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Matthieu Legrand
Rick Bezemer
Can Ince

The role of renal hypoperfusion in development of renal microcirculatory dysfunction in endotoxemic rats: reply to Ji et al.

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Dear Editor,

We would like to thank Ji et al. [1] for their comments regarding our recently published study [2]. The authors raised two very interesting and relevant points of concern.

First, they point out that we might have missed the initial peak in TNF-α expression shortly after LPS infusion and therefore cannot conclude that neither immediate nor late fluid could prevent systemic inflammatory activation. However, although we may have missed the peak expression, we could still detect increased TNF-α levels at the end of our protocol group which evidently indicates that neither immediate nor late fluid resuscitation could completely prevent systemic inflammatory activation. Furthermore, plasma TNF-α may not accurately reflect TNF-α kinetics in tissue. For instance, Detmer et al. [3] found that TNF-α increased until 360 min after LPS exposure in smooth muscle cells. The kinetics of TNF-α release may also been modified by interaction of TNF-α with other cytokines. Andersson et al. [4] found a reciprocal functional relationship between cytokines with HMG-1 extending and amplifying the secretion of TNF-α. Thus, if anything, the point raised by Ji et al. does not preclude our conclusion. Nonetheless, we must acknowledge that the main aim of our study was not to investigate the whole picture of the LPS-induced cytokine response spectrum, but to investigate the role of LPS-induced hypotension and renal hypoperfusion in the development of renal microcirculatory dysfunction and systemic and renal inflammatory activation. The method we used fits this goal.

Second, Ji et al. raised concerns regarding the relatively small sample size. This might be a valid point here. However, although we can not exclude a lack of power, we believe that increasing the sample size would not show a different result with respect to the very similar TNF-α plasma levels in the immediately and delayed resuscitated groups. The authors also pointed out that there was a clerical error in the abstract of the article. For this we would like to apologize.

Finally, the authors state that the data presented in our study should be interpreted with some caution. Of course, as should the data presented in every study. Furthermore, the authors state that more research is needed. Again, we agree. Although we could explore the role of renal hypoperfusion in the development of renal microcirculatory failure, application of immediate fluid resuscitation is clinically impossible. Hence, future research could focus on developing therapeutic strategies protecting the renal microcirculation in endotoxemia, hemorrhage, ischemia/reperfusion injury, and other scenarios in which the kidney might suffer from hypoperfusion and inflammation.

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M. Legrand · R. Bezemer · C. Ince
Department of Translational Physiology, Academic Medical Center, University of Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands

M. Legrand (✉)
Department of Anesthesiology and Critical Care, Lariboisière Hospital, Assistance Publique-Hopitaux de Paris, University of Paris, 7 Denis Diderot, 2 rue Ambroise-Paré, 75475 Paris Cedex 10, France
e-mail: matthieu.m.legrand@gmail.com
Tel.: +33-1-49958085
Fax: +33-1-49958073