

## Ventilation-induced diaphragm atrophy impacts clinical outcomes



Diaphragm atrophy developing during mechanical ventilation is associated with prolonged mechanical ventilation and ICU admission and an increased risk of complications of acute respiratory failure, according to new research published in the American Journal of Respiratory and Critical Care Medicine. The findings suggest the need for clinicians to target an inspiratory effort level similar to that of healthy subjects at rest, which could accelerate liberation from ventilation.

Prolonged mechanical ventilation contributes to increased risk of death, poor long-term functional outcomes, and markedly higher healthcare costs. Diaphragm weakness is a leading cause of difficult weaning from mechanical ventilation. It remains uncertain, however, whether the changes in the diaphragm specifically due to mechanical ventilation significantly impact clinical outcomes.

The current study sought to determine the impact of diaphragm injury resulting from ventilation on clinical outcomes. Researchers evaluated the effect of both decreases and increases in diaphragm thickness on the risk of prolonged ventilator-dependence. Diaphragm thickness was measured daily by ultrasound in adults requiring invasive mechanical ventilation; inspiratory effort was assessed by thickening fraction. The primary outcome was time to liberation from ventilation. Secondary outcomes included complications (reintubation, tracheostomy, prolonged ventilation, or death). Associations were adjusted for age, severity of illness, sepsis, sedation, neuromuscular blockade, and comorbidity.

The research team reported these key findings:

- · Of 211 patients enrolled in the study, 191 had two or more diaphragm thickness measurements. Thickness decreased more than 10% in 78 patients (41%) by median Day 4 (interquartile range, 3-5).
- Development of decreased thickness was associated with a lower daily probability of liberation from ventilation (adjusted hazard ratio, 0.69; 95% confidence interval [CI], 0.54-0.87; per 10% decrease), prolonged ICU admission (adjusted duration ratio, 1.71; 95% CI, 1.29-2.27), and a higher risk of complications (adjusted odds ratio, 3.00; 95% CI, 1.34-6.72).
- Development of increased thickness (n = 47; 24%) also predicted prolonged ventilation (adjusted duration ratio, 1.38; 95% CI, 1.00–1.90).
- Decreasing thickness was related to abnormally low inspiratory effort; increasing thickness was related to excessive effort.
- Patients with thickening fraction between 15% and 30% (similar to breathing at rest) during the first three days had the shortest duration of ventilation.

"Our findings suggest that prolonged ventilator-dependence due to deleterious diaphragmatic changes resulting from ventilation might be potentially mitigated by targeting levels of inspiratory effort during ventilation similar to that of healthy subjects breathing at rest," the authors write. "Previous work has shown that diaphragm inactivity causes diaphragm atrophy while excess inspiratory efforts can exacerbate ventilatorinduced lung injury and injure the diaphragm.'

The authors note that observed associations may derive from residual confounding related to unmeasured patient or illness characteristics, hence they cannot definitively conclude a causal effect. They say causality can only be demonstrated in the context of a randomised study of interventions known to prevent deleterious changes in the diaphragm during mechanical ventilation.

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