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LETTER TO EDITOR
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Dual Role of Angiopoietine II in the Complex Management of Critically Ill Patients with Sepsis

To the Editor

I read with great interest the article entitled "The role of Angiopoietine-2 in the diagnosis and prognosis of sepsis", published by Szederjesi et al in the issue no.1/2015 of JCCM journal [1]. As the authors pointed out, the prognosis of patients with sepsis is highly dependent on the early establishment of a proper diagnosis and on the early initiation of the adequate therapy. Therefore, identification of new biomarkers characterising this critically ill condition can be considered extremely important for a better understanding of this condition, leading to a more rapid and accurate diagnostic. The study identified angiopoietine-2 (ANG-2) as such a new biomarker characterising septic shock, demonstrating a good correlation between ANG-2 levels, duration of stay in the intensive care unit and the most widely used ICU mortality prediction scores. At the same time, the study showed a good sensitivity and specificity of this biomarker for diagnosis of sepsis and the authors should be congratulated for their results.

However, an interesting observation of this study is related to the fact that there was no correlation between the level of angiopoietine-2 and the alteration of renal function in patients with severe sepsis. In a recent study, Tsai et al demonstrated that ANG-2 is an independent predictor of adverse renal outcome in patients with chronic kidney disease (CKD), without clearly establishing the role of ANG-2 in progression of this disease [2]. Therefore, a link between this biomarker and the renal function has been demonstrated in non-septic population. The lack of correlation between ANG-2 levels and the renal function in the sepsis population included in the present study could raise the hypothesis that there are other pathways of action of ANG-II in patients with sepsis, different from the one encountered in the CKD population.

It is also well-known that ANG-2 is an endothelium-specific growth factor, and the production of this factor is stimulated by pro-inflammatory mediators, which present significantly increased levels in sepsis. Another study published by Orfanos et al showed a strong relationship between serum ANG-2 and serum tumour necrosis factor-alpha suggesting that the latter may play a role in ANG-2 production in sepsis [3].

Therefore, the ANG–II could play a dual role in the complex management of critically ill patients with sepsis:

- On one hand, it can be considered as a biomarker, indicating the severity of the disease. In this case further studies should be performed to find a potential role of this biomarker in the complex clinical scoring systems expressing the prognostic of this severe condition.
- On the other hand, ANG II could play the role of an effector biomolecule, involved in the progression of the disease and deterioration of the clinical status of these patients, and in this case more complex studies are required to elucidate the role on this molecule in the pathophysiologic mechanisms of multiple organ failure associated with sepsis.

A study on the potential relationship between inflammatory mediators and ANG-II production could add significant further value to this interesting study.

Monica Marton-Popovici

Swedish Medical Center, Department of Internal Medicine and Critical Care, Edmonds, Washington, USA

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* Correspondence to: Monica Marton-Popovici, Swedish Medical Center, Department of Internal Medicine and Critical Care, 21601, 76th Ave W, Edmonds, Washington, 98026, USA.
E-mail: Monica.Marton-Popovici@Swedish.org