Histopathologic evidence of ventilator-induced lung injury in COVID-19

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Ventilator-induced lung injury (VILI) has been an old and well-established concept and the term "respiratory lung" has been used to describe the diffuse alveolar infiltrates and hyaline membranes that were found on post-mortem examinations of mechanically ventilated patients (1). A low tidal volume ventilation strategy has been widely adopted to decrease VILI due to the benefits shown in clinical trials (2).

The COVID-19 pandemic has posed new challenges for clinicians regarding the initiation and management of mechanical ventilation. Early in the pandemic, many experts argued that an early intubation approach might be beneficial due to the prevention of lung injury from vigorous spontaneous inspiratory efforts, the so-called patient self-induced lung injury (P-SILI) (3). However, others questioned this approach citing the known risks of mechanical ventilation including VILI (4). As new data became available, there seemed to be little benefit from an early intubation approach (5) and the mortality rates for intubated COVID-19 patients were alarmingly high (6). Moreover, barotraumas such as pneumothorax was reported in 12.8–23.8% of mechanically ventilated COVID-19 patients and their occurrences were associated with a high mortality of up to 100% (7). These highlighted the importance of VILI in severe COVID-19 patients requiring mechanical ventilation.

In the current issue of *Annals of Translational Medicine*, Saegeman and colleagues did a narrative case-control literature review on histopathological changes consistent with VILI in the lungs of COVID-19 patients who were mechanically ventilated for more than 24 hours (8), using COVID-19 patients who were not mechanically ventilated or mechanically ventilated for less than 24 hours as controls. The samples were mainly from postmortem cases (60/62). The histopathologic changes included epithelial and endothelial injury, leading to diffuse alveolar damage (DAD) and microcirculatory thrombotic events, followed by squamous metaplasia as early as 7 days after symptom onset, and subsequent fibrosis. Through multivariate analysis, they found that mechanical ventilation for more than 24 hours was associated with the histopathologic patterns of DAD and fibrosis, consistent with possible VILI.

As in all such studies on VILI, it can be hard to determine how much of the histopathologic changes were attributable to the underlying disease instead of VILI. Nevertheless, the study along with other studies on VILI in COVID-19 patients will help us to fill in pieces in the big puzzle of understanding VILI in COVID-19 and potentially selecting better mechanical ventilation strategies.

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