## Letter to the Editor

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## Interference of glucose and total protein on Jaffe based creatinine methods: mind the covolume – reply

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To the Editor,

We thank Dr. Oyaert and colleagues for their interest in our study [1] and appreciate their response to the issues we raised [2]. They argue that the interference of glucose and total protein in the Jaffe creatinine and enzymatic assays is even more complex than we presented because of the covolume effect. We agree that, apart from the analytical interference, both the Jaffe method and the enzymatic method are - in vivo - affected by the redistribution of creatinine in the available water content of the blood circulation in case of severe hypo-/hyperproteinemia. This may be of particular importance in intensive care patients and lead to additional difficulties in the interpretation of creatinine results, and unreliable eGFR calculations for this patient group. Given the large absolute effects on creatinine concentrations that we demonstrated in our study, the impact of analytical interference by glucose in particular is likely to be higher than the impact of the volume displacement effect.

We here would like to clarify why we did not observe increases in creatinine concentrations with increasing total protein concentrations. To generate IDMS traceable creatinine measurements, we adjusted the patient results according to the deviations from the target calibrator values. Then the target values of the patient samples were defined as the mean of the IDMS traceable patient results of the four enzymatic methods. We intended to specifically demonstrate the impact of glucose and total protein interference on the creatinine test results *in vitro*, beyond volume displacement effects that indeed further hamper the interpretation of real patient test results.

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