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Dyspnea and Mechanical Ventilation
The Emperor Has No Clothes

Dyspnea, or breathing discomfort (1), is a common yet underappreciated problem for hospitalized patients. Although regulatory bodies in the United States require regular assessments of pain, similar requirements for evaluation of dyspnea do not exist. Dyspnea during a hospital admission has been shown to be associated with higher mortality during that admission and in the 2 years after discharge (2), and dyspnea after extubation is associated with greater risk of recurrent respiratory failure (3). For patients with acute respiratory failure, however, dyspnea has often been given less attention owing to difficulty assessing it in individuals who are frequently unable to communicate and the common use of sedation, and because the focus of care is directed at managing the underlying illness. Nevertheless, dyspnea among critically ill patients has been shown to be the most distressing of 10 symptoms studied (4) and has been found to afflict a significant percentage of patients during mechanical ventilation (5). In this issue of the *Journal*, Demoule and colleagues (pp. 917–926) extend earlier work of this group (5) to rectify this deficit and to demonstrate the relationship between breathing discomfort during mechanical ventilation and long-term mental health consequences (6).

Dyspnea has historically been associated with increased work of breathing and the now decades-old concept of length–tension inappropriateness (7). This has subsequently led many clinicians to equate dyspnea with mechanical loads on the inspiratory muscles and an increased effort to breathe. With this mindset, the institution of positive pressure ventilation, by relieving the work of breathing, should greatly relieve, if not eliminate entirely, respiratory distress. The reality is that the origins of dyspnea are more complicated; the breathing discomfort may arise from stimulation of pulmonary and vascular receptors, chemoreceptors, and other factors that may be the source of the discomfort and/or enhance the drive to breathe (1). Furthermore, dyspnea is worsened when the output of the ventilatory system (e.g., V_T and inspiratory flow) is not consistent with the expected or desired output. This concept has been termed neuromechanical uncoupling or efferent–reafferent dissociation (8, 9). For example, in individuals with normal lungs with high spinal cord lesions and quadriplegia requiring permanent mechanical ventilation, a decrease in V_T leads to breathing discomfort even in the absence of gas exchange abnormalities (10).

For the past 20 years, with the report of the ARDSNet (Acute Respiratory Distress Syndrome Network) study (11), critical care physicians have assiduously adhered to a low-V_T strategy, sometimes necessitating permissive hypercapnia and acute respiratory acidosis, to avoid ventilator-induced lung injury not only for patients with the acute respiratory distress syndrome but for most patients with acute respiratory failure necessitating mechanical ventilation. The restriction of V_T in patients with acute lung disease and a strong drive to breathe is likely to cause an intense sense of "air hunger" (12). Management of the ventilator in these patients may also be complicated by dyssynchrony. Although there are multiple types of dyssynchrony associated with different mechanisms (13), patient discomfort may play a role. Of those individuals who survive mechanical ventilation, a significant percentage will have emotional and behavioral problems, including symptoms consistent with post-traumatic stress disorder (PTSD), in the months and years after extubation (14), and a case has been made for dyspnea as a contributing factor for this outcome (15).

Sedation is commonly used to treat patients with acute respiratory failure, often triggered by apparent discomfort. When selecting medications, however, we need to distinguish drugs such as benzodiazepines, which may be anxiolytics but have little effect on dyspnea, from analgesics, such as opiates, which will reduce the intensity of dyspnea (15). Although an individual may be unconscious with sedation, experimental studies with propofol suggest that painful stimuli may still be "perceived," as evidenced by activation of the insular cortex, a part of the limbic system in which noxious experiences are processed, on brain imaging (16).

Can we assess dyspnea in a patient who is mechanically ventilated? Dyspnea, as with any symptom, is ideally reported by the individual. Yet, we suspect that unconscious patients can perceive pain based on their behavior (e.g., withdrawing from a noxious stimulus) and on the results of neural imaging (14). With respect to dyspnea, clinicians frequently make inferences from findings on physical exam that indicate "respiratory distress," although these findings are generally reflecting an increase in respiratory drive (e.g., use of accessory muscles of ventilation or nasal flaring). Validated instruments have been developed to incorporate facial

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expressions and associated clinical observations into the assessment of dyspnea in patients unable to communicate directly (17). Furthermore, patients with endotracheal tubes in place may not be able to speak, but often they can communicate in other ways if we would just ask the question (18).

Demoule and colleagues (6) confirm earlier findings (5) that a significant fraction of patients with acute respiratory failure experience dyspnea while treated with mechanical ventilation. They have extended these observations, however, by now demonstrating the relationship between dyspnea and subsequent PTSD. In their study of over 600 patients with acute respiratory failure, 34% reported dyspnea before initiation of spontaneous breathing trials. Although mortality and ICU length of stay were not different between the two groups, nearly 30% of patients reporting dyspnea were subsequently determined to have probable PTSD compared with 13% in those without dyspnea. In addition, they have introduced the concept of "density of dyspnea" to reflect the duration and/or frequency of dyspnea, which was found to be independently associated with PTSD. The multiinstitutional study design strengthens the findings, which are likely representative of ICUs around the world.

To the extent that the measurements were made just before a spontaneous breathing trial, this suggests that patients were not in the most severe phase of their respiratory failure (e.g., with very high degrees of positive end-expiratory pressure or $F_{I_{O_2}}$) and may not capture dyspnea occurring when our ventilatory strategies are most likely to exacerbate dyspnea arising from the underlying pulmonary insult, a challenge given the difficulty communicating with patients at those times owing to the common use of sedation. Furthermore, the prevalence of dyspnea among mechanically ventilated patients is likely higher than described here, as their sample was limited to patients who could report their experience. Ascertaining the prevalence across all patients using both self-report and validated observation scales would extend our knowledge further.

These results are a clarion call to intensivists to consider the presence of dyspnea in their patients receiving mechanical ventilation and to respond to dyspnea with measures to reduce the intensity of the discomfort. Changes in ventilator settings (e.g., inspiratory flow, positive end-expiratory pressure, and V_T) when possible without risking lung injury, nonpharmacological measures, and use of analgesics rather than sedation (15) should all be considered essential if we are to avoid these often devastating long-term sequelae of mechanical ventilation. ■

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