Neurally Adjusted Ventilatory Assist in Difficult Weaning

Promising Findings on a Prickly Issue

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Weaning from mechanical ventilation is defined as a separation of the patient from the ventilator. Because prolonged mechanical ventilation is associated with a risk of multiple complications (*i.e.*, hospital-acquired infections, intensive care unit–acquired neuromuscular disorders, ventilator-induced lung injury, diaphragm dysfunction, *etc.*), shortening the weaning phase clearly constitutes a major clinical challenge, especially in the case of difficult-to-wean patients, who are particularly exposed to the devastating consequences of prolonged mechanical ventilation. Over recent decades, manufacturers and researchers have worked together and developed various tools to hasten weaning. Proportional assist modes of mechanical ventilation seem promising techniques with which a level of assistance is proportional to the need of the patients. Neurally adjusted ventilatory assist is one of these proportional assist modes. Neurally adjusted ventilatory assist delivers a level of assistance that is proportional to the electromyographic activity of the crural diaphragm (monitored by a nasogastric feeding tube equipped with electrodes), a close surrogate for the respiratory drive.

"…neurally adjusted ventilatory assist may become the preferred mode of mechanical ventilation in difficult-to-wean patients."

In this issue of Anesthesiology, Liu *et al.*[1] report a randomized clinical trial that evaluates the impact of neurally adjusted ventilatory assist in difficult-to-wean patients. Difficult weaning was defined as one failure of the spontaneous breathing trial or one reintubation within 48 h after extubation. Over a 6-yr period, 99 patients were randomly assigned to neurally adjusted ventilatory assist or pressure support ventilation. The primary outcome was the duration of weaning, defined as the time from study enrollment to successful ventilator liberation. Clinically relevant secondary outcomes were the proportion of patients with successful weaning, ventilator-free days, and mortality. The two groups were correctly balanced on inclusion. Patients were mechanically ventilated for 5 days. The predefined ventilator strategy from randomization to extubation was clearly described for both groups. The main and major result of the study was the shorter duration of weaning in the neurally adjusted ventilatory assist group compared to the pressure support ventilation group (3 *vs.* 7 days). In addition, the proportion of patients with successful weaning from invasive mechanical ventilation was higher in the neurally adjusted ventilatory assist group (33 of 47, 70%) than in the pressure support ventilation group (25 of 52, 48%). Finally, the number of ventilator-free days at day 14 and day 28 was higher in the neurally adjusted ventilatory assist group than in the pressure support ventilation group. However, mortality was not significantly different between the two groups (48% *vs.* 34% in the pressure support ventilation group and neurally adjusted ventilatory assist group, respectively).

Neurally adjusted ventilatory assist has been available for clinicians for more than 10 yr. Physiologic studies have demonstrated that neurally adjusted ventilatory assist improves load/capacity balance and patient–ventilator interaction, prevents lung overdistension, and improves patient–ventilator asynchrony.[2] However, to date, few studies had evaluated the benefit of neurally adjusted ventilatory assist in terms of clinical outcomes. In a study comparing neurally adjusted ventilatory assist and pressure support ventilation, neurally adjusted ventilatory assist did not improve the weaning process and did not reduce the duration of mechanical ventilation in an unselected population of critically ill patients.[3] While neurally adjusted ventilatory assist is

Image: J. P. Rathmell.

This editorial accompanies the article on p. 1482.

Accepted for publication February 25, 2020. From Sorbonne University, Institut National de la Recherche Scientifique, UMRS1158, F-75005 Paris, France (A.D., M.D.); and AP-HP, Groupe Hospitalier Universitaire Assistance Publique - Hôpitaux de Paris, site Pitié-Salpêtrière, Medical Intensive Care Unit and Respiratory Division, Paris, France (A.D., M.D.).

not superior to pressure support ventilation in simple weaning, it seems to be beneficial in a population in which the quality of patient–ventilator interactions is essential, such as difficult-to-wean patients.[4] This is the major strength of the study by Liu *et al.*[1] If these results are further confirmed by future studies, neurally adjusted ventilatory assist may become the preferred mode of mechanical ventilation in difficult-to-wean patients. Indeed, by reducing the duration of weaning and increasing the weaning success rate, it may significantly improve the prognosis of these patients. It also means that clinicians will need to learn how to use neurally adjusted ventilatory assist, which requires some training.

The study suggests that neurally adjusted ventilatory assist was especially beneficial in the population of difficult-to-wean patients because it provides a more lung- and diaphragm-protective ventilation. Indeed, it has been clearly established that neurally adjusted ventilatory assist prevents lung overdistension by reducing the level of assistance when the electromyographic activity of the diaphragm decreases,[5] which protects the lung against ventilator-induced lung injury. Neurally adjusted ventilatory assist may also protect the diaphragm against ventilator-induced diaphragm dysfunction, as neurally adjusted ventilatory assist reduces the level of assistance when the electromyographic activity of the diaphragm is too low, thereby constantly maintaining a certain level of diaphragm activity. It is not unrealistic to hypothesize that strict lung- and diaphragm-protective ventilation would be more beneficial in difficult-to-wean patients that in an unselected intensive care unit population, especially in tracheostomized patients, as tracheostomy is generally performed in the most difficult-to-wean patients. Another explanation could be the beneficial impact of neurally adjusted ventilatory assist on dyspnea,[6] because neurally adjusted ventilatory assist adjusts the level of assistance to the patient's neural respiratory drive, thereby reducing the prevalence of dyspnea,[3] which is associated with more difficult weaning.[7] It is of notice that the reduction of patient–ventilator asynchrony observed in the neurally adjusted ventilatory assist group does not seem sufficient to explain this benefit, as in a previous study in unselected patients, a dramatic reduction of patient–ventilator asynchrony was not associated with a shorter duration of weaning or smoother weaning.[3]

This study has limitations. First, this was a single-center trial conducted by a team reporting a high level of experience with neurally adjusted ventilatory assist. The results of this study may therefore not be automatically transposable to another intensive care unit. However, they remind us that a ventilatory mode such as neurally adjusted ventilatory assist requires expertise and that a team wishing to use neurally adjusted ventilatory assist must complete systemic and adequate training. Second, and this is a major limitation of the study, tracheostomy was performed after randomization in a high proportion of patients (40% in the pressure support ventilation group and 28% in the neurally adjusted ventilatory assist group), and the indication for tracheostomy was not clearly defined in the protocol. In addition, while a very precise weaning protocol was applied in intubated patients, a less rigorous weaning protocol was applied in tracheostomized patients. Sensitivity analyses showed that the primary outcome, duration of weaning, was shorter in the neurally adjusted ventilatory assist group, but only for the 34 tracheostomized patients (5 *vs.* 14 days in the pressure support ventilation group). It is noteworthy that the duration of weaning was not significantly different among the 65 nontracheostomized patients (3 days in the neurally adjusted ventilatory assist group *vs.* 5 days in the pressure support ventilation group). Similar results were observed for ventilator-free days at day 14 and day 28. What is the explanation for this difference? First, patients who underwent tracheostomy after randomization were ventilated for a longer period of time (7 *vs.* 4 days) than those who remained intubated. Second, the duration of weaning was much longer in tracheostomized patients of the pressure support ventilation group than in the other patients. Any intervention decreasing the duration of weaning in these patients would, therefore, be beneficial.

In conclusion, Liu *et al.* demonstrate the clinical benefit of neurally adjusted ventilatory assist in difficult-to-wean patients. They should be commended for having conducted such a complicated study over such a long period of time. In the near future, neurally adjusted ventilatory assist could definitely become a major tool to facilitate weaning in difficult-to-wean patients. Because of the discrepancy of the results between tracheostomized and nontracheostomized patients in this single-center study, further multicenter studies are needed to ensure their finding can be generalized. Liu *et al.* have paved the way for future studies to determine the role of neurally adjusted ventilatory assist facilitating weaning certain populations such as very asynchronous, severe chronic obstructive pulmonary disease, or severely dyspneic patients.

Competing Interests

Dr. Demoule reports personal fees from Medtronic (Dublin, Ireland), grants, personal fees, and nonfinancial support from Philips (Carlsbad, California), personal fees from Baxter (Deerfield, Illinois), personal fees from Hamilton (Bonaduz, Switzerland), personal fees and nonfinancial support from Fisher & Paykel (Auckland, New Zealand), grants from the French Ministry of Health (Paris, France), personal fees from Getinge (Gothenburg, Sweden), grants and personal fees from Respinor (Oslo, Norway), and grants and nonfinancial support from Lungpacer (Exton, Pennsylvania), unrelated to the submitted work. Dr. Dres reports personal fees from Lungpacer (Exton, Pennsylvania), unrelated to the submitted work.

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