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First, Do No Harm

Caution Against Use of Tocilizumab in COVID-19



To the Editor:

I read with great interest the case report by Radbel et al¹ in *CHEST* (July 2020) on their use of tocilizumab in severe coronavirus disease 2019 (COVID-19) and two adverse outcomes. Their call for caution regarding the use of IL-6 inhibitors is justified. The “hyperinflammatory state” as a major driver of morbidity and mortality in severe COVID-19 is still a hypothesis. C-reactive protein levels in COVID-19 are no different from other etiologies of pneumonia and ARDS.²⁻⁴ Although it has been posited that reducing IL-6 may be beneficial because high IL-6 levels are associated with poor outcomes in COVID-19 and other diseases, this question is far from settled. The assumption that IL-6 in this disease is pathologic and not an appropriate response to the infection has not been proven, and in fact, the opposite has been shown in other viral infections.⁵ I question the uncontrolled use of tocilizumab in severe cases of COVID-19 given the possible protective effect of IL-6 in this disease. Its off-label use should only be carefully considered in the setting of a clinical trial.

The proliferation of unreviewed manuscripts on preprint servers, study results released via press release, and large number of uncontrolled retrospective studies should give us all pause. As this pandemic worsens in the Americas, Africa, and the Indian subcontinent, those suffering from COVID-19 would benefit from well-controlled trials capable of providing high-quality, actionable treatment and diagnostic interventions. Small, uncontrolled trials are vulnerable to well-known biases that affect the direction and magnitude of treatment effects. With so many critically ill patients, there is a temptation to do something, but our first commitment should be to do no harm.

Radbel et al¹ should be commended for publishing this result.

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Risk Factors for Postextubation Dysphagia in the Presence of Competing Risks and Immortal Time Bias



To the Editor:

We read with great interest the study exploring the risk factors for dysphagia in ICU patients after invasive mechanical ventilation (IMV) in this issue of *CHEST*.¹ The authors identified several risk factors after complex statistical modeling, including baseline neurologic disease, emergency admission, and duration of IMV. However, we propose that the occurrence of dysphagia should be considered in the context of competing risks. The occurrence of death can be a competing risk for dysphagia. In other words, patients who die before extubation preclude the occurrence of dysphagia, despite that these patients can also have high risk of dysphagia had death not occurred. Suppose an extreme case where the baseline neurologic disease is associated with increased risk of postextubation dysphagia, and is also a risk factor for death. If most patients with baseline neurologic disease die before extubation, a limited number of postextubation dysphagia can be observed (ie, these patients are not included for analysis) in patients with baseline neurologic diseases. In this case, patients without baseline neurologic disease are more likely to be included for analysis. In other words, the selection of the cohort is influenced by mortality outcome. More critically ill patients who die early are less likely to be included. To better capture the