Reviewer's report

**Title:** Procalcitonin and procalcitonin kinetics for diagnosis and prognosis of intravascular catheter-related bloodstream infections in critical care: a prospective observational study

**Version:** 1 **Date:** 6 August 2012

**Reviewer:** Pierre-Emmanuel Charles

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Theodorou et al present herein the results of an interesting study about PCT diagnosis and prognosis value in the setting of suspected catheter-related BSI. They show that in selected patients from their ICU, PCT is likely to predict reliably the risk of CR-BSI (Se = 92%; Sp = 100% with a 0.7 ng/mL cut-off). Comparatively, neither WBC nor CRP was likely to differentiate between the patients with or without proven CR-BSI. In addition, the authors show that PCT kinetic analysis allows an earlier diagnosis and provides relevant information regarding the outcome of the infection.

The topic is timely and the study well conducted. I have however several concerns.

**Major comments:**

First, I am concerned about the fact that the included patients look peculiar, precluding therefore the external validity of the study. Accordingly, these patients are “young”, with a low rate of underlying disease, mainly surgical with neurological admission diagnosis. In other words, most of the included patients are likely to be trauma patients. As a result, the findings of this study cannot be translated to other groups of patients. In addition, the authors have excluded all the patients with any infection prior to the suspicion of CR-BSI. This limitation should also be clearly stressed within the discussion section since the remaining patients are clearly different from those we use to deal with in the ICU setting. Although this point weakens the presented findings, it represents one of its strength. Accordingly, sepsis biomarkers such as PCT often prove useful when confounders have been withdrawn. The discussion section should be deeply modified accordingly. The authors should say that the conflicting findings met in the literature could result for such case-mix concerns.

Secondly, I have concerned about the isolated bacterial pathogens. Thus, gram negative are predominantly recovered from the patients with proven CR-BSI. Since gram positive bacteria are usually encountered in this setting, the authors should comment this point within the discussion. Interestingly, this could account for the fact that PCT elevation is more elevated than expected if you consider the study from Schuetz et al (ref 28), focusing on coagulase-negative staphylococci CR-BSI. This point should be discussed since it has been shown previously that
PCT elevation was greater in the patients with GNB bacteremia as compared to those with gram-positive BSI.

Another issue to be addressed is about the way the authors categorized the included patients as “proven” or “not proven” CR-BSI. First of all, the authors should replace “group 1” and “group 2” by proven and unproven, respectively, in order to clarify their manuscript. Although the criteria are well described, the reader cannot know exactly which one(s) was(were) mandatory: all or almost one? Which one(s)? Please clarify. In addition, criteria fulfillment should be detailed for each group in a new table.

Minor comments

English expression should be improved

Title: “in selected critically ill patients” instead of “in critical care”

p. 5, 2nd §: “catastrophic” should be avoided. “septic shock” instead of “severe sepsis”.

p. 6: 3methods”: the CRBSI criteria should be described before exclusion criteria and clarified as told above.

p. 7: given the isolated bacteria in your study, which antibiotics are recommended in the patients with CR-BSI? What is the proportion of appropriate treatments in your cohort? Such data should be provided since the outcome was evaluated.

p. 8, 3rd §: the fact that the Kryptor test was not available should be discussed as a limitation of the study.

p. 12: The first sentence of the discussion should be modified. It should be clearly said that the cohort is made of selected patients as mentioned above. In addition, the discussion should be shorten.

p. 15: it should be said as a perspective that beyond larger observational studies, clinical trials would be the best way to demonstrate any impact of PCT dosing when dealing with ICU patients with suspected CR-BSI.

References:
The number of references should be reduced.

Tables:
The likelihood ratios should be provided in a new Table instead of electronic supplemental, in addition to Se, Sp, PPV and NPV.

Table 2:
The number of patients with PCT measurement actually available for analysis from D1 to D4 should be provided
Table 5: the same comment as in Table 2

Figures 2 & 4: standard deviations should be shown on the graph
**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I have received lecture fees from Brahms AG during the past 5 years.