Beyond Ventilator-induced Diaphragm Dysfunction

New Evidence for Critical Illness-associated Diaphragm Weakness

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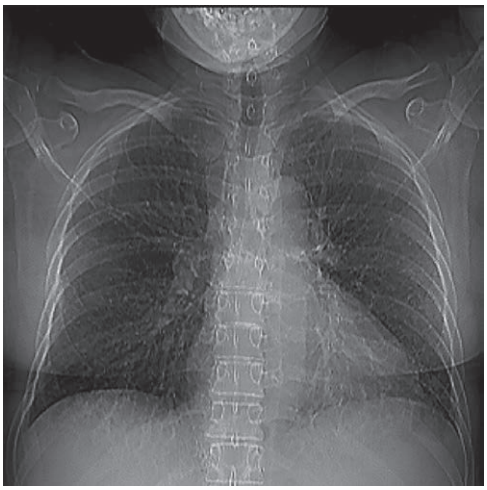
Respiratory muscles are essential to ensure the vital function of breathing. The diaphragm is a unique respiratory muscle, because it contracts throughout the individual's life span without resting, not even during sleep. Any diaphragm rest—even brief—is therefore potentially harmful. Mechanical ventilation is a life-supporting therapy that intrinsically induces diaphragm rest. Consequently, mechanical ventilation induces time-dependant diaphragm weakness in animals[1] and critically ill patients, and is referred to as *ventilator-induced diaphragm dysfunction*.[2] However, many other factors, such as disease severity on admission and sepsis may cause diaphragm weakness in the intensive care unit, which is why the term *critical illness–associated diaphragm weakness* may be preferable.[3] As the load/capacity balance of the respiratory system is a major determinant of weaning success, diaphragm weakness may cause weaning failure and subsequently prolong the time spent on mechanical ventilation, which in turn worsens the prognosis.[3,4] Critical illness is also associated with the development of peripheral muscle weakness, a factor associated with poor outcome.[5]



"[E]arly diaphragm atrophy …was observed in most of the patients treated by invasive mechanical ventilation."

In this issue of Anesthesiology, Vivier *et al.* report original and insightful data in the field.[6] The primary objective of their study was to detect diaphragm atrophy by ultrasound during the first 5 days of intensive care stay. They also evaluated pectoral muscle thickness as a control measure. The authors formulated the hypothesis that diaphragm atrophy (induced by mechanical ventilation) would be more severe than pectoral muscle atrophy (which is supposedly not influenced by mechanical ventilation). They report serial ultrasound measurements of the right hemidiaphragm and right pectoral muscle in 97 critically ill patients: 62 mechanically ventilated patients and 35 spontaneously breathing patients. Using a robust and well-established ultrasound protocol, the authors measured the thickness of the two muscles on admission in all patients and after 5 days in the intensive care unit in the remaining 35 patients, 28 of whom were still on mechanical ventilation and 7 of whom were breathing spontaneously. The authors defined muscle atrophy as greater than or equal to a 10% decrease in muscle thickness on day 5 compared to day 1. The main finding was that diaphragm atrophy (17 of 35 [48%]) occurred more frequently than pectoral muscle atrophy (10 of 34 [29%]). The other major result was that diaphragm atrophy was preferentially associated with more severe disease on admission, mechanical ventilation (all patients with diaphragm atrophy were mechanically ventilated *vs.* 61% of patients without diaphragm atrophy), sepsis, and use of sedation, but not neuromuscular blockers. In contrast, steroid administration was the only factor associated with pectoral muscle atrophy. The most remarkable finding is that pectoral muscle and diaphragm atrophy were observed not only in mechanically ventilated patients, but also in spontaneously breathing patients, supporting the concept that mechanical ventilation is only one of several risk factors for critical illness–associated muscle atrophy. In conclusion, the main message of this study is that ultrasound can detect early diaphragm atrophy that was observed in most of the patients treated by invasive mechanical ventilation. Pectoral muscle atrophy was also observed independently of the use of mechanical ventilation, but was associated with poorer outcome.

The main strength of this study is the assessment of atrophy in two muscles (one of which is directly impacted by mechanical ventilation) in two distinct populations of critically ill patients: mechanically ventilated and spontaneously

Image: J. P. Rathmell.

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breathing patients. Vivier *et al*. confirm previous studies showing that diaphragm atrophy can be detected by ultrasound.[7] They highlight the rapid onset (fewer than 5 days) of diaphragm atrophy in the intensive care unit. It is noteworthy that only a few patients in the study by Vivier *et al*. presented an increase in diaphragm thickness, in contrast with the findings of a recent study that reported that approximately 20% of mechanically ventilated patients exhibit an increase in diaphragm thickness.[8] No clear explanation has yet been proposed for this increase in diaphragm thickness and the discordant results between these two studies require further investigation. The combined results of diaphragm and pectoral muscle thickness are important, as they support the hypothesis that the diaphragm is more susceptible to rest and immobilization atrophy than limb muscles.[3,4]

When a muscle contracts, it thickens and produces a force: these two features are related. Physiologically, diaphragm function can be assessed by measuring its pressure-generating capacity. However, this approach requires complex and sophisticated technology. As muscle atrophy is one of the features of diaphragm weakness, the use of ultrasound to evaluate diaphragm thickness and diaphragm thinning has become increasingly popular over recent years. Nevertheless, it is important to highlight that atrophy, *per se,* is not a marker of force or function, as no correlation has been observed between diaphragm thickness and the pressure-generating capacity of the diaphragm.[9]

This study presents several limitations that are acknowledged by the authors. First, while the sample size was calculated *a priori* and required 40 mechanically ventilated patients and 40 spontaneously breathing patients, only 28 mechanically ventilated patients and 7 spontaneously breathing patients were finally analyzed, which is a much smaller sample size than planned. Due to the small sample size (n = 35) of patients followed until day 5, no relevant association with outcomes can be reasonably established. Second, the magnitude of the changes in muscle thickness is only a few millimeters. The reproducibility of ultrasound measurements therefore cannot be guaranteed, although the authors carefully ensured the robustness of their ultrasound protocol. Finally, the mode of ventilation and more precisely the amount of spontaneous breathing efforts generated by the patients while on mechanical ventilation are not described. However, these efforts likely may play a role in diaphragm thinning.

Vivier *et al*. have produced an elegant study that provides new evidence that the diaphragm is a preferential target during the intensive care unit stay.[6] Importantly, their findings support the concept of critical illness–associated diaphragm weakness. Further investigations are now required to confirm whether diaphragm atrophy has a major impact on clinical outcomes and, if so, how this impact might be prevented, mitigated, and ultimately treated.

Competing Interests

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