Reviewer's report

Title: Procalcitonin as markers of sepsis and outcome in patients with Neurotrauma a prospective observational study

Version: 3 Date: 19 September 2013

Reviewer: Michael Meisner

Reviewer's report:

Major remarks.

1. The APACHE II score should not be addressed as a severity score.

2. Does the reader understand correctly that this is isolated brain/head injury or are there other types of trauma coexisting?
   This should be – if this is the case – expressed by an Injury Severity Score (ISS...),
   because in this case the GCS is maybe not enough to correlate trauma severity of brain, PCT and overall tissue damage.

3. Does the reader understand well that onset of sepsis is possible also during the later course (e.g. day 1-28), or does it mean that sepsis came up during the initial days of the PCT observation period (e.g. day 2, 3, 5, 7?)?

Independent from this systemically remarks the reviewer asks to provide more analysis regarded the following question:

4. The difference of SIRS/no SIRS and the Sepsis groups is maximum at day 2. The authors should also provide the statistical analysis and data for this day, because results may be much better and because of the below mentioned consequences.

4b) in Figure 2 the error bars cannot be separated. Thus, the numbers should be mentioned in a table e.g. with median, 90-percentiles etc.

5. The consequences of the data should be updated:

Presently PCT is also used to guide antibiotic therapy. Especially the negative predictive value to exclude a risk of sepsis is used. The major strength of the manuscript is using the quite sensitive assay of Roche (see detection thresholds). Hence, the NPV of negative PCT values (< 0.1ng/ml PCT) should be discussed and analysed, e.g. for the following procedure:

If only a single shot antibiosis after trauma is given on day 0 or 1, and PCT remains low < 0.1ng/ml, it should be questioned whether further AB therapy is required? What about the data regarded this discussion point, at least it should be mentioned as a possible use of the data presented. Again, during the further course, do negative PCT levels e.g. < 0.1 ng/ml indicate that there is no sepsis and hence no antibiotics are required?
Since we cannot look into the future, this must be a daily approach and daily analysis, not a prospective „prediction of sepsis“, since this does not help the patient, and the ROC values are also quite low for this purpose (around 0.7x...). But using on a daily base the NPV would be clinically helpful.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

No competing interest.