

LETTER TO THE EDITOR

Therapeutic-dose heparin in preventing COVID-19-associated acute kidney injury: What about bleeding risk?

We would like to offer thoughtful insights into a recent randomized trial by Smilowitz et al. [1] that reported the benefits of therapeutic-dose heparin in preventing acute kidney injury (AKI). This trial enrolled participants hospitalized due to COVID-19 who did not require intensive care or extended hospitalization beyond 72 hours [1]. Participants were randomized to either therapeutic-dose heparin or usual-care pharmacologic thromboprophylaxis in line with local practice guidelines. Of the 1922 participants, 83 (4.9%) experienced the primary endpoints of severe (stage 2 or 3) AKI or death, with 40 out of 908 participants (4.4%) in the therapeutic-dose heparin group and 43 out of 786 participants (5.5%) in the usual-care pharmacologic thromboprophylaxis group (adjusted relative risk, 0.72%; 95% credible interval, 0.47-1.10). Specifically, severe AKI occurred less frequently in participants administered therapeutic-dose heparin compared to those receiving usual-care pharmacologic thromboprophylaxis (3.4% vs 3.9%).

COVID-19-associated AKI is a common complication as it tends to complicate the course of hospitalization among patients with COVID-19, often linked to increased severity of illness and heightened risk of mortality [2]. Various factors contribute to COVID-19-associated AKI, including acute tubular injury (regional inflammation, renal compartment syndrome, and nephrotoxic-induced injury), vascular injury (microthrombi, thrombotic microangiopathy, and endotheliitis), glomerular injury, and interstitial injury. Autopsies of patients with COVID-19-associated AKI have reported a 9-fold higher incidence of macrovascular and microvascular thrombosis in the lungs compared to those with influenza pneumonia [3]. Additionally, platelet-rich peritubular fibrin microthrombi were identified in the renal microcirculation. Therefore, therapeutic-dose heparin can be beneficial as it may prevent acute inflammation and alleviate microvascular thrombosis [1].

Based on the findings reported by Smilowitz et al. [1], clinicians may consider the use of therapeutic-dose heparin in patients with COVID-19 at risk of AKI given the substantial adverse outcomes associated with AKI in this patient population [2]. However, it is imperative to lay a comprehensive strategy when considering the use of therapeutic-dose heparin. Populations at risk of AKI that may benefit from therapeutic-dose heparin include individuals hospitalized for COVID-19 with underlying chronic kidney disease, as well as other long-term comorbidities such as diabetes mellitus, heart failure, and liver disease, and severe COVID-19 illness, among others. One critical aspect that requires attention is the potential occurrence of major bleeding events associated with the use of therapeutic-dose heparin.

These events are more likely to occur in patients with the characteristics described beforehand. Therefore, it is essential to weigh the potential benefits against the risks, particularly concerning major bleeding.

Given the complexities involved, it is evident that further clinical trials are warranted to comprehensively investigate the net benefit of therapeutic-dose heparin in preventing AKI, paying specific attention to the risk of major bleeding. While the potential benefits may be apparent, as indicated by the study conducted and reported by Smilowitz et al. [1], we strongly urge practitioners to thoroughly assess the risks of bleeding before initiating this therapy in patients at risk of COVID-19-associated AKI. This precaution should be taken while awaiting more conclusive evidence from future research endeavors.

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There are no competing interests to disclose.

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