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Letter to the Editor

Reply to: Why would procalcitonin perform better in patients with a SOFA-score less than 8?

We appreciate the comments made by Dr van Oers and colleagues concerning the effect of procalcitonin (PCT)-guided cessation of antibiotics in patients with a Sequential Organ Failure Assessment (SOFA) score of less than 8. Our meta-analysis revealed that PCT-guided cessation of antibiotic therapy decreased the short-term mortality in patients with an average SOFA score of <8, suspected sepsis, or lower algorithm adherence (<70%), but not in those with a score >8, confirmed sepsis, or higher adherence (Peng et al., 2019). Compared to the standard care group, PCT-guided antibiotic therapy failed to decrease the mortality or shorten the length of intensive care unit (ICU) stay, as reported in previous trials (Bouadma et al., 2010; Jensen et al., 2011; Bloos et al., 2016). Therefore, we concluded that PCT-guided antibiotic therapy would not be suitable for severely critically ill patients.

The accuracy of PCT monitoring is far from perfect and sepsis is a heterogeneous and complex syndrome. Organ injury or failure, such as acute kidney injury and thermal injury, contribute to hyperprocalcitonemia (Carsin et al., 1997; Grace and Turner, 2014). Thus, the PCT level does not veritably reflect the infection in those sepsis patients with higher SOFA scores. Moreover, the risk factors, such as the presence of septic shock or acute respiratory distress syndrome (ARDS), contribute to the occurrence of multidrug-resistant organisms, which promote antibiotic use, prolong hospital stay, increase the mortality, and eventually lead to biases in the effect of PCT guidance. In addition, there was no original study exploring the effect of PCT-guided antibiotic therapy that compared patients in the emergency department and general ward with those in the ICU. Based on our evidence, we did not recommend PCT-guided antibiotic therapy in critically ill patients.

We agree with Dr van Oers that analyses on an individual patient level should be done to measure whether the SOFA score influences the effect of antibiotic therapy. It is known that an individual patient data meta-analysis offers several advantages in bias assessments and in explaining the heterogeneity. The recent patient-level meta-analysis on PCT-guided antibiotic therapy by Wirz and colleagues included different severity subgroups based on SOFA score (0 to 6, 7 to 10, and 10 to 24); however, the results indicated no significant difference due to the subgroup effect, with all p-values >0.05 and odds ratio (OR) and 95% confidence interval (95% CI) values from OR 0.85 (95% CI 0.66, 1.10), OR 0.92 (95% CI 0.73, 1.17) to OR 0.86 (95% CI 0.72, 1.01) (Wirz et al., 2018). Furthermore, several studies that enrolled infectious patients in the ICU were not included in this meta-analysis (Stolz et al., 2009; Jensen et al., 2011; Najafi et al., 2015; Wang et al., 2016; Daubin et al., 2018), which would distinctly contribute to the bias. The SISPCT trial enrolled 1076 patients with a mean APACHE II score of 24.2 ± 7.6 and mean SOFA score of 10.0 ± 3.3, illustrating a comparable difference in 28-day mortality between the PCT guidance (25.6%) and no PCT guidance groups (28.2%; $p = 0.34$) (Bloos et al., 2016). Therefore, we considered that the effect of PCT-guided antibiotic therapy in patients with different severities of illness was not conclusive and needed further validation.

We agree with Dr van Oers that PCT would be better suited for the cessation of antibiotic therapy, as suggested by our results. If we excluded the SAPS-trial, the significance on short-term mortality of PCT-guided cessation of antibiotic therapy was moderate (OR 0.89, 95% CI 0.72, 1.10; $p = 0.30$). We noted that the first treatment course was insufficient in the SAPS-trial, which was launched in the Netherlands, where physician prescribing of antibiotics is quite low (de Jong et al., 2016). Moreover, the PRORATA trial reported a non-significant absolute increase in the risk of death of 3.8% (95% CI −2.1, 9.7) on day 60 (Bouadma et al., 2010). Hence, we insist that antibiotics should be initiated or withheld according to symptoms, signs, and positive laboratory examinations and should not be based on PCT alone.

Author contributions

All authors (Fei Peng, Wei Chang, Chun Pan and Yi Yang) made equal contributions.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

Not applicable.

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