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EDITORIAL

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NAVA: brain over machine?

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The goal of mechanical ventilation in the acute setting is to "buy time" to give a patient a chance to recover from some catastrophe. The ideal ventilator would not damage the respiratory muscles or lung parenchyma. Over the last few years we have become increasingly aware of potential morbidity and mortality associated with overzealous [1–3] or insufficient [4] ventilator support. In addition, accumulating evidence suggests that patient-ventilator dyssynchrony may be a harbinger of poor outcome[5]. To overcome the problems of excessive (or insufficient) support and dyssynchrony, an ideal ventilator should be able to record the activity of the respiratory neural system, and use that measurement to select a satisfactory tidal volume. At this time, it is not feasible to record the activity of the respiratory centers in patients. The newly introduced neurally adjusted ventilatory assist (NAVA), with the recording of the electrical activity of the diaphragm, comes close. NAVA provides pressure assistance in proportion to the electrical activity of the diaphragm [6]. Like proportional assist ventilation [7], NAVA ensures a positive relationship between the ventilator assistance and the patient's spontaneous effort. With NAVA, this relationship is based upon a gain factor, set by the clinician, which translates a given electrical activity of the diaphragm into pressure assist. The positive relationship between ventilator assistance and patient effort ensured by NAVA (and proportional assist ventilation) contrasts with volume or pressure controlled modes [8, 9].

In the current issue of *Intensive Care Medicine*, Colombo et al. [10] show, for the first time, that compared to pressure support ventilation, NAVA avoids over-assistance and patient-ventilator dyssynchrony. NAVA enabled greater variability in tidal volume than did pressure support, and thus a more natural ("noisy") breathing pattern [11]. No data on the comfort of these critically ill and partially sedated patients in response to NAVA as compared to pressure support was provided. Does this mean that the quest for the ideal ventilator is over?

Central to the delivery of NAVA is the assumption that the electrical activity of the diaphragm accurately represents the output of the respiratory centers. In critically ill patients, though, this assumption is not necessarily true—at least when employing pressure support ventilation [12]. A second fundamental assumption is the appropriateness of the neuroventilatory coupling. Is the output of the respiratory centers appropriate to the ventilatory needs of that patient? The latter point rests on at least three suppositions. One, that the feedback mechanisms linking the respiratory system (bellows, gas exchange units, and chemoreceptors) with the respiratory centers are intact. Two, that the mechanical and chemical receptors responsible for monitoring respiratory function have the proper sensitivity. Three, that the response of the respiratory centers to perturbations has, at any given time, the proper gain. Do these assumptions always hold in critically ill patients? Probably not. Pulmonary inflammation or insults to the central nervous system can lead to excessive output of the respiratory centers for any given

ventilatory requirement. Impaired connections between the peripheral receptors and the respiratory centers, sedatives, and organic insults to the central nervous system can have the opposite effect. How can NAVA support patients where there is an uncoupling between respiratory motor output and respiratory demands? Will the intensivist be able to identify the correct NAVA gain—one not too small to prevent muscle injury due to overuse or one too large to cause ventilator-induced diaphragmatic dysfunction [13] or ventilator-induced lung injury? [2, 3] Despite the encouraging results of Colombo et al. [10], it is not possible to answer these questions at this time.

Notwithstanding current theoretical difficulties in setting the gain of NAVA in different clinical conditions, NAVA has the potential for rendering obsolete any discussion of patient-ventilator dyssynchrony. A common reason for dyssynchrony is the lack of sensitivity of triggering systems that rely only on flow or airway pressure signals to identify the start of inspiratory effort. NAVA, by relying "also" on the electrical activity of the diaphragm, overcomes the limitations of flow- and pressure-triggering. As suggested by the findings of Colombo et al. [10], a properly operating NAVA system should be free of dyssynchrony. Most exciting, and unique to NAVA, is the identification of the start of neural exhalation. The start of neural exhalation is not recognized by assist-control ventilation [14] or pressure support ventilation [15]. Of the commercially available modes, only proportional assist ventilation comes close to this type of synchrony [7]. The potential for improved "on" and "off" ventilator triggering, and thus elimination of dyssynchrony, by NAVA could have important clinical implications. These may include improved patient's comfort [16] and consolidation of sleep [17, 18]. By ensuring that the duration of assisted mechanical inflation parallels the duration and timing of neural inhalation, NAVA may prevent possible damage to respiratory muscle fibers due to plyometric contractions. These are eccentric muscle contractions or contractions occurring while a muscle is being stretched [19]. In peripheral muscles, eccentric contractions can induce cytokine release [20] and Z-band disturbances, which are more pronounced in Type 2 fibers than in Type 1 fibers [21]. As such, Type 2 fibers appear to be recruited more than Type 1 fibers during eccentric contractions [22]. We remain unsure, however, whether eccentric contractions contribute to the diaphragmatic weakness seen in critically ill, mechanically ventilated patients [23].

In vivo recordings of the electrical activity of the diaphragm are always contaminated by electrical signals originating in the heart. In a remarkable technical feat, NAVA can deal with this contamination in real time. For any identified cardiac artifact, NAVA removes the contaminated segment and substitutes it with a computed signal. The correction for cardiac artifacts, however, may affect the shape, timing, and duration of NAVA's ventilator support. And the fact that most patients in respiratory distress are tachycardic raises the question of whether this correction for cardiac artifacts impacts the adequacy of tidal volume delivered by NAVA, patient comfort, and patient-ventilator synchrony.

Could a progressive decrease in the gain of NAVA expedite weaning? Probably not. Such a strategy would be similar to a progressive decrease in pressure-support ventilation. Although progressive decreases in pressure-support ventilation are usually associated with improvement in patient-ventilator synchrony [24], this strategy does not hasten weaning [25].

The right niche for NAVA is not clear. One of the main benefits should be improved patient-ventilator synchronization. I would also expect a more noisy, more natural breathing pattern. Altogether, we can expect patients experience greater respiratory comfort—even those at risk of dynamic hyperinflation. NAVA represents true assertion of brain over machine.

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