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Authors and Disclosures

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From Expert Review of Respiratory Medicine

The Difficult-to-wean Patient

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Posted: 10/27/2010; Expert Rev Resp Med. 2010;4(5):685-692.

Abstract and Introduction

Abstract

Up to 20% of patients requiring mechanical ventilation will suffer from difficult weaning (the need of more than 7 days of weaning after the first spontaneous breathing trial), which may depend on several reversible causes: respiratory and/or cardiac load, neuromuscular and neuropsychological factors, and metabolic and endocrine disorders. Clinical consequences (and/or often causes) of prolonged mechanical ventilation comprise features such as myopathy, neuropathy, and body composition alterations and depression, which increase the costs, morbidity and mortality of this. These difficult-to-wean patients may be managed in two type of units: respiratory intermediate-care units and specialized regional weaning centers. Two weaning protocols are normally used: progressive reduction of ventilator support (which we usually use), or progressively longer periods of spontaneous breathing trials. Physiotherapy is an important component of weaning protocols. Weaning success depends strongly on patients' complexity and comorbidities, hospital organization and personnel expertise, availability of early physiotherapy, use of weaning protocols, patients' autonomy and families' preparation for home discharge with mechanical ventilation.

Introduction

Up to 40% of patients admitted to intensive care units (ICUs) may require mechanical ventilation (MV) due to acute respiratory failure (ARF) or acute on chronic respiratory failure (ACRF),[1] and this need is increasing.[2] Most ACRF patients and, to a lesser extent, some patients with *de novo* ARF, may be treated with noninvasive MV,[3,4] whereas a minority of these patients in the ICU need invasive MV. There is evidence that 65–85% of these patients undergoing invasive MV, under appropriate clinical conditions, can be successfully extubated, whereas up to 20% of patients will need a prolonged ICU length of stay (LOS) due to difficult weaning.[2] As a consequence of advances in intensive care that have allowed increasing numbers of patients to survive, there is a large and growing population of patients with partial or complete dependence on MV and other intensive care therapies. Recent estimates indicate that there are more than 100,000 such patients in the USA, a number that is also increasing in many other developed countries. This condition is devastating for patients and imposes heavy burdens on healthcare systems (exceeding US$20 billion each year for the US healthcare system as a whole) and family members, who may suffer from depression and practical and financial hardships, with patients' nonprofessional caregivers having to face tasks that require high skills.[5]

Definition of Difficult-to-wean Patient

Patients who need prolonged MV have high resource utilization and relatively poor outcomes, especially the elderly, and are increasing in number.[6] The most recent data suggest that the global prevalence of ventilator-assisted individuals in Europe ranges from two to 30 per 100,000 population in different countries.[7] Difficult-to-wean patients have been variously defined.[8–12] According to the European Respiratory Society (ERS) Task Force, difficult-to-wean patients are those requiring more than 7 days of weaning after the first spontaneous breathing trial (SBT; prolonged weaning).[13] These patients may represent up to 14% of patients admitted to the ICU for intubation and MV and are associated with a in-hospital mortality of up to 32%.[14] The National Association for Medical Direction of Respiratory Care Consensus Conference defined prolonged MV as the need for more than 21 consecutive days of MV for more than 6 h a day.[8] There is evidence that 3–7% of patients fulfill this definition.[12] Some authors suggest that placement of a tracheotomy after at least 10 days of MV defines the onset of prolonged weaning because this definition involves the concept that the patient is not expected to die or to wean from the ventilator in the immediate future.[5]

Causes of Prolonged MV

The most frequent cause of prolonged MV is a severe acute condition over a severe chronic disease.[2] Several pathophysiological factors can lead to prolonged weaning as described in Box 1.[8,13,15–17]

Box 1. Factors associated with prolonged weaning.

Systemic

- Chronic diseases, comorbidities, nutrition and metabolic disturbances
- Severity of illness

Impaired cardiovascular performance

- Left ventricular dysfunction, myocardial ischemia and cardiomyopathy

Neurologic

- Critical illness neuromuscular abnormalities

Respiratory

- Unresolved causes of respiratory failure
- Imbalance between work of breathing and respiratory muscle capacity
- Upper airway obstruction

Treatment complications

- Ventilator-associated pneumonitis and infections
- Barotrauma
- Tracheostomy
- Sedation

Cognitive

- Delirium, depression and anxiety

- Sleep deprivation

Treatment setting

- Weaning protocols
- Staffing
- Staff training

Careful research of potentially reversible pathologies should be conducted in all patients who do not succeed in simple weaning. The pathophysiologic mechanisms leading to weaning failure in this group may be complex and multifactorial, with several potentially reversible etiologies for weaning failure, including: respiratory and/or cardiac load; neuromuscular competence (central and peripheral); critical illness neuromuscular abnormalities; neuropsychological factors; and metabolic and endocrine disorders (Box 1). These factors should be considered in patients requiring MV for more than 7 days.

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In this group of chronically critically ill patients, there is the need for a comprehensive approach to ongoing surveillance for any reversible or irreversible factors.[13] Since long-term MV 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.[18]

Clinical Consequences of Prolonged MV

As a consequence of weaning failure, patients will undergo prolonged ventilator dependence, a component of the 'chronic respiratory illness'. Besides prolonged ventilator dependence, chronic critical illness comprises additional features such as weakness due to myopathy and neuropathy, and body composition alterations such as loss of lean body mass, increased adiposity and anasarca.[5] Other features of this syndrome include specific neuroendocrine changes of anterior pituitary hormones, such as growth hormone, thyrotrophin and prolactin, contributing to low target organ hormone levels and impaired anabolism;[19,20] increased susceptibility to difficult-to-eradicate infections;[21,22] coma or protracted or permanent delirium;[23] nutritional deficiency-associated skin breakdown, edema, incontinence and prolonged immobility.[24]

Some of these features (e.g., brain dysfunction and symptom distress) may also be present in the acute critical illness (or other conditions). Other features (e.g., changes in body composition and neuroendocrine patterns) have only been described in the chronic phase. Chronic critical illness is defined by the presence of this clinical constellation associated with prolonged dependence on MV.[5] Although currently available bedside methods of assessment of respiratory and peripheral muscle function in critically ill patients may be considered somewhat inadequate, evidence suggests that respiratory muscles may be relatively spared from damage resulting from immobility, prolonged MV and systemic inflammation in critical illness.[25] Furthermore, the consciousness of total or partial dependence on a machine for breathing may induce emotional stress in patients requiring prolonged MV (and in their caregivers). The stress may negatively impact ventilator weaning and survival. Depressive disorders have been diagnosed in 42% of difficult-to-wean patients, and patients with depressive disorders seem to be more likely to suffer from weaning failure and reduced survival.[26]

Where to Treat the Difficult-to-wean Patient

It has been claimed that ICUs are expensive resources[2] and probably lack the necessary focus, personnel and organization to care for difficult-to-wean patients.[13,14] Therefore, alternative solutions have been investigated. Two types of units have been proposed as solutions to the problem of the inappropriate use of ICUs:[27]

- Respiratory intermediate care units (RICUs) within acute care hospitals manage patients with ARF or ACRF with noninvasive ventilation, resulting in a significant reduction in ICU admissions and need for invasive MV,[3,4] with an adequate level of assistance, which is less costly than in a ICU. These units may also provide multidisciplinary rehabilitation[28] and serve as a bridge to home care programs or long-term care facilities.[29] Some of these RICUs may work also as 'step-down' units for difficult-to-wean patients;[30,31]
- Specialized regional weaning centers (WCs), often located within rehabilitation hospitals, treat difficult-to-wean patients transferred from several acute care hospitals. Dedicated WCs offer specialized teams (e.g., nurses, respiratory therapists, nutritionists, psychologists and speech therapists) and also relieve pressure on scarce ICU beds at a lower costs. Variable mortality and weaning success rate have been reported.[9–11,31–33]

How to Manage these Patients

Weaning Protocols

Difficult-to-wean patients usually undergo two weaning protocols,[9] namely either a strategy of progressive reduction of level of assistance, such as pressure support ventilation,[34] or progressively longer periods of SBT.[35] Intermittent mandatory ventilation has been proved to be less effective than pressure support ventilation or SBT.[35,36] Indeed, no significant difference in weaning success and mortality rate, duration of ventilatory assistance, WC or total hospital LOS was reported between these two weaning techniques in difficult-to-wean patients,[9] although there is some evidence of a reduction in the duration of MV, weaning duration and LOS with the use of standardized protocols, both in the ICU and in the RICU.[9,37,38] The usefulness of noninvasive ventilation in shortening the weaning time in 'acute weaning' is well defined, whereas similar evidence is lacking in difficult-to-wean patients.[39] In our practice, we usually adopt progressive reduction of ventilatory support and, less frequently, progressively longer periods of SBT according to previously described protocols.[9] On occasion we use a combination of both methods on an empirical basis.

Early Physiotherapy

An important component of the weaning protocols is the availability of physiotherapy. The early mobilization of critically ill patients is a relatively new management approach advocated to address ARF and reduce the disability associated with ICU-acquired weakness.[40] This therapeutic approach has been reported in clinical studies and is recommended by the ERS and the European Society of Intensive Care Medicine Task Force on Physiotherapy for Critically Ill Patients.[41] It has been demonstrated that early physiotherapy results in benefits in critical patients in the ICU.[42–48] On the basis of these reports, the ERS Task Force suggests that efforts to prevent or treat respiratory muscle weakness might have a role in reducing weaning failure through appropriate implementation of physiotherapy in the ICU or transferring patients to dedicated units.[13,41,49,50] In our practice, we use physiotherapy protocols as previously described.[46]

Enteral Nutrition

Weaning from artificial nutritional intake with the subsequent possibility to eat is an essential rehabilitative outcome in severe tracheostomized difficult-to-wean chronic obstructive pulmonary disease (COPD) patients who may undergo different weaning protocols.[18] In tracheostomized difficult-to-wean spontaneously breathing COPD patients, meals may induce an increase in respiratory rate, end-tidal carbon dioxide and dyspnea. Inspiratory pressure support ventilation may prevent dyspnea from worsening during meals.[51]

Percutaneous endoscopic gastrostomy (PEG) as a measure of enteral tube feeding has gained wide acceptance, and it is currently 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 with the nasogastric tube feeding in patients with dysphagia due to chronic neurological diseases. PEG insertion is a quick procedure that is generally well tolerated by patients and a relatively low complication rate in the outcome has been described.[18]

Outcome

Weaning Success

Proposed definitions of weaning success (i.e., patients discharged alive without needing breathing assistance) for these difficult-to-wean patients have included 48 h, 7 days or 14 days without need of MV, or liberation from ventilator support at the time of hospital discharge[8–10,13] or at 6 months–1 year after the onset of MV. Between 30 and 53% of chronically critically ill patients are liberated from MV in the acute care hospital.[52] Average time to

ventilator liberation varies with the severity and type of illness or injury, but typically ranges from 16 to 37 days after intubation for respiratory failure.[53] If the patient fails to wean from ventilator dependence within 60 days, they will probably not do so later.[54] Better outcomes are reported for some specialized WCs, but they often select patients with a higher potential for ventilator liberation and rehabilitation.[13,54,55] The literature reports great variability in the clinical outcomes of WCs.[8,13,56] Observational studies indicate a 34–60% successful weaning rate in WCs.[57,58] Recently it has been shown that the sequential activity of a RICU and a WC resulted in an additive weaning success rate (up to 80%) of difficult-to-wean patients with reduced costs compared with the ICU.[32] Such differences in weaning success definition may be related to differences in patient population, discharge criteria and specific characteristics of the institutions.[8] Similarly, hospital mortality and LOS are widely variable.[59]

Hospital Mortality

Hospital mortality varies from 6 to 50%, depending on admission criteria, severity of clinical status and underlying diseases, and likelihood of transfer to a different facility when patients become acutely ill.[9–12,24] While patients who remain ventilator dependent are at a higher risk of death, successful weaning does not assure long-term survival as most patients have underlying comorbid conditions, residual organ dysfunction and intercurrent complications. Acute hospital mortality for unselected patients is generally reported in the range of 20–49%.[23,52,53] Across study populations, 1-year mortality is 48–68%, with little change over the past 20 years.[31,52,54] Compared with patients requiring short-term MV, the risk of death in patients with prolonged MV remains particularly high between 60 and 100 days after MV initiation.[60,61] However, comparison among studies of different centers and different periods may be not appropriate, as weaning success seems to strongly depend on patients' complexity and comorbidities,[33] hospital organization and personnel expertise,[62,63] availability of early physiotherapy,[43–45] use of weaning protocols,[9] patients' autonomy and families' preparation for home discharge with MV.[64] When evaluating outcomes, it is necessary to consider the severity of patients at admission, as Schonhofer *et al.* showed that use of the Acute Physiological And Chronic Health Evaluation II prognostic system at admission was able to successfully differentiate from unsuccessfully weaned patients.[65]

Tracheostomy

Studies have identified chronically critically ill patients by elective placement of a tracheostomy to facilitate prolonged MV and weaning efforts.[66–68] The need of elective tracheostomy means that the patient will neither wean nor die in the immediate future, a point of demarcation between acute and chronic critical illness that is considered both clinically meaningful and practical.[5] The use of tracheostomy seems to increase in patients requiring prolonged MV,[69] although the advantage of this strategy on outcome is still discussed. In some studies, tracheostomy did not favorably influence ICU survival,[70,71] whereas it has been reported that tracheostomy performed in ICU for long-term MV patients was associated with lower ICU and in-hospital mortality rates.[72] There is considerable variability in the indications and time considered optimal for performing tracheostomy. Among mechanically ventilated adult ICU patients, early tracheotomy compared with late tracheostomy did not result in a statistically significant improvement in the incidence of ventilator-associated pneumonia.[73] Nevertheless, some authors support the usefulness of tracheostomy protocols based on a standardized approach to ventilator weaning.[74] Consequently, the decision to perform tracheostomy is more of an experience- than an evidence-based decision and should be made with caution. Efforts should be made to identify patients who might clearly benefit from this technique to avoid unnecessary and unwanted prolonged MV.

Tracheostomy tube malposition is a relatively common complication in patients with ARF who are recovering from critical illness and is associated with need for prolonged MV;[75] therefore, it should be considered in mechanically ventilated patients who unexpectedly fail to be liberated from MV. Although surgical expertise is a risk factor, identifying patients who are at risk for this complication is difficult.[76] A recent survey on 719 patients from 22 Italian RICUs shows that tracheostomy was maintained in a substantial proportion of patients without any need for home MV.[77] The clinical relevance of decannulation at discharge is supported by a recent study that showed that a lack

of decannulation of conscious tracheostomized patients before ICU discharge to the general ward was associated with higher mortality.[78]

Customer Satisfaction

The reported outcome of prolonged weaning may be not satisfactory for patients and relatives. In a study of 1-year patient outcomes for prolonged MV, patients were significantly worse than expected by patients' relatives and physicians. Lack of prognostication about outcomes, discordance between relatives and physicians about potential outcomes and relatives' unreasonably optimistic expectations seem to be potentially modifiable deficiencies in relative–physician interactions.[79] Recently, we studied the families' perception of care in patients under home MV during the last 3 months of life.[80] In 11 respiratory units, we submitted a 35-item questionnaire to relatives of 168 deceased patients exploring six domains: symptoms, awareness of disease, family burden, dying, and medical and technical problems. The response rate was 98.8%. The majority of patients complained of respiratory symptoms and were aware of the severity and prognosis of the disease. Family burden was high, especially in relation to money need. During hospitalization, 74.4% of patients were admitted to the ICU. A total of 78 patients died at home, 70 patients in a medical ward and 20 in the ICU. Overall, 27% of patients received resuscitation maneuvers. Hospitalizations and family economic burden were unrelated to diagnosis and MV. Families of the patients did not report major technical problems with the use of ventilators.[80] In comparison with mechanically invasively ventilated patients, noninvasively ventilated patients were more aware of prognosis, used more respiratory drugs, changed ventilation time more frequently and died less frequently when under MV.

Costs

Although advances in intensive care have enabled more patients to survive an acute critical illness, they also have created a large and growing population of chronically critically ill patients with prolonged dependence on MV and other intensive care therapies.[81] Chronic critical illness is a devastating condition: mortality exceeds that for most malignancies, while functional dependence persists for most survivors. Costs of treating the chronically critically ill in the USA already exceed US$20 billion and are increasing.[5] Long-term weaning units may be cost-effective alternatives to acute ICUs in the management of difficult-to-wean patients. Several observational studies estimate lower daily costs of care for ventilator-dependent patients in WC, primarily through reduced need of personnel, and reduced costs for monitoring (e.g., noninvasive), technical equipment (e.g., portable ventilators), diagnostics and therapeutics.[11,32,82]

Expert Commentary

Although advances in intensive care have allowed an increasing number of patients to survive an episode of ARF or ACRF, they have also created a large and growing population of patients with partial or complete dependence on MV and other intensive care therapies. These patients who neither die nor recover in the ICU have also been defined as 'chronically critically ill'. Recent estimates indicate that there are more than 100,000 such patients in the USA, a number that is also increasing in many other developed countries. This condition is devastating for patients and their families, and is also expensive. Incidence and expenditures are rising mainly due to older elderly adults receiving aggressive medical and surgical treatments. Most patients with chronic critical illness leave the hospital with severe derangements of physical and cognitive status, and therefore require institutional care or home familial or nonprofessional assistance. Hospital re-admission rates during the year after hospital discharge exceed 40%. Patients discharged to extended-care facilities who cannot return to home by 6 months usually remain institutionalized until death, if healthcare services provide these facilities. When facilities are lacking, this condition imposes heavy burdens on family members, who may suffer from depression and practical and financial hardships. Studies of the nonprofessional caregivers of patients requiring prolonged MV indicate that depressive symptoms are more severe in this group than among caregivers of patients with Alzheimer's disease or spinal cord injury and that

depression continues for months after the patient is discharged from the hospital or dies. Moreover, these caregivers also report a decline in physical health and increase in 'caregiving overload' during the post-discharge period. These nonprofessional caregivers have to face tasks requiring high skills, such as management of tracheostomy, setting of ventilators and enteral nutrition, with relevant economical, psychological and emotional consequences, such to require hospital admission in order to give physical and psychological relief to the caregiver. In other words, these difficult-to-wean patients represent an example of the future challenges for public or private healthcare services, with disturbing questions such as these: 'In a globalized world is it worthwhile to spend human and financial resources to 'prolong suffering' of such patients whereas in some parts of the globe children have no water to survive?.'; 'Is it ethical to perform aggressive medical and surgical therapies for such patients with low life duration and high sufferance expectancy?.' This turns us to end of life decision making, an issue deserving a dedicated chapter, not only a commentary. A suggested approach has been the use of noninvasive MV in palliative care, a position still discussed.[83] There are different approaches among different countries on withholding and withdrawal of care, depending on religious, ethical and organizational factors. In a survey of European respiratory intermediate-care units and high-dependency units, an 'end of- life decision' was taken for 30% of the patients admitted. The most common practices were withholding treatment, the use of noninvasive MV as a ceiling therapy and provision of a do-not-resuscitate/do-not-intubate order, the latter occurring significantly more frequently in North Europe compared with South Europe. Patients, when competent, and their families were often involved, together with nurses, in reaching these key decisions.[84] Use of advance directives should be encouraged and accepted in all countries.[85,86]

Five-year View

The aforementioned fundamental questions are relevant, but, independent of ethical, religious and even economical considerations, the present evidence does not allow a definite response and it is hard to believe that it will be found in the next 5 years. Many factors prevent research on this topic. The successes of ICUs in achieving short-term survival have prevented this area to be recognized as an important focus of scientific investigation. Areas to be researched in the near future are the different facilities available to care for these patients, with the problem of generalization from one setting to another. In the near future, a consensus on a definition of this condition needs to be reached. A common definition would be beneficial for interventional studies in which patients are prospectively enrolled. A large multicenter, multicountry research network including a broad range of venues for care of the chronically critically ill should be supported and developed. Studies on pathobiology and pathophysiology of chronic critical illness as distinct from acute critical illness are needed. We also need well-designed trials testing approaches to the best management of prolonged MV (including setting, protocols and interfaces), nutritional support, delirium, symptoms (drug therapy of dyspnea) and physical weakness. Comparative research of economic analyses should be conducted to compare the cost–effectiveness of care in acute hospitals versus at specialized facilities versus home.

Sidebar

Key issues

- Patients admitted to intensive care units requiring mechanical ventilation may suffer from difficult weaning.
- Reversible causes for weaning failure may be: respiratory and/or cardiac load, neuromuscular abnormalities, neuropsychological factors, and metabolic and endocrine disorders.
- As a consequence of weaning failure, patients may undergo need for prolonged ventilator dependence, a component of the 'chronic respiratory illness'.
- These difficult-to-wean patients may be managed in two type of units: respiratory intermediate-care units and specialized regional weaning centers.
- Usually two weaning protocols are used: progressive reduction of ventilator support, or progressively longer periods of spontaneous breathing trials.

- Physiotherapy is an important component of weaning protocols.
- Studies report great variability in the clinical outcomes of weaning protocols.
- The decision to perform tracheostomy should be made with caution, and efforts should be made to identify patients who might clearly benefit from this technique to avoid unnecessary and unwanted prolonged mechanical ventilation.

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Papers of special note have been highlighted as:
• of interest
•• of considerable interest

Financial & competing interests disclosure
The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.
No writing assistance was utilized in the production of this manuscript.

Expert Rev Resp Med. 2010;4(5):685-692.