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CORRESPONDENCE

A way towards ventilator-associated lower respiratory tract infection research

Ignacio Martin-Loeches[1,2*], Pedro Povoa[3,4,5] and Saad Nseir[6,7]

Dear Editor,

We read with interest the systematic review and meta-analysis by Fernando et al. recently published in *Intensive Care Medicine* evaluating the diagnostic performance of ventilator-associated pneumonia (VAP) of physical examination findings (fever, purulent secretions), chest radiography, endotracheal aspirate cultures, bronchoscopic cultures, and Clinical Pulmonary Infection Score (CPIS) in comparison with either histopathology of lung tissue, or quantitative BAL cultures as reference standards [1]. Despite the findings of poor accuracy for diagnosis of VAP of individual clinical indicators, we believe that there are several shortcomings that were not fully discussed.

The first point that must be addressed is the so-called gold standard of VAP diagnosis—the histopathologic criteria of pneumonia (intense infiltration of the intraalveolar spaces by neutrophils, fibrinous exudates, and cellular debris, particularly around terminal bronchioles, and the presence of an infectious agent at that level). However, as the authors clearly pointed out these criteria are themselves "*subject to disagreement between pathologists*". How could the authors use as gold-standard criteria that are not well defined? Besides, as Osler has already noted over 100 years ago with the so-called terminal pneumonia—that we now classified as HAP or VAP—this is not lobar pneumonia as CAP but more patchy pneumonia characterized by infiltrates being spread heterogeneously in the lung; in this way, a single normal biopsy does not exclude the presence of HAP/VAP since the biopsy could have reached normal lung area and, a few centimetres away, we could have alveolar infiltration.

The second point is that the authors suggested ventilator-associated events (VAEs) as a better surveillance tool that VAP rates, but VAE includes a criterion that was not evaluated, that is, changes in oxygen requirement after a period of stability [2]. In addition, VAEs have shown a poor correlation with both VAP and ventilator-associated tracheobronchitis (VAT) and have been associated with higher consumption of resources (ICU and hospital length of stay), but not with mortality. Since VAE was designed only as a surveillance tool and the assessed criteria "*have poor accuracy for diagnosing*" VAP, what do the authors propose for clinical use at the bedside?

The third point is that no one uses these criteria individually. In addition, the clinicians use them together and also monitor the longitudinal changes, in conjunction with the changes in organ dysfunction like oxygenation assessed by the P/F ratio [3]. The authors did not take into account this common practice at the bedside.

Finally, using the aforementioned criteria, we showed that VAT and VAP are interconnected diseases, both associated with an increase in length of stay in both ICU and hospital, but with different impacts on mortality. In addition, we also showed that adequate antibiotic therapy had a significant impact on outcomes. And recently, we found that the impact of the adequacy of antibiotic therapy on mortality was conferred only to patients without cardiovascular failure [4].

Therefore, in the light of the poor definitions of the histopathologic criteria of pneumonia, inability to propose other alternative criteria, ignoring the usual clinical use of the diagnostic criteria, and finally the impact of adequacy of antibiotics on VAT and VAP, we think that the conclusions of this systematic review and meta-analysis should be regarded with great caution.

*Correspondence: drmartinloeches@gmail.com
[1] Department of Intensive Care Medicine, Multidisciplinary Intensive Care Research Organization (MICRO), St. James's Hospital, St. James Street, Dublin 8, Dublin, Eire, Ireland
Full author information is available at the end of the article

Author details
[1] Department of Intensive Care Medicine, Multidisciplinary Intensive Care Research Organization (MICRO), St. James's Hospital, St. James Street, Dublin 8, Dublin, Eire, Ireland. [2] Hospital Clinic, IDIBAPS, Universidad de Barcelona, Ciberes, Barcelona, Spain. [3] Polyvalent Intensive Care Unit, São Francisco Xavier Hospital, Centro Hospitalar de Lisboa Ocidental, Lisbon, Portugal. [4] NOVA Medical School, CHRC, New University of Lisbon, Lisbon, Portugal. [5] Center for Clinical Epidemiology and Research Unit of Clinical Epidemiology, OUH Odense University Hospital, Odense, Denmark. [6] Critical Care Center, CHU Lille, 59000 Lille, France. [7] Medicine Faculty, Lille University, 59000 Lille, France.

Compliance with ethical standards

Conflicts of interest
No conflicts of interest to disclose.

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References

1. Fernando SM, Tran A, Cheng W, Klompas M, Kyeremanteng K, Mehta S, English SW, Muscedere J, Cook DJ, Torres A, Ranzani OT, Fox-Robichaud AE, Alhazzani W, Munshi L, Guyatt GH, Rochwerg B (2020) Diagnosis of ventilator-associated pneumonia in critically ill adult patients-a systematic review and meta-analysis. Intensive Care Med. https://doi.org/10.1007/s00134-020-06036-z
2. Pouly O, Lecailtel S, Six S, Preau S, Wallet F, Nseir S, Rouze A (2020) Accuracy of ventilator-associated events for the diagnosis of ventilator-associated lower respiratory tract infections. Ann Intensive Care 10(1):6. https://doi.org/10.1186/s13613-020-0624-6
3. Ferrer M, Sequeira T, Cilloniz C, Dominedo C, Bassi GL, Martin-Loeches I, Torres A (2019) Ventilator-associated pneumonia and PaO2/FIO2 diagnostic accuracy: changing the paradigm? J Clin Med. https://doi.org/10.3390/jcm8081217
4. Martin-Loeches I, Torres A, Povoa P, Zampieri FG, Salluh J, Nseir S, Ferrer M, Rodriguez A (2019) The association of cardiovascular failure with treatment for ventilator-associated lower respiratory tract infection. Intensive Care Med 45(12):1753–1762. https://doi.org/10.1007/s00134-019-05797-6