Inspiratory Muscle Activity in Neurally Adjusted Ventilatory Assist

More than Sonata for "Solo Diaphragm"

Nicolas Terzi, M.D., Ph.D., Paolo Navalesi, M.D.

MECHANICAL ventilation (MV) is the form of supportive therapy most frequently used in the intensive care unit. Although a life-saving intervention for patients admitted to intensive care unit with acute respiratory failure, MV is not free of side effects. Well-known complications of MV are ventilator-induced lung injury, high oxygen concentration toxicity, upper airway damage or dysfunction, inappropriate and delayed sedation, acquired pulmonary infections, altered hemodynamics, sleep disturbances, and psychic distress. Two additional issues have been increasingly recognized in the last decade as major problems associated with MV, ventilator-induced diaphragmatic dysfunction[1] and a poor patient–ventilator interaction leading to dyssynchrony between spontaneous respiration and ventilator assistance.[2] Both ventilator-induced diaphragmatic dysfunction and dissynchrony have received growing attention because they are potential determinants of prolonged MV and intensive care unit stay.[3] In this issue of Anesthesiology, Cecchini *et al.*[4] provide novel information on inspiratory muscle activity during assisted MV.

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Experimental data confirmed in humans that even relatively brief periods of controlled MV can induce ventilator-induced diaphragmatic dysfunction.[1] Accordingly, forms of partial mechanical assistance, where the patient's respiratory muscles and the ventilator contribute to generate the ventilatory output, have been privileged in recent years, whenever possible and safe. Ideally, because with these modes the ventilator is triggered by the patient's inspiratory effort, the respiratory muscles should be active enough to avert the risk of ventilator-induced diaphragmatic dysfunction, and the respiratory rhythm should be under control of the patient's respiratory centers, thereby assuring patient–ventilator synchrony.

Unfortunately, things are not as straightforward as we would like them to be. On the one hand, it has been recently shown that during pressure support ventilation (PSV), probably the most widely used assisted mode, protracted high levels of ventilator assistance may drastically reduce diaphragm activity and promote atrophy and contractile dysfunction.[5] On the other hand, several studies repeatedly proved that patient–ventilator synchrony is not guaranteed with the conventional forms of partial assistance, such as PSV, assist/control, and the various mandatory modes, irrespective of the underlying disease.[6–8]

For these reasons new forms of partial ventilator assistance emerged, aimed to avoid excessive support and guarantee persistent diaphragm activity, enhance patient–ventilation interaction and synchrony, and facilitate the natural breath-to-breath variability, while maintaining adequate gas exchange and optimal patient comfort.[9] In particular, two "proportional" modes were developed and are presently available for clinical use, proportional assist ventilation and neurally adjusted ventilator assist (NAVA), where the effort exerted by the respiratory muscles directly (NAVA) or indirectly (proportional assist ventilation) drives and regulates ventilator functioning.[9] Ventilation with both modes remains under patient control, and although proportional

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assist ventilation uses the "conventional" pneumatic signals, that is, flow and volume, NAVA has the unique feature to control ventilator functioning through the electrical activity of the diaphragm (EAdi).

In NAVA, the inspiratory assistance is proportional to EAdi, which corresponds to muscle fibers depolarization, occurring immediately after the output of the central respiratory centers and just before the intrathoracic pressure variations induced by muscle contraction.[10] In addition to proportionality, the "neural" on–off triggering of the mechanical support also offers potential advantages, especially for the patients with severely impaired respiratory mechanics and muscle function. Compared to the conventional pneumatically driven modes, in fact, NAVA reduces the inspiratory trigger delay, harmonizes the patient's offend-inspiration with the cycling off of the ventilator, and reduces the asynchronies that occur between the patient and the ventilator during either invasive[6,7] and noninvasive[11,12] ventilation. In the end, during NAVA, the ventilator assistance is ideally synchronous and proportional, to an extent that depends on a preset gain factor, to the activity of the principal inspiratory muscle. Though the principal inspiratory muscle is the diaphragm, it is not the only one. Indeed, the act of breathing resembles the symphony produced by the synchronous and synergic activity of a variety of instruments (the inspiratory muscles), rather than a sonata for solo instrument (the diaphragm). When the activity of one muscle prevails, chest wall paradoxical movements and distortion occur, leading to expensive and energetically inefficient breathing.

Cecchini *et al.*[4] assess and compare the effects of PSV and NAVA, set at comparable levels of assistance, on EAdi, as obtained by transesophageal electromyography, and on the electrical activity of the scalene (EAscal) and *alae nasi* (EAan) muscles, both assessed by means of surface electromyography. Both modes reduced EAdi and the overall extradiaphragmatic inspiratory muscle activity in rapport to the level of assistance. While the decrease in EAdi was similar to the two modes, NAVA produced a significantly greater reduction in EAscal, as opposed to PSV, at highest and lowest levels of assistance. The reduction in EAan was also greater in NAVA, though it did not achieve statistical significance, likely because of the limited patient sample. Overall, EAscal/EAdi and EAan/EAdi ratios were lower in NAVA than during PSV. In sum, diaphragm contribution to the overall inspiratory effort resulted to be higher during NAVA than in PSV, which is rather unanticipated. In fact, one would expect the assistance in NAVA, being directly proportional to EAdi, to have more inhibitory effect on the diaphragm rather than on the other inspiratory muscles.

As acknowledged by the authors, this physiological study is of limited size and has some methodological limitations. Also, it does not fully elucidate the mechanisms underlying its findings and leaves open a bunch of possible explanations generating further hypothesis. For instance, it remains unclear whether the greater extradiaphragmatic muscle activity may depend on the worse triggering function in PSV, as opposed to NAVA. This study provides, nonetheless, novel and sound information on the physiological effects of different modes of partial support. Unloading the extradiaphragmatic inspiratory muscles greatly contributes to reducing dyspnea in patients with acute respiratory failure. Extending the findings of previous work in patients undergoing PSV,[13] this study shows that both PSV and NAVA have nonspecific inhibitory effects on the respiratory drive, as indicated by the progressive reduction of the electrical activity of all muscles evaluated at increasing support levels. The EAdi is the only neural source for the NAVA feedback loop, and the distribution of neural drive to the other muscles of respiration is not altered during NAVA.

It is of particular interest that despite the upper airway being bypassed by the endotracheal tube, the activity of the upper airway dilator muscle *alae nasi* was still influenced with both modes by the amount of assistance delivered. Indeed, while surface electromyography appears to be quite problematic for the rib cage (cross talking between inspiratory and expiratory muscles) and neck muscles (placement of central venous catheters), placing an electrode on the external surface of the nose seems pretty simple to accomplish. If confirmed by further studies, this noninvasive approach might be utilized to facilitate and improve the adjustment of the level of assistance, irrespective of the ventilator in use.

As pointed out by the authors, these findings are not necessarily better or worse for NAVA *versus* PSV or *vice versa*. As a matter of fact, however, the work by Cecchini *et al.*[4] eliminates from the list another potential drawback of NAVA. Indeed, most of the physiological comparisons between NAVA and the conventional modes of partial assistance, in general, and PSV, in particular, have shown advantages for this new mode.[14] Clearly, we need further physiological studies; we also need to assess whether NAVA is truthfully applicable over the long period; in the end, however, we need to know whether, and for which patients, the physiological benefits translate into clinical advantage.

Competing Interests

Dr. Terzi has been a member of a board sponsored by Covidien (France). Dr. Navalesi contributed to the development of a new interface (neither used or mentioned in the current work), whose license for patent belongs to Intersurgical S.p.A. (Mirandola, Italy), and received royalties for that invention. His research laboratory has received equipment and grants from Maquet Critical Care (Italy), which produces the mechanical ventilator with the NAVA (neurally adjusted ventilator assist) mode, and Intersurgical S.p.A. He also received honoraria/speaking fees from Maquet Critical Care, Breas (Italy), Covidien AG (Mansfield, Massachusetts), GSK (Philadelphia, Pennsylvania), and Linde AG (Arluno, Italy).

Correspondence

Address correspondence to Dr. Terzi: terzi-n@chu-caen.fr

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