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ABSTRACT
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# Abstract 261: Tissue Factor Pathway Inhibitor Prolongs The Initiation Of Thrombin Generation And Is Associated With Acute Kidney Injury In Covid-19

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## Abstract

COVID-19 can cause profound inflammation and coagulopathy, yet the mechanisms underlying the thrombo-inflammatory state are not fully elucidated. Patients with COVID-19 have elevated plasma levels of not only procoagulant factors but also anticoagulant proteins, such as tissue factor pathway inhibitor (TFPI), and very little research has been done to test the role of COVID-19 infection on anti-coagulant pathways. We tested the mechanistic contribution of TFPI to thrombin generation and its association with renal failure during the initial wave of COVID-19 (April 2020 to January 2021). We utilized blood plasma collected from a clinical trial of hospitalized COVID-19 patients (NCT04360824) and recruited healthy subjects as controls. We first confirmed that there was increased thrombin generation potential in the COVID-19 cohort, reflected by greater peak thrombin ($p$ = 0.020), velocity index ($p$ = 0.022), and endogenous thrombin potential (ETP) ($p$ = 0.006); however, the time to initiation of thrombin generation (lag time) was delayed ($p$ = 0.037). Plasma levels of TFPI in were elevated in COVID-19 patients compared to controls ($p$ < 0.0001) and TFPI concentration was positively associated with lag time ($p$ = 0.002). Treatment of plasma with anti-TFPI blocking antibody shortened the lag time in both controls ($p$ = 0.001) and COVID-19 patients ($p$ < 0.0001) and normalized the difference in lag time between healthy subjects and COVID-19 patients without affecting peak thrombin, velocity index, or ETP. Interestingly, the levels of TFPI in the plasma of

COVID-19 patients positively correlated with acute kidney injury ($p = 0.026$) but not with mortality, admission to the intensive care unit, or thrombosis. Together these data indicate that TFPI affects the pro-thrombotic state and is associated with clinical outcome in COVID-19.