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REVIEW

Chronic respiratory care for neuromuscular diseases in adults

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ABSTRACT: Neuromuscular diseases (NMD) may affect respiratory muscles, leading to respiratory failure. Studies show that long-term noninvasive mechanical ventilation (NIV) improves symptoms, gas exchange, quality of life and survival. NIV improved these parameters in muscular dystrophies and also in patients with amyotrophic lateral sclerosis without severe bulbar dysfunction. NIV should be started at the onset of nocturnal hypoventilation. In selected cases, NIV may be simpler, better accepted by patients and cheaper than invasive mechanical ventilation, but it cannot be used as an alternative. Tracheostomy may be preferred by patients unable to protect their airways and wishing to survive as long as possible, or by ventilator-dependent patients.

Glossopharyngeal breathing consists of taking air and propelling it into the lungs. Chest percussions and vibrations can help to mobilise airway secretions but they cannot substitute coughing. Manually assisted coughing requires substantial lung inflation through air stacking or deep lung insufflation, followed by an abdominal thrust with open glottis. The combination of mechanical in-exsufflation with an abdominal thrust is a mechanically assisted cough.

In conclusion, recent advances in respiratory care of NMD have improved prognosis and many caregivers have changed from a traditional noninterventional to a more aggressive, supportive approach.

KEYWORDS: Chronic respiratory insufficiency, chronic ventilatory support, cough capacity, health-related quality of life, home ventilation, inspiratory muscles

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Most neuromuscular diseases (NMD) are characterised by progressive muscular impairment leading to loss of ambulation, being wheelchair-bound, swallowing difficulties [1, 2] respiratory muscle weakness and, eventually, death from respiratory failure. Rapidly progressive NMD are characterised by muscle impairment which worsens over months and results in death within a few years, such as amyotrophic lateral sclerosis (ALS) and spinal muscular atrophies (SMA). Relatively rapid progression is seen in Duchenne muscular dystrophy (DMD), resulting in muscle impairment within a few years and a significantly reduced life expectancy; death occurs within young adulthood. Other myopathies, such as Becker muscular dystrophy, facioscapulohumeral muscular dystrophy, limb-girdle muscular dystrophy and myotonic dystrophy, experience a slowly progressive reduction in muscular function and only mildly reduced life expectancy [3]. Respiratory failure is the most common cause of morbidity and mortality in these patients with chronic or rapidly progressive NMD (table 1). In fact, reduction in inspiratory muscle strength, with related ineffective alveolar ventilation, and expiratory muscle weakness, with related difficult airway secretions clearance, lead to chronic respiratory insufficiency, as well as to potentially life-threatening problems (table 2).

The muscular components of the respiratory system are as follows. 1) The inspiratory muscles contribute most to ventilation; 2) the expiratory muscles carry out forced expiration and expulsive efforts including coughing; and 3) the bulbar muscles protect the airways [1]. Due to progressive inspiratory muscle weakness and increasing elastic load induced by reduced lung and thorax compliance, these patients suffer from a progressive decline in vital capacity (VC) and increase in work of breathing. A rapid–shallow breathing pattern may be associated with increased work of

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TABLE 1 Neuromuscular diseases affecting respiratory function

Neuropathic disease
Motor neuron disease
Amyotrophic lateral sclerosis
Poliomyelitis, post-polio syndrome
Spinal muscular atrophy
Paralytic rabies
Peripheral neuropathies
Guillain–Barré syndrome, Chronic inflammatory demyelinating polyneuropathy
Critical illness polyneuropathy
Unilateral or bilateral diaphragm paralysis
Charcot–Marie–Tooth disease
Disorders of the neuromuscular junction
Myasthenia gravis, congenital myastenic syndrome, Lambert–Eaton myasthenic syndrome
Botulism, poisoning with curare and organophosphate
Myopathies
Acquired myopaties
Polymyositis, dermatomyositis
Critical illness myopathy
Inherited myopathies
Progressive muscular dystrophy
Duchenne muscular dystrophy
Becker muscular dystrophy
Facioscapulohumeral muscular dystrophy
Limb-girdle muscular dystrophy
Myotonic dystrophy
Congenital myopathies
Nemaline myopathy, core diseases, myotubular myopathy
Congenital muscular dystrophy
Ullrich congenital muscular dystrophy, Emery–Dreifuss muscular dystrophy, merosin-deficient congenital muscular dystrophy, merosin-positive congenital muscular dystrophy, rigid spine muscular dystrophy
Metabolic myopaties
Mitocondrial myopaty, glycogen storage disease type 2

TABLE 2 Signs and symptoms of respiratory failure

Symptoms
Increasing generalised weakness
Dysphagia
Dysphonia
Dyspnoea on exertion and at rest
Fatigue
Sleepiness
Clinical signs
Rapid shallow breathing
Tachycardia
Weak cough
Staccato speech
Accessory muscle use
Abdominal paradox
Orthopnoea
Weakness of trapezius and neck muscles
Single-breath count
Cough after swallowing
Laboratory data
VC $\leqslant$15 mL·kg^{-1}, VC $\leqslant$1 L or 50% drop from value in stable state, or >20% drop from sitting to supine position
Maximum inspiratory pressure $\leqslant$30 cmH_2O
Maximum expiratory pressure $\leqslant$40 cmH_2O
Nocturnal desaturation
P_{a,CO_2} >45 mmHg (6.7 kPa)

VC: vital capacity; P_{a,CO_2}: arterial carbon dioxide tension.

breathing and an inability to take deep breaths, leading to chronic microatelectasis and decreased lung and chest wall compliance [4–8]. NMD may also be associated with obstructive or central sleep-disordered breathing, particularly during rapid eye movement sleep. During this condition, respiratory muscle weakness and/or mechanical disadvantage may result in severe alveolar hypoventilation leading to sustained oxygen desaturation and hypercapnia [9, 10], depending on the involvement of upper airway muscles and respiratory centre neurons (*e.g.* in myotonic dystrophy) [4, 11], and comorbidities, such as obesity. Due to the patients' difficulty in moving, dyspnoea usually appears late in the disease history, accordingly early lung function and respiratory muscle function monitoring should be mandatory and both are considered to be the best prognostic indicators in these patients [12, 13]. Serial measurements of spirometry provide a simple and reliable means of follow-up. Lung function is useful to predict nocturnal hypercapnia, with a VC of <680 mL being very sensitive to predict daytime hypercapnia [12]. Individual variation in the rate of forced vital capacity (FVC) decline is an important variable to be considered. A reduction in VC when changing from a sitting to a supine position and serial measurements in respiratory muscle strength, as assessed by maximal inspiratory pressure (MIP) and maximal expiratory pressure, are also useful in follow-up. There is no clear evidence as to how MIP should be measured, although plateau pressures sustained for 1 s and measured at residual volume are usually recommended. Measurements of peak and plateau pressures are comparably useful for the assessment of inspiratory muscle strength and can be reliably measured at functional residual capacity and at residual volume [14, 15].

Effective cough requires full pre-cough inspiration, followed by glottis closure and adequate expiratory muscle strength to generate sufficient intra-thoracic pressures and obtain high-peak expiratory flows. Expiratory muscles weakness combined with inadequate lung inflation prevents effective coughing and airway clearance, altering airway resistance and increasing the risk of developing atelectasis and pneumonia.

Bulbar muscle weakness (facial, oropharyngeal and laryngeal muscles) can affect the ability to speak, swallow and clear airway secretions, with the possibility of an increased likelihood of aspiration. Drooling is an indicator of a severe swallowing impairment. Patients with NMD usually experience mild-to-moderate bulbar dysfunction with the exception of patients with ALS, type 1 SMA and with other rapidly progressive NMD who may develop a severe glottis functional impairment.

Although respiratory failure is the major cause of morbidity and mortality in NMD, there is inadequate awareness of how

to manage respiratory problems in these patients. Recent advances in respiratory care of NMD have improved prognosis and expectations, and many caregivers have changed from a traditional noninterventional approach to a more aggressive, supportive approach, resulting in new unsolved problems [16, 17]. The increasing interest in this topic is demonstrated by the increasing number of papers published over time (fig. 1). We researched the literature from 1966 to 2009 using the key word ''Neuromuscular disease AND Respiratory Failure'' which generated 3,324 references, of these 576 were reviews. We will review the most relevant tools in the care of chronic respiratory problems of these patients. Management of acute respiratory failure in these patients will only be reviewed briefly as it has been addressed elsewhere [18].

VENTILATORY ASSISTANCE

Whereas patients with rapidly (ALS and SMA) or relatively rapidly (DMD) progressive NMD may develop acute respiratory failure (ARF) secondary to an acute and dramatic decrease in respiratory muscle strength, patients with chronic NMD, such as other myopathies, experience a slowly progressive reduction in respiratory muscle function. Therefore, they initially suffer from nocturnal hypoventilation and recurrent respiratory infections, progressing to daytime hypercapnia and eventually to death. In these patients, long-term mechanical ventilation (LTMV) delivered either invasively or noninvasively (noninvasive mechanical ventilation: NIV) is the main therapeutic intervention to support the respiratory muscle function and to increase life expectancy and health-related quality of life (QoL) [16]. A detailed survey of home LTMV use in 16 European Countries [19] showed that NMD represented 35% of chronically ventilated patients with large differences between countries. Overall, 24% of the NMD population received ventilation *via* a tracheostomy with 60% using a nose mask and 40% using a face mask or a mouthpiece [20]. Volume pre-set positive pressure ventilators were used in less than half of NMD patients, indicating a trend to also use bilevel pressure ventilators in these patients [21, 22].

Noninvasive mechanical ventilation

Long-term NIV has improved survival in patients with some NMD, and improved the QoL in most patients [23–25]. Herein, we address two examples of the effect of NIV in relatively rapidly or rapidly progressive diseases, such as DMD and ALS.

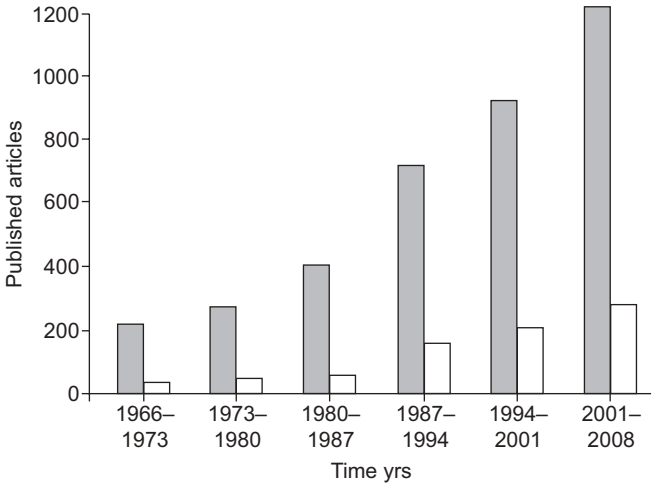

FIGURE 1. Time course of published original articles (■) and reviews (□) on neuromuscular diseases and respiratory failure listed on PubMed from 1996–2008.

DMD

DMD is an X-linked recessive trait occurring in 1:3,000 male births, due to a mutation of the dystrophin gene. As with other NMD it causes progressive loss of muscle strength, eventually resulting in loss of ambulation, respiratory muscle weakness and death from respiratory insufficiency. The majority of patients also develop cardiomyopathy. Diagnosis depends on medical history, physical findings and elevated serum creatine kinase level. DMD is confirmed by finding an abnormal dystrophin gene by mutation analysis of blood leukocyte DNA. If DNA analysis is normal (as is the case in one out of three patients), a diagnosis should be confirmed by finding absent or abnormal dystrophin using immunohistology or protein analysis of muscle tissue.

The natural history of DMD is more predictable than many of the other NMD. Significant reduction in VC and restrictive ventilatory pattern is usually seen after the initiation of wheelchair use; increasing nocturnal hypoxaemic dips are seen in subsequent teenage years, and respiratory insufficiency occurs between 18–20 yrs of age. An FVC <1 L is a predictor of poor outcome, with a 5-yr survival rate of only 8% if assisted ventilation is not provided. Some studies [26, 27] showed deterioration of nocturnal ventilation and oxygenation, sleep quality and symptoms when NIV was withdrawn from patients who had gained benefits. Improvement of these parameters was seen after NIV was restarted. Although controlled, randomised studies are lacking, several large series [28–30] have shown excellent long-term survival rates for patients receiving long-term NIV with less rapidly progressive muscular dystrophies. One study evaluated the effects of nocturnal NIV on survival in 23 symptomatic DMD patients with established diurnal and nocturnal hypercapnia [30]; 1- and 5-yr survival rates were 85% and 73%, respectively. Early changes in arterial blood gas tensions following NIV occurred with mean arterial oxygen tension increasing from 7.6 to 10.8 kPa and mean arterial carbon dioxide tension falling from 10.3 to 6.1 kPa. Improvements in arterial blood gas tensions were maintained over 5 yrs. Health perception and social aspects of QoL index were reported as equivalent to other groups with nonprogressive disorders using NIV.

Other studies also consistently show that long-term NIV may improve symptoms and QoL, although the effects on sexual activity are unclear [31, 32]. One study assessed physical disability, pulmonary function and QoL using Short-Form 36 of the medical outcome questionnaire in 35 patients with DMD [31]. All patients required a wheelchair and help for dressing and eating. In total, 14 patients were on long-term NIV. In ventilated patients, mean FVC was 12% predicted and the physical disability score was 65; the corresponding values in spontaneously breathing patients was 48% pred and 51, respectively. Short-Form 36 physical function scores were reduced in both groups but vitality, role-emotional, social function and mental health scores were nearly normal, and did not differ between groups. KOHLER *et al.* [31] concluded that QoL in DMD is not correlated with physical impairment or the need for NIV.

NIV therapy has also reduced the risk of pregnancy in stable patients with NMD. Careful assessment and pre-pregnancy counselling are required [33], but, in the absence of cardiomyopathy or pulmonary hypertension, successful maternal and foetal outcomes have been reported in NIV users with a VC of 800 mL and even in a few cases of patients lacking a detectable VC. Preconception genetic advice and a full cardiopulmonary assessment are mandatory [22].

ALS

ALS is the NMD for which NIV is most frequently prescribed [34, 35]. Uncontrolled studies [36, 37] observed improvements in QoL and functional scores, as well as better survival of patients who tolerated NIV compared to those who were intolerant, especially in patients without bulbar involvement. Criteria to perform NIV in these studies included orthopnoea, intact bulbar function, hypercapnia and nocturnal oxygen desaturation [38]. A controlled randomised study by BOURKE *et al.* [39] in patients with orthopnoea and MIP <60% pred or symptomatic daytime hypercapnia showed that NIV improved QoL and sleep-related symptoms, and prolonged survival by almost 7 months in patients without severe bulbar dysfunction compared with control subjects. These improvements were considered as greater than those achievable with any currently available drug therapy, justifying a trial of NIV. Patients with severe bulbar dysfunction were often intolerant and gained no survival benefit from NIV, but considering that in the study by BOURKE *et al.* [39] and in other studies [40] sleep-related symptoms and some domains of QoL improved in tolerant patients, a trial of NIV was considered as justified even in these patients. Advanced age at diagnosis and relevant bronchial secretions are poor prognostic indexes of ALS patients treated with NIV. In addition, the severity of bulbar impairment and the nutritional status of the ALS patients at the start of ventilation may predict tolerance and survival [41].

As a consequence of the studies in DMD, ALS and other NMD, current evidence about the therapeutic benefit of NIV is defined as weak but consistent [42]. Usually, NIV is performed at night, but additional daylight hours of NIV are suggested as this may unload respiratory muscles and reverse breathlessness more effectively than night NIV alone [43].

Timing of NIV

Current international consensus guidelines identify a number of indicators for the establishment of long-term NIV for patients with NMD but do not address the possible clinical differences between each of the underlying disorders [44]. Several studies have examined the timing issue of when to start NIV. A randomised study has shown increased mortality compared with control subjects among NIV users when patients with DMD were started on ''elective'' NIV before daytime symptoms or hypoventilation developed [45]. A more recent study randomised NMD patients with nocturnal but no daytime hypercapnia to begin NIV promptly or to start when daytime hypercapnia or symptoms develop [46]. ''Awaiting'' patients had to start NIV within the next 2 yrs because of the development of daytime hypercapnia or symptoms; most within the first year. In addition, a retrospective study [47] found that tracheostomy-free survival from the time of ALS diagnosis was significantly longer in patients who started NIV when their FVC was >65% pred compared with patients starting NIV when FVC was <65% (2.7 yrs *versus* 1.8 yrs, respectively). Awaiting the onset of daytime hypercapnia before initiating NIV may be risky, whereas beginning NIV before the onset of symptoms or nocturnal hypoventilation may offer no benefit. Therefore, a ''therapeutical window'' should be evaluated. It has been suggested to begin NIV at the onset of nocturnal hypoventilation as demonstrated by sustained nocturnal oxygen desaturations. Whether ALS patients with FVC <65% pred should routinely undergo NIV awaits confirmation in prospective randomised trials. One study has assessed the differences in the physiological parameters of 66 NMD patients (19 ALS, 12 DMD and 35 slowly progressive disease), assigned to long-term NIV for symptomatic chronic hypercapnia over a 9-yr period [48]. Mean FVC at NIV onset was 40.3% pred in all patients, but was >50% pred in 12% patients. ALS patients were more hypercapnic and more hypoxaemic, but had better forced expiratory volume at 1 s at NIV onset compared with DMD patients. Mean MIP was 3.0 kPa in all patients, but values were lower compared with international consensus guidelines (5.88 kPa). Median survival in DMD, slowly progressive diseases and ALS was 132, 82 and 16 months, respectively. This study indicates that physiological parameters such as lung function, blood gases or MIP substantially differ between different underlying conditions causing NMD when long-term NIV is being considered [48].

NIV versus *tracheostomy*

Compared to tracheostomy ventilation, NIV greatly simplifies administration of care, is more comfortable for patients and reduces costs [49–51]. Night-time NIV means that patients are not restricted in the daytime and enables them to be cared for at home, whereas with long-term tracheostomy ventilation patients may need admission to healthcare services or highly trained and well-motivated home professional or familiar caregivers. Because of the advantages over tracheostomy ventilation in most patients and the consistency of supporting evidence, despite the lack of randomised trials, NIV should be considered as the preferred ventilatory modality for home mechanical ventilation in NMD patients. Although LTMV prolongs survival through both interfaces, NIV is preferred by patients over tracheostomy for speech, sleep, swallowing, comfort, appearance and security [52]. One study also demonstrated a 77% cost saving when NIV was used for ventilator-dependent individuals, by facilitating community placement with personal care attendants rather than nursing care or long-term institutionalisation [53].

Despite the reported benefits of NIV, there is no consensus that it can be used as an alternative to invasive ventilation. NIV must be used selectively; tracheostomy ventilation may be preferred by patients unable to protect their airways and who wish to maximise survival or when the patient is ventilator dependent for most of the day [44]. The decision to perform tracheostomy should only be taken with the patient's informed consent and after careful discussion of the impact of social factors and living arrangements. Access to the resources necessary to support patients living at home with tracheostomy ventilation varies widely throughout Europe [19]; mouthpiece ventilation may be especially valuable in countries where

these resources are scarce [20, 52]. MARCHESE *et al.* [54] described survival, predictors of long-term outcome and attitudes in patients treated by home tracheostomy-mechanical ventilation for respiratory failure during a 10-yr period. Patients were divided into three groups: NMD, pulmonary and nonpulmonary patients. There was statistically significant longer survival in NMD compared to pulmonary patients. The median survival in ALS patients was lower than the whole group of NMD patients (49 months). Major tracheostomy complications were <3%. The vast majority of patients were pleased they had chosen trascheostomy and almost all would choose it again. More than half of the caregivers were pleased that the patients had chosen home ventilation, despite reporting major burdens.

Feeding and ventilatory assistance

Malnutrition is common in NMD patients. Impaired swallowing compromises the patient's ability to meet intake needs. In these patients, deglutition is fragmented in several swallows over several breathing cycles. In tracheostomised patients swallowing is better under mechanical ventilation than in spontaneous breathing [55, 56]. However, there is no consensus of whether time for tracheostomy should be the same for percutaneous endoscopic gastrostomy (PEG). NIV and PEG have been included in standard treatment of ALS [57].

Glossopharyngeal breathing

Glossopharyngeal breathing (GPB) is the act of the glottis taking air and propelling it into the lungs. One breath usually consists of six to nine gulps of 60–100 mL each. According to some authors, GPB can sustain normal ventilation throughout daytime hours without using a ventilator, and safely in the event of ventilator failure during sleep in patients with reduced or no inspiratory muscle function [58]. It is claimed that both inspiratory and, indirectly, expiratory muscle activity can be assisted by GPB and that the safety and versatility afforded by GPB may avoid tracheostomy or substitution of a tracheostomy with NIV. Appoximately 65% of patients with functional bulbar-innervated musculature have been reported to be able to use GPB to increase tidal volumes if taught [59]. Despite the enthusiasm of some researchers, in the opinion of the present authors, there is not enough evidence for generalised use of GPB alone in order to avoid invasive ventilatory assistance.

CLEARING AIRWAYS

Effective secretion clearance is critical for patients with chronic NMD to prevent atelectasis, pneumonia, acute respiratory failure and hospitalisation. The use of airway clearance techniques, including assisted coughing techniques, both manual and mechanical, and secretion mobilisation techniques, is strongly recommended. These techniques should always be included in the treatment of chronic NMD patients. Chest percussion and vibration can help to mobilise peripheral airway secretions but they are not substitutes for coughing and, unlike for assisted coughing, have never been shown to decrease pulmonary morbidity and mortality. Cough can be assisted by manual and mechanical means [60, 61].

Manually assisted coughing

Manually assisted coughing requires substantial lung inflation through air stacking or deep lung insufflation, followed by an abdominal thrust applied as the glottis opens. If the VC is <1.5 L, air stacking is especially important before the abdominal thrust [62]. Whereas inspiratory, expiratory and bulbar-innervated muscles are needed for spontaneous coughing, only bulbar-innervated muscle function is required for assisted coughing as airway pressure changes and abdominal thrusts substitute for respiratory muscles but nothing can substitute for glottic function. Manually assisted coughing requires a co-operative patient, good coordination between the patient and caregiver, adequate physical effort and often frequent application by the caregiver. Forced exhalation is augmented by pushing on the upper abdomen (*i.e.* abdominal thrust) or chest wall (*i.e.* anterior chest compression) in synchrony with the subject's own cough effort. Moreover, chest wall stiffness has also been suggested as a contributing factor to cough ineffectiveness [16].

Mechanical in-exsufflation

When manually assisted coughing is not enough, the most effective alternative is mechanically assisted coughing. The combination of mechanical in-exsufflation with an abdominal thrust is a mechanically assisted cough (fig. 2) [63–67]. Mechanical in-exsufflation delivers deep insufflations followed immediately by deep exsufflations. The cough volumes normally exceed 2 L at flows of 10 $L \cdot s^{-1}$. Inspiratory–expiratory pressures of 40– -40 cmH_2O delivered *via* oronasal interface or adult tracheostomy with the cuff inflated are usually the most effective. Independent of delivered pressures, the importance is to fully expand and then fully and quickly empty the lungs. Pneumothorax has been reported with mechanical in-exsufflation [68].

Whether *via* the upper airway or indwelling airway tubes, routine airway suctioning misses the left main stem bronchus ~90% of the time. This explains the high rates of left lower lobe pneumonia. However, mechanically assisted cough provides the same exsufflation flows in both left and right airways without discomfort, fatigue or airway trauma and it can be effective even when suctioning is not. Patients who benefit from mechanically assisted cough have weak respiratory muscles but adequate bulbar-innervated muscle function for

FIGURE 2. The technique of mechanical in-exsufflation.

airway patency but insufficient function for air stacking to assisted cough peak flow (CPF) to >5 $L \cdot s^{-1}$. Mechanically assisted cough is not usually necessary for patients with intact bulbar-innervated muscle function who can air stack sufficiently for CPF to exceed 6 $L \cdot s^{-1}$ with an abdominal thrust. Mechanically assisted cough cannot avoid a tracheostomy if bulbar innervation is inadequate, as in advanced bulbar ALS. Secretion mobilisation techniques that induce a more efficient airway secretion clearance are also helpful and include manual chest percussion and postural drainage. Provision of mechanical in-exsufflation in combination with standard chest physical treatments may improve the management of airway mucous obstruction in NMD [67]. Bronchoscopy should only be considered in cases of persistent atelectasis after all noninvasive airway clearance techniques have been proven to be unsuccessful [16].

ACUTE ON CHRONIC RESPIRATORY FAILURE

Many episodes of ARF usually appear late in the natural history of diseases. Nevertheless, on occasion they may discover a previously undiagnosed disease. Such episodes are usually precipitated by chest infections, as the progression of expiratory muscle weakness, which reduces cough effectiveness, parallels that of the inspiratory muscles. Acute on chronic respiratory failure due to NMD is an important indication for NIV. Despite the lack of randomised controlled studies [69–71], there is agreement on the effectiveness of NIV in preventing endotracheal intubation and avoiding mortality during these episodes. In one study [70], three out of four patients who previously had rejected tracheostomy, but not continuous NIV, survived an episode of ARF treated with NIV. After obtaining the patient's informed consensus and in the absence of severe bulbar involvement, continuous NIV during ARF in NMD must be performed in a specific designated hospital unit by skilled staff with prompt availability of tracheal intubation. Important issues are the appropriateness of the ventilation devices, the availability of several types of interfaces, combining nasal or oronasal masks with a mouthpiece, and the effectiveness of noninvasive aids to clear the patient's airway secretions [72]. Patients should be carefully monitored and, if NIV fails, those who previously have accepted tracheostomy should be intubated without delay. In the patients who reject tracheostomy, all of the futile procedures (including NIV) should be interrupted, and adequate palliative care should be instituted. Once secretions have improved, the patient can often be extubated and NIV resumed. NIV should be used with extreme caution in NMD patients with rapidly progressive NMD syndromes, such as myasthenia gravis or Guillian–Barré syndrome, especially when bulbar muscles are involved.

ANTICIPATORY AND END OF LIFE RESPIRATORY CARE

The World Health Organization defined palliative care as: ''patient and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering. Palliative care throughout the continuum of illness involves addressing physical, intellectual, emotional, social and spiritual needs and to facilitate patient autonomy, access to information and choice'' [73, 74]. As such, palliative care is aimed at: improving QoL; optimising function; supporting medical decision-making and identifying the goals of care; and addressing the needs of family and other caregivers [75]. In contrast, the term ''end-of-life care'' usually refers to care in the final stage of life and focuses on giving care to the dying person and their family. The time period for end-of-life care is arbitrary and is variable depending on the patient's history of disease [76, 77]. The European Respiratory Society (ERS) Task Force on ethics and decision-making in end stage lung disease has defined the end-stage ''restrictive'' respiratory patient as: ''a patient with an FVC of <0.6 L and/or at least one admission for hypercapnic respiratory failure. An additional criterion is the need for assistance with at least one instrumental activity of daily living (*e.g.* housework or shopping), in order to improve the prognostication with respect to life expectancy'' [78]. Using these definitions, palliative care includes end-of-life care, but is broader and also includes care focused on improving QoL and minimising symptoms before the end-of-life period [73].

There are recommendations [79, 80] based on systematic evidence review [81, 82]. The recommendations are as follows.

In patients with serious illness at the end of life, clinicians should regularly assess patients for pain, dyspnoea and depression, and administer therapies of proven effectiveness for pain, dyspnoea (including opioids and oxygen) [83] and depression. They should ensure that advance care planning, including completion of advance directives, (in countries where available and/or legal) takes place for all patients with serious illness. Providing patients and their families with information about treatment options and anticipating possible future needs are crucial steps to appropriately tailor the management of the respiratory issues of NMD patients. NIV is often the only way to sustain NMD patients who decline endotracheal intubation and invasive mechanical ventilation [84]. Since NMD are characterised by a progressive clinical deterioration, these patients must be involved in the decision-making process on treatment escalation, such as endotracheal intubation, tracheotomy and, eventually, the option of palliative care. Although end-of-life care usually refers to care in the final months, weeks or days, there is growing evidence that communication with patients and families about their preferences for end-of-life care should occur early in the course of a chronic life-limiting illness to facilitate high-quality palliative and end-of-life care. Discussing in advance a treatment plan should be a standard of care in these patients, in particular, with patients diagnosed with type 1 SMA and ALS, who are the most fragile subjects.

As expected there are differences in attitudes toward end-of life decisions in different European countries. A survey promoted by the ERS [78] has shown that in European respiratory intermediate care and high dependency units, an end-of-life decision is taken for 30% of the patients admitted. The most common practices were withholding treatment, the use of NIV as a ceiling therapy and provision of a do-not-resuscitate/do-not-intubate order, the latter occurring significantly more frequently in Northern Europe compared with Southern Europe. Patients, when competent, and their families are often involved, together with nurses, in reaching these key decisions.

CONCLUSION

The care of respiratory problems, resulting in prolonging survival by many years and improving QoL in a previously

lethal condition should be considered as a major progress in medicine. Such gains have been made possible mainly due to the use of LTMV in patients with a range of neuromuscular conditions associated with premature death. Even when survival is not prolonged, such as in ALS patients with severe bulbar involvement, NIV therapy may still improve QoL. Having said that we must remember that no care is possible without the sacrifice of the patient's family and caregivers.

STATEMENT OF INTEREST

A statement of interest for N. Ambrosino can be found at www.erj.ersjournals.com/misc/statements.dtl

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