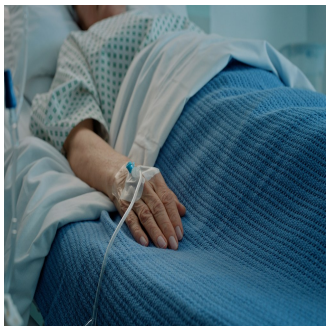
ICU
MANAGEMENT & PRACTICE

Inflammatory Subphenotype and Brain Dysfunction in Mechanically Ventilated Patients



Up to 80% of mechanically ventilated ICU patients experience acute brain dysfunction, commonly manifesting as delirium or coma. Both conditions are linked to increased mortality and long-term cognitive impairment in survivors. The underlying pathophysiology of acute brain dysfunction during respiratory failure is poorly understood.

Previous studies have explored the relationship between delirium and individual host-response biomarkers, suggesting the involvement of specific physiological pathways. However, these studies may not capture the full biological complexity. Subphenotypes of ARDS and sepsis have been identified using latent class analyses of multiple biomarkers and clinical variables, indicating potential for predicting therapy responses.

A recent study tested the hypothesis that the hyperinflammatory subphenotype is associated with worse acute brain dysfunction in mechanically ventilated ICU patients. This study enrolled adults with acute respiratory failure requiring invasive mechanical ventilation. Participants were endotracheally intubated adults aged 18-90. Clinical and radiographic data classified participants into four categories: ARDS, at-risk for ARDS, congestive heart failure, or intubated for airway protection.

Inflammatory subphenotypes were identified using a four-variable model (angiopoietin-2, soluble tumour necrosis factor receptor-1, procalcitonin, and bicarbonate). Biomarker concentrations in plasma samples were measured within 48 hours of intubation. Acute brain dysfunction, defined as delirium or coma, was assessed using the Richmond Agitation-Sedation Scale (RASS), Confusion Assessment Method for the ICU (CAM-ICU), Riker Sedation-Agitation Scale, and Intensive Care Delirium Screening Checklist (ICDSC).

The primary outcome was 14-day delirium/coma-free days (DCFDs). Additional analyses included associations between subphenotype and delirium days, coma days, and 14-day mortality.

Three hundred forty mechanically ventilated ICU patients were enrolled: 103 (30%) with ARDS, 147 (43%) at risk for ARDS, 35 (10%) with CHF, and 55 (16%) intubated for airway protection. Of these, 94 (28%) were classified as having the hyperinflammatory subphenotype. Acute brain dysfunction was common, with 51% of participants comatose and 71% delirious on at least one study day.

In unadjusted analyses, hyperinflammatory participants had fewer delirium/coma-free days (DCFDs), indicating more acute brain dysfunction, compared to hypoinflammatory participants. This association remained after adjusting for age, preexisting comorbidities, and sedative doses. The reduction in DCFDs in the hyperinflammatory subphenotype was driven by increased odds of all DCFD components (delirium days, coma days, and death), although these individual associations were not statistically significant. An exploratory analysis showed that patients with low inflammation on day 1 but high inflammation on day 5 had significantly lower odds of DCFDs, affecting 7 of the 134 patients with day-5 data. Other groups did not show significant changes in DCFD odds.

Overall, findings show that in patients with acute respiratory failure, the hyperinflammatory subphenotype was linked to greater acute brain dysfunction than the hypoinflammatory subphenotype, even after adjusting for age, comorbidities, and sedative use. This supports the idea that systemic inflammation triggers acute brain dysfunction during critical illness, extending previous research that focused on individual biomarkers. The findings suggest that host-response subphenotyping could help identify factors affecting treatment heterogeneity beyond clinical diagnosis alone. Validation in an external cohort is necessary to generalise these findings to other critically ill populations.

Source: Annals of the American Thoracic Society

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Published on : Wed, 3 Jul 2024