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Role of increased neutrophil extracellular trap formation on acute kidney injury in COVID-19 patients

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Objectives: A close association between increased neutrophil extracellular trap (NET) levels and poor clinical outcomes in patients with coronavirus infection 2019 (COVID-19) has been reported. However, while acute kidney injury (AKI) is a common complication of COVID-19, the role of NETs in COVID-19-associated AKI is unclear. We examined the relationship between elevated NETs and AKI as well as the prognostic role of NETs in COVID-19 patients.

Methods: Two representative markers of NETs, circulating nucleosomes and myeloperoxidase-DNA, were measured from 115 patients and 50 controls. Serum levels of interleukin [IL]-6, monocyte chemotactic protein-1 [MCP-1], plasma von Willebrand factor (vWF) and urine biomarkers of renal tubular damage (β2-microglobulin [β2M] and kidney injury molecule 1 [KIM-1]) were measured

Results: AKI was found in 43 patients (37.4%), and pre-existing chronic kidney disease (CKD) was a strong risk factor for AKI. A higher circulating NET level was a significant predictor of increased risk of initial intensive care unit admission rate, in-hospital mortality (adjusted HR 3.21, 95% CI 1.08–9.19), and AKI (OR 3.67, 95% CI 1.30-10.41), independent to age, diabetes, pre-existing CKD and IL-6 levels. There were strong correlations between circulating nucleosome levels and urinary KIM-1/creatinine ($r=0.368$, $p=0.001$) and β2M ($r=0.218$, $p=0.049$) levels. Furthermore, NETs were closely associated with serum vWF ($r = 0.356$, $p<0.001$) but not with IL-6 or MCP-1 levels.

Conclusions: Elevated NETs were closely associated with AKI, which was a strong predictor of mortality. The close link between NETs and vWF might suggest a role of NETs in COVID-19-associated vasculopathy causing AKI.