feeding[66] has gained wide acceptance and it is, nowadays, the preferred method for providing enteral nutrition in long-term settings with the aim to prevent the most serious complications. Short-term studies have demonstrated the advantages of PEG as compared to the naso-gastric tube feeding in patients with dysphagia due to chronic neurological diseases.[67,68] PEG insertion is a quick procedure generally well tolerated by patients and a relatively low complication rate in the outcome has been described. Hull and coworkers[69] showed that, in 49 consecutive patients undergoing PEG insertion due to dysphagia, 27 complications (site infections, mechanical problems, gastrointestinal dysfunction) occurred after 30 days or more, whereas 51% of patients had

no problem at all. Reflux and aspiration are also significantly reduced by PEG.[70] For this reason PEG is considered a good solution for an early discharge home, leaving also the opportunity to be easily removed in the case, if any, of reversibility or improvement of dysphagia and it does not contraindicate oral feeding. In patients needing long-term ventilatory support with impaired swallowing such as in neurological diseases, PEG is often proposed. It ensures an enhanced daily dietary intake toward recovery and reduced major complication (i.e. infections),[71] and may be a bridge solution toward oral feeding.

## Nutrition and food intake-related problems in children with LTMV

Nutritional problems are common in children with chronic respiratory failure, particularly in infants with chronic lung diseases[72] leading to failure to thrive and malnutrition. The effects of malnutrition on respiratory function are well described in animals and humans and include reduction of respiratory muscle mass and reduced contractile strength, leading to reductions in respiratory muscle strength, endurance and vital capacity.[27,28,31,73] These deleterious effects of malnutrition are generally reversible with nutritional repletion. In children, a multitude of factors is frequently responsible for this, including gastro-oesophageal reflux, oromotor dysfunction, behavioural feeding refusal. The importance of the composition of feeding has been recognised for sometime with diets high in carbohydrates leading to excessive carbon dioxide production. This finding has prompted many to provide up to 50% of non-protein calories as fat.

The most important problems are described in mechanically ventilated children with neuromuscular disease, many of whom have high caloric requirements.[74] Even normal caloric intakes based on patient age and weight, may lead to obesity, which will further embarass the patient respiratory function and mobility. Attempts to limit caloric intake may however inadvertently lead to excessive protein mineral and oligoelements depletion in children with chronic respiratory failure.

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