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Reply to Gibot

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Dear Sir: Herewith we respond to comments on our paper [1] made by Dr. Gibot.

The fact that the study was performed retrospectively is stated clearly, but it was not reported explicitly that part of the samples were used in a previous study [2]. All samples were stored at -80°C in different aliquots until further processing. They were not subject to freeze-thaw cycles, since one aliquot was used in the study by Linssen et al. [2] and a different aliquot was used for our study.

Despite the fact that centrifugation at $250\times g$ for 10 min might not have been sufficient to eliminate all cells present in the bronchoalveolar lavage (BAL) fluid, samples from the confirmed ventilator-associated pneumonia (VAP) group and the nonconfirmed VAP group were subject to the same procedure. Although we cannot completely exclude that persistence of cells expressing triggering receptor expressed on myeloid cells-1 (TREM-1) might have confounded results, it is unlikely that this explains the lack of difference between VAP and non-VAP, since the mean cell count was higher in the confirmed VAP group ($p < 0.001$).

In case of antibiotic use, percentage intracellular organisms (ICO, $\geq 2\%$) will still be a reliable diagnostic tool for diagnosis of VAP [2]. The number of VAPs diagnosed using ICO percentage and negative quantitative culture was 16 of 97 cases (17%). Since standard practice at our intensive care unit (ICU) is to start antibiotics after performance of BAL, this suggests that no VAPs were misdiagnosed due to prior antibiotic use. The final diagnosis in nonconfirmed VAP patients could not be retrospectively established in all cases, but varied from acute respiratory distress syndrome (ARDS) to *Pneumocystis pneumonia* (PCP).

Finally, we were not aware of the fact that the assay was recalled by R&D Systems, a fact for which we apologise. However, the assay was recalled because the kit had a bias towards detection of recombinant TREM-1, thereby underestimating natural TREM-1 levels. Since the recombinant TREM-1 was only used to determine the standard concentrations and was not used in the actual assay, the underestimation occurred in samples of both VAP and non-VAP patients. Moreover, differences in outcome between studies on the diagnostic value of sTREM-1 may be readily explained by factors other than the assay itself, as stated in Table 2 of our paper [1]. Three studies [3–5] indicated that sTREM-1 levels in BAL had potential for the diagnosis of VAP [using immunoblot or DuoSet enzyme-linked immunosorbent assay (ELISA, R&D Systems)], and three studies [1, 6, 7] suggested that sTREM-1 levels in BAL fluid may not be helpful in diagnosing VAP (using DuoSet or Quantikine ELISA, R&D Systems). Additionally, the number of cases, the general everyday ICU setting, and the correction for dilution of BAL and type of BAL may have had a role in the difference in outcome of the studies.

In conclusion, in our opinion, this study (despite its limitations) contributes to the debate about the value of sTREM-1 as a diagnostic marker for VAP because the study was performed in a large general ICU population. This is the population in which sTREM-1 should be used and in which sTREM-1 levels may not be helpful for clinicians to establish the diagnosis of VAP.

Conflicts of interest statement None.

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