

# **Reduced Vitamin K Status and Coronavirus Disease 2019: An Epiphenomenon of Impaired Kidney Function?**

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Dear Editor,

Dofferhoff et al. [1] recently hypothesized that enhanced thrombogenicity related to low vitamin K status is implicated in coronavirus disease 2019 (COVID-19), linking pulmonary and thromboembolic disease. This hypothesis was corroborated by the finding of markedly elevated plasma dp-ucMGP – a marker of poor extrahepatic vitamin K status – in hospitalized patients with COVID-19 compared with healthy controls. Furthermore, among patients, plasma dp-ucMGP was higher in those with poor outcome (i.e., those whom required invasive ventilation or died in-hospital) compared with good outcome (i.e., those whom were discharged without the need for invasive ventilation). These differences were independent of age, sex, and use of vitamin K antagonists as potential confounders. Nonetheless, there are reasons to believe that the differences in plasma dp-ucMGP between hospitalized patients with COVID-19 and healthy controls and between poor and good outcome were driven by differences in kidney function.

Impaired kidney function is common among hospitalized patients with COVID-19 and the degree of impairment strongly relates to disease severity. Acute kidney injury is experienced by 32% to 46% of patients [2,3], of which 80% develops within one day of hospitalization [3]. Interestingly, in the study by Dofferhoff et al., three hospitalized patients with COVID-19 versus none of the healthy controls were dialysis-dependent, which may be a sign thereof.

Importantly, it has been consistently reported that there is a strong cross-sectional association between plasma dp-ucMGP and kidney function, with circulating dp-ucMGP progressively increasing for decreasing kidney function [4,5]. In 2018, it was postulated that higher plasma dp-ucMGP is also associated with increased risk of incident chronic kidney disease (CKD) [6]. However, this study did not account for the cross-sectional association between plasma dp-ucMGP and kidney function at baseline. Indeed, a subsequent replication study showed that the prospective association between higher plasma dp-ucMGP and increased risk of incident CKD disappears if baseline kidney function is accounted for [7].

Given the strong and established association between plasma dp-ucMGP and kidney function on the one hand and the high prevalence of kidney dysfunction in hospitalized patients with COVID-19 on the other hand, we postulate that the observation of elevated plasma dp-ucMGP in hospitalized patients with COVID-19 may be confounded by impaired kidney function. It is imperative to know whether the observations by Dofferhoff et al. [1] would remain statistically significant after baseline kidney function is accounted for. Otherwise, their findings should be interpreted with great caution, as the observed between-group differences in plasma dp-ucMGP could be an epiphenomenon of actual differences in kidney function. We therefore cordially invite the authors to report on the association of extrahepatic vitamin K status with accelerated elastic fiber degradation and thrombosis after having accounted for time-matched kidney function.

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