LETTER

New molecular semi-quantification tool provides reliable microbiological evidence for pulmonary infection

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Dear Editor,

Ventilator-associated pneumonia (VAP) remains one of the most commonly encountered hospital-acquired infections worldwide, despite recent national surveillance data suggesting its declining incidence [1]. Many reports have been published on the use of large multiplex rapid diagnostic methods for various community-acquired infections, but their validity for the microbiological diagnosis of VAP using a semi-quantitative approach has not yet been assessed [2, 3].

Bronchoalveolar lavage (BAL) specimens from a prospective, non-randomized, non-interventional, multi-center clinical trial enrolling 120 patients [4] were used to evaluate the new BioFire® Pneumonia Panel (BPP). A total of 117 BAL specimens were tested with the BPP, which enabled the detection of 18 bacteria, 8 viruses, and 7 antimicrobial resistance-associated genes in 1 h. Results were compared with conventional culture methods (CC). Assessment of concordance for the identification of 15 commonly detected bacteria was done, according to an agreed semi-quantitative threshold to report a positive result [5]. Clinicians were left blinded to the rapid test results and patients were treated according to local guidelines.

We found that the most frequent bacterial species in BAL were *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Haemophilus influenzae* with 14 (12%) of the

specimens positive for the *ctx-m* gene and 12 (10%) for viruses. Overall bacterial identification concordance with CC was 89.0% positive percentage agreement (PPA) and 95.9% negative percentage agreement (NPA). A total of 74 (39%) identification calls were discrepant between both techniques. In 26 (14%) cases, the same microorganism was detected by both BPP and CC, even though they were considered as apparent discrepancies, as a result of the different positivity threshold call used for each technique. Eleven (6%) were false positive BPP calls that could be explained by an active antimicrobial therapy ongoing at the time of BAL collection. Overall concordance increases to 93.1% PPA and 98.2% NPA (Fig. 1) when reconsidering these discrepancies as true positive results. Additional investigations were carried out on the 10 (5.2%) false negative identification calls remaining. While 4 (2.0%) were linked to a wrong identification provided by CC, 6 (3.1%) remained unexplained. This latter number appears acceptable when considering overall usual microbiological documentation in VAP with CC methods. If the molecular method was used to choose initial therapy, in 28 (29.1%) patients, initial antimicrobial treatment should have been larger, as at least one microorganism reported by BPP was not covered; and in 16 (16.7%) patients, initial antimicrobial therapy could have been more targeted, as prescription of at least one antimicrobial agent would not have been supported by the BPP results.

Our study is the first comparing concordance of a multiplexed molecular method with conventional culture, based on the use of specific semi-quantitative thresholds for positivity calls, enrolling more than 100 homogeneous

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patients with suspected VAP. The availability of rapid reliable microbiological results and resistance information can be of major utility to effectively manage critically ill patients in the ICU with suspected or confirmed VAP but more comprehensive prospective studies are required to understand if the use of the BPP would have an overall positive impact in the management of VAP, including effect on antimicrobial use, clinical outcomes, and emergence of resistance even when considering some false negative results.

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Compliance with ethical standards

Conflicts of interest

BF, OB, and MCP institutions have received funding from bioMérieux to run the VALIBI study. JYM, AI, CAS, AP, and VM are employees of bioMérieux S.A. CG is an employee of bioMérieux Inc. MR is an employee of BioFire Diagnostics LLC.

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