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Letter to Editor

## Continuous renal replacement and removal of inflammatory mediators in sepsis: Still an open debate



Dear Editor,

We read with great interest the article by Wu et al about the role of continuous renal replacement therapy (CRRT) in sepsis-associated kidney failure; the authors reported that in septic patients CRRT allowed a better recovery of renal function and a reduction of inflammatory biomarkers.<sup>1</sup> Particularly, the authors found that the expression levels of IL-9, TNF- $\alpha$ , and INF- $\gamma$  were significantly reduced after a CRRT performed with a flow rate of 40 ml/kg/h.<sup>1</sup> More recently CRRT has been used in COVID-19 patients developing acute kidney injury both to treat renal failure and to remove the mediators of cytokines storm.<sup>2</sup> Dialysis dose is crucial to determine the efficacy of CRRT in septic patients, but the correct dose is still a matter of debate.<sup>3</sup> The flow rate is conventionally set between 20 and 35 ml/kg/h; CRRT performed with a dialysis dose greater than 35 ml/kg/h is defined high volume hemofiltration. Both mediators and pro-mediators of inflammation are removed by high volume hemofiltration not only from the blood but also from the interstitial fluids and the tissues; when the concentration of these molecules falls below a certain threshold, the inflammatory cascade is blocked.<sup>4</sup> Indeed, in septic patients, a high flux hemofiltration at 60 ml/kg/h was found to progressively reduce the circulating cytokines and to increase the transcriptional activity of IL-6 produced by peripheral blood mononuclear cells.<sup>5</sup> Since we strongly believe that CRRT not only removes inflammatory mediators in a non-selective way during sepsis<sup>5</sup> but also may affect the transcription of inflammatory mediators we would ask the authors to add more details about the choice of a flow rate of 40 ml/kg/h. Furthermore, the authors should better specify which routine therapies have been applied to the control group and discuss their role on cytokine modulation.

### Declaration of competing interest

The authors have no conflict of interest.

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