Reviewer’s report

Title: Causes and consequences of coagulation activation in sepsis: an evolutionary medicine perspective

Version: 1 Date: 7 January 2015

Reviewer: Massimo Girardis

Reviewer’s report:

The author proposed an interesting (but not new) perspective on the role of coagulation in sepsis. The hypothesis that coagulation activation is beneficial for pathogen clearance is well supported in the manuscript by concepts of evolutionary medicine and animal models. Although this view may be acceptable and important particularly in re-thinking the design of clinical trials, I guess that the other side of the matter is also important. Indeed, numerous experimental data supported the idea that an excessive coagulation may be detrimental and that the use of anticoagulants in this specific condition may be beneficial. The key is perhaps the correct identification of the pathophysiological ‘moment’ of the septic patient. I strongly suggest to insert a paragraph to briefly discuss the limitations of the approach proposed and the contrasting data from in vitro and animal models.

The in vivo observation of tissue microcirculation by Microvideoscopic techniques methods clearly showed strong disturbances of tissue perfusion during both early and late phases of sepsis. These disturbances has been attributed to deregulated coagulation processes and seem to be the main cause of cellular dysoxia and organ dysfunction observed in sepsis. A discussion of this point is needed.

Differently from RCTs, several systematic reviews and meta-analysis showed a possible beneficial effect of anticoagulant therapy (e.g. heparin, protein c (activated)) in specific populations of septic patients. Please add this information.

A table(main data supporting the concept that coagulation activation is beneficial for pathogen Clearance) and a figure (mode of action of coagulation system as defense against pathogens) may help the reader.

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests