Author’s response to reviews

Title: Serum procalcitonin elevation in the critically ill patients at the onset of bacteremia caused by either gram negative or gram positive bacteria

Authors:

Pierre emmanuel charles (pierre-emmanuel.charles@chu-dijon.fr)
sylvain ladoire (sylvain.ladoire@chu-dijon.fr)
serge aho (ludwig-serge.aho@chu-dijon.fr)
jean-pierre quenot (jean-pierre.quenot@chu-dijon.fr)
jean-marc doise (jean-marc.doise@chu-dijon.fr)
sebastien prin (sebastien.prin@chu-dijon.fr)
Nils-Olivier olsson (nils.olsson@chu-dijon.fr)
Bernard Blettery (bernard.blettery@chu-dijon.fr)

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ANSWER TO REVIEWER 1 (V. Nobre)

General comments:

Title: We do not agree with the title suggested by the reviewer since we believe that PCT is not reliable enough to really help the physician in the clinical setting as mentioned in the text and by both reviewers as well.

Major compulsory revisions:

1. We agree with the fact that the antibiotic therapy choice is based on the clinical judgment including the infection source knowledge as well as the patient origin (i.e., community-acquired vs nosocomial sepsis) rather than on the level of any biomaker. Accordingly, PCT predictive value does not appear as sufficiently high to be helpful per se. This point is more clearly discussed within the conclusion section (p 12) and emphasized within the conclusion.

2. We agree with the reviewer statements about the fact that PCT elevation should be milder if soft tissue infection is considered. Firstly because such infections are localized ones. Secondly, because they should have been diagnosed earlier which could account for a better outcome and lower PCT levels as well. Since soft tissue infections are more likely caused by gram positive bacteria, one cannot exclude therefore that « soft tissue » behaves as a confusing variable in our statistical model. However, it is worth noting that whereas the « soft tissue » variable was entered into our multivariate analysis model, a low PCT value remains independently associated with the isolation of gram positive bacteria in blood culture. In addition, the large difference between gram positive and gram negative bacteremia in terms of PCT level remains after the exclusion of the patients with soft tissue infections. This point is now clarified.
within the discussion section (p. 11 last §).

There is a balance between both groups (i.e., GP and GN bacteremia) in terms of surgical patients number (5 [11.1%] and 6 [11.5%], respectively). In addition, PCT levels were similar in surgical patients than in medical patients (log10PCT=1.03 vs 1.07, p=0.90).

<table>
<thead>
<tr>
<th>PCT (ng/mL)</th>
<th>Infection source</th>
<th>Isolated bacteria</th>
<th>Age</th>
<th>gender</th>
<th>SAPS II</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.41</td>
<td>lung</td>
<td>Pseudomonas aeruginosa</td>
<td>29</td>
<td>F</td>
<td>24</td>
</tr>
<tr>
<td>0.34</td>
<td>Soft tissue</td>
<td>S aureus</td>
<td>61</td>
<td>M</td>
<td>33</td>
</tr>
<tr>
<td>0.36</td>
<td>unknown</td>
<td>Propionibacterium acnes</td>
<td>54</td>
<td>F</td>
<td>76</td>
</tr>
<tr>
<td>0.36</td>
<td>catheter</td>
<td>S aureus</td>
<td>56</td>
<td>M</td>
<td>31</td>
</tr>
<tr>
<td>0.08</td>
<td>unknown</td>
<td>S aureus</td>
<td>58</td>
<td>F</td>
<td>58</td>
</tr>
<tr>
<td>0.07</td>
<td>catheter</td>
<td>S non-aureus</td>
<td>52</td>
<td>F</td>
<td>19</td>
</tr>
</tbody>
</table>

3. A PCT < 0.5 was found in 6 patients (1 with GN and 5 with GP bacteremia). The clinical findings are the following:

The content of this table has now been summarized and included in the results section (p. 8 2nd §).

Minor essential revision:
We apologize for the mistake. ¿appropriate¿ has been replaced by ¿inappropriate¿.

ANSWER TO REVIEWER 2 (B. Tang)

1. We acknowledge that there is a discrepancy between the text and the table 3. The logistic regression analysis results are now suitably presented. Variables coding has been modified and new odd ratios have been calculated. The legend if the table 3 has also been modified.

2. The fact that our findings do not allow the use of PCT as a reliable tool to distinguish between gram negative and gram positive bacteremia is now more clearly emphasized within the discussion section, as also suggested by the other reviewer (p 12). This point has also been added to the conclusion.

3. The required confidence intervals are now provided in the Table 4.

4. We agree with the reviewer comment. It is now mentioned within the abstract that there was no difference between groups in terms of SOFA score values in order to support the conclusion.

English expression has been revised.