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Letter to the Editor

Reply - Letter to the Editor: Vitamin D deficiency in critically ill COVID-19 ARDS patients

**Keywords:**

Acute respiratory distress syndrome
Vitamin D
Critical care
Nutrient supplementation
Immune response

We thank our colleagues for their valuable thoughts and interest in our explorative study on vitamin D deficiency and supplementation in critically ill COVID-19 ARDS patients [1]. While we agree that age is an important risk factor, both for vitamin D deficiency [2], and for severe COVID-19, including ICU admission and death [3], there is currently no evidence to support a causal relationship. Our study was conducted in a specialized center for extracorporeal membrane oxygenation (ECMO) and only included a small number of elderly COVID-19 patients. There was no age difference, when comparing patients with and without vitamin D deficiency (Table 3, original manuscript). Also, patients ≤ 55 and patients > 55 years of age had the same serum levels (Table 1). We could not confirm a correlation between age and either 25-hydroxyvitamin D or

1,25-dihydroxyvitamin D levels at any point of time. In addition, viral loads, as determined via cycle thresholds (ct) of the reverse transcription polymerase chain reaction (RT-PCR), were not associated with the patient's vitamin D status (Fig. 1). On admission to our intensive care unit the median ct-value was 25 (23–33) for tracheal secretions and 33 (26–40) for throat swabs. This indicates a rather low viral load [4], most likely due to delayed referral to our center.

Four patients received vitamin D supplementation prior to the COVID-19 infection. Their long-term medication included daily doses between 1000 and 20,000 IE of vitamin D, whereas no more details on the compliance and the exact duration of administration were available. Despite acknowledging the potential relevance of vitamin D pretreatment [5], we think that this aspect is far beyond the scope of our observational study.

At the time of study inclusion, vaccines against COVID-19 were not available. Whether vitamin D has a potential influence on vaccine effectiveness via promotion of B cells and antibody production remains highly speculative [6]. Although, it may be worth mentioning that we observed an isolated increase in circulating plasmablasts as a function of 25-hydroxyvitamin D levels, it is equally important not to overinterpret explorative findings. We consider our study as solely hypothesis generating and hope to encourage further research in this area.

Table 1

After exclusion of four patients with vitamin D pretreatment, 11 patients were ≤ 55 years and 11 patients were > 55 years old. Two patients in each group did not receive vitamin D supplementation during their stay on the intensive care unit. IQR, interquartile range. The Mann–Whitney test was used.

Age [years]	Admission			10 to 15 days		
	≤ 55	> 55	p	≤ 55	> 55	p
25-hydroxyvitamin D, ng/ml (median, IQR)	11 (9–26)	15 (13–20)	0.6	23 (16–31)	27 (21–34)	0.3
1,25-dihydroxyvitamin D, pg/ml (median, IQR)	27 (19–37)	22 (14–34)	0.4	11 (8–52)	21 (11–24)	1.0

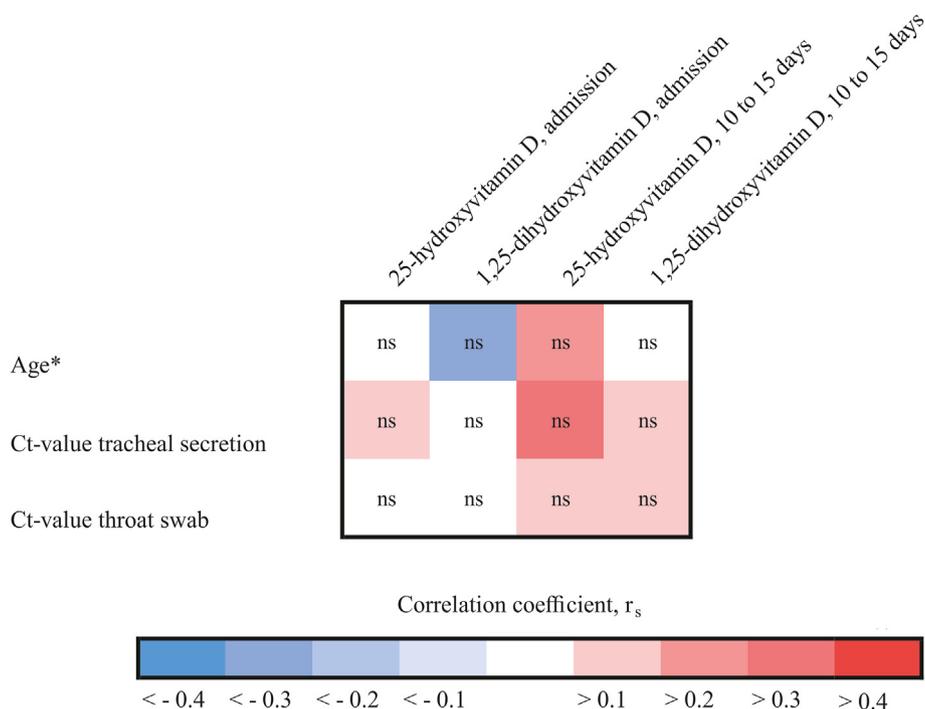


Fig. 1. Spearman's correlation between vitamin D levels, age and cycle thresholds (Ct) of COVID-19 ARDS patients did not indicate an association. *Patients with vitamin D supplements in their longterm medication, as well as patients without supplementation during their intensive care stay were excluded. Ns, not significant.

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Author contributions

QN, CS drafted the response.

Conflict of interest

None.

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