Patient–Clinician Alliance during Prolonged Mechanical Ventilation

"Never Give Up on a Dream"

Perception is often quite different from reality. This observation fits very well in medicine. In fact, despite extensive experience, many clinicians tend to under- or overestimate the outcomes of their patients (1). The perception of a poor prognosis in patients requiring prolonged mechanical ventilation is a classic example of this phenomenon, which can lead to dramatic ethical dilemmas about the value of continuing the "artificial" support at the expense of the patient's quality of life, which is often presumed to be miserable (2).

In this issue of the *Journal*, Jubran and colleagues (pp. 1508–1516) challenge this idea in a prospective 1-year study conducted in 315 consecutive patients from a large cohort of subjects enrolled in a previous clinical trial, comparing weaning methods in long-term ventilated patients admitted to a long-term acute care hospital (LTACH) (3, 4).

In line with previous findings from LTACH studies (4, 5), more than 50% of the patients were liberated from mechanical ventilation. However, the most important and novel results were that the majority of subjects at discharge regained the ability to perform daily activities independently, and 85% of survivors indicated a willingness to undergo ventilation again if deemed necessary.

Interestingly, in patients who were still alive at 12 months, respiratory muscle strength was quite well preserved at LTACH admission and did not change during the following year, whereas peripheral strength was very impaired but recovered with time, allowing an overall satisfactory quality of life (3). This was not the case for the patients who died, as they had a severe generalized muscle weakness (in both limb and respiratory muscles) that did not improve during the LTACH stay.

The study by Jubran and colleagues is important because it raises several considerations concerning the weaning process in the ICU, the best location where weaning should be performed in cases of prolonged ventilation, the mechanisms that lead to long-term functional recovery, and lastly, the patient's perception of this often devastating experience.

First, patients experiencing prolonged ventilation represent a relatively small subset of patients admitted to an ICU, and although many survivors in Jubran and colleagues's study regained satisfactory autonomy, it should be kept in mind that more than half of the 315 patients died within the 12-month follow-up period (3).

The question that arises is, were these individuals already very sick at ICU admission or did they deteriorate because of prolonged ventilation and the ICU stay? In other words, did these patients receive the best weaning practice, as they did during the LTACH stay?

Little details can make a big difference in the care of mechanically ventilated patients, including the ventilator setting, which can result in under- or overassistance of the diaphragm (6); the judicious use of sedation (7) and medical therapy; the use of care bundles to prevent infections (8); the avoidance of delirium; the prompt recognition of weanibility by means of the appropriate tests (9); and last but not least, early mobilization while patients are on mechanical ventilation (9).

Whatever the medical history of these patients, LTACHs are probably the best settings in which to attempt to liberate them from prolonged ventilation.

On arrival, each patient was evaluated by rehabilitation professionals (occupational therapist, physical therapist, and speech-language therapist) to determine his or her functional status and rehabilitative needs. An exercise-training program was initiated thereafter for a minimum of 30 min/d. In addition, the weaning protocol using pressure support or a tracheostomy collar was strictly supervised (being the procedural part of a randomized controlled trial) (4). Interestingly, 109 of the 315 patients (35%) were not randomized, because they were able to be liberated from the ventilation after the first attempt in the LTACH, suggesting that in the originating ICU the feasibility of weaning was probably not always evaluated at the proper time.

Given the increasing number of patients undergoing prolonged ventilation and tracheotomy, over the last two decades there has been a rapid rise in LTACH use in the United States (10). The main benefits of these units are related to the environment itself, which offers less sleep disturbance, lower light and noise intensity (11), and more liberal visiting hours. In addition, the LTACH enables clinicians to respond to sudden changes in a patient's clinical condition, allows enough time for a multidisciplinary rehabilitation approach, and serves as a bridge to home-care programs or other forms of continuous assistance (e.g., telemedicine or dedicated long-term units). However, the levels of assistance in LTACHs are not homogeneously distributed, so the conclusions of Jubran and colleagues may not be generalizable.

Upon enrollment the patients who survived at 12 months had a relatively preserved respiratory muscle strength that did not improve between admission and discharge, whereas handgrip strength was very low on arrival and increased during the LTACH stay. The comprehensive rehabilitation program that was continued after LTACH discharge could probably explain this result. In fact, only 11.8% of the patients were sent directly home, and the others were transferred either to a rehabilitation facility or to skilled nursing centers.

As discussed by the authors, physiological studies performed in the ICU showed that diaphragm contractility, assessed using phrenic nerve stimulation, was not different between patients who were successfully weaned and those who failed to wean (12). However, other investigators have demonstrated that the development of diaphragm atrophy during mechanical ventilation strongly impacts clinical outcomes (6). In addition, it was shown that diaphragm dysfunction occurs twice as frequently as limb muscle weakness and has a direct negative impact on weaning outcomes, and that the two types of muscle weakness have only limited overlap (13). It should also be kept in mind that strength itself represents only one side of the so-called load/capacity index (14), i.e., the ratio between the tidal effort that the diaphragm needs to face to overcome the inspiratory load, and the maximal pressure that can be elicited (which unfortunately was not recorded in Jubran and colleagues's study).

Lastly, the authors reported that 85% of the patients said that they would be willing to undergo the experience of prolonged

The quote in the title is from "Never Give Up on a Dream" by Rod Stewart (November 6, 1981).

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mechanical ventilation again if deemed necessary, and they speculated that the "remembering-self" was probably the leading reason for this affirmation.

This is in keeping with another study that showed that patients would choose to receive aggressive treatment, but only if survival was not associated with severe functional or cognitive impairment (15).

The major factor in a patient–clinician interview is how it is conducted, and this detail is not specified in the article. It has been suggested that "little white lies" in this bidirectional communication are quite common; sometimes in an attempt to "please my doctor who saves my life," a patient may minimize his or her symptoms or bad experiences (16).

In conclusion, this study, besides being well conducted and providing important clinical information, clarifies the issue that perception in medicine may be very misleading. Therefore, the patient and clinician, allied together, should never give up on the dream to liberate the patient from prolonged ventilation and recover a satisfactory quality of life. ■

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Stefano Nava, M.D., F.E.R.S.
Lara Pisani, M.D.
Sant'Orsola Malpighi Hospital
Alma Mater Studiorum, University of Bologna
Bologna, Italy

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Defining the Cell Types That Drive Idiopathic Pulmonary Fibrosis Using Single-Cell RNA Sequencing

Few novel technologies have been welcomed with more excitement by the scientific community than single-cell RNA sequencing (scRNA-seq). The report by Reyfman and colleagues (pp. 1517–1536) in this issue of the *Journal* provides important insight into pathogenic cell types in lung fibrosis on an unprecedented scale (1), making idiopathic pulmonary fibrosis (IPF) the first chronic lung disease to be analyzed using scRNA-seq (#CureIPF).

A single cell is the fundamental unit of life. Dissecting the heterogeneity, dynamics, and interactions of cells will truly unravel how we, as well as diseases we are trying to cure, develop and grow. Until recently, the characterization of specific cell types (of the lung) relied on *ex vivo* labeling or generating large numbers of cells based, at times, on poorly understood isolation techniques, followed by analysis of pooled RNA or proteins for hybridization or sequencing. Although these approaches have revealed robust cell

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