Intensive Care Med (2024) 50:789–791
https://doi.org/10.1007/s00134-024-07375-x

CORRESPONDENCE

Rapid multiplex PCR panels for the management of ventilator-associated pneumonia: pondering strengths and weaknesses

Mara Tomasello[1,2], Davide Mangioni[1*], Mauro Panigada[3], Caterina Matinato[4] and Alessandra Bandera[1,2]

We read with interest the review by Kreitmann et al. on intensive care unit (ICU)-acquired infections in immunocompromised patients [1]. The authors nicely discussed conditions associated with immunosuppression in ICU and mechanisms of infections. Their review offers also an up-to-date description of epidemiology and diagnostic–therapeutic management of ventilator-associated lower respiratory tract infections (VA-LRTIs) in this population.

However, we do not agree with the authors' view on the role of multiplex polymerase chain reaction (mPCR)-based tests in VA-LRTIs. While they stated that mPCR pneumonia tests are probably less useful for ICU-acquired than for community-acquired infections, we believe they are actually quite the opposite. Recent guidelines on community-acquired pneumonia suggest mPCR testing only "whenever nonstandard antibiotics are prescribed or considered" [2]. Conversely, multicenter randomized controlled trials on nosocomial pneumonia showed that mPCR-based tests could increase the sensitivity of microbial sampling and/or shorten the duration of inappropriate antibiotic therapy, supporting their use to improve antibiotic stewardship in ICU [3].

*Correspondence: davide.mangioni@policlinico.mi.it
[1] Infectious Diseases Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
Full author information is available at the end of the article

This comment refers to the article available online at https://doi.org/10.1007/s00134-023-07295-2

In the prospective cohort study CoV-AP, we previously evaluated the concordance between mPCR-based test BIOFIRE®FILMARRAY® Pneumonia Panel plus (BAL_{FAPPP}) and standard cultures (BAL_{CX}) on bronchoalveolar lavage (BAL) of ICU patients with coronavirus disease 2019 (COVID-19) and suspected ventilator associated pneumonia (VAP) [4].

Based on a secondary analysis of the CoV-AP study, here we want to share some food for thought on the impact of mPCR-based tests on therapeutic decisions of VA-LRTIs in real-life settings.

1. *Strength point #1*: *very short turnaround time*.

   In the CoV-AP cohort, the median time from BAL acquisition to definitive microbiological results differed greatly between techniques (6.3h, interquartile range (IQR) 4.5–7.7h for BAL_{FAPPP} and 70.6h, IQR 49.7–77.8h for BAL_{CX} results).
2. *Strength point #2*: *ability to anticipate (the majority of) therapeutic choices*.
   Therapeutic decisions based on BAL_{FAPPP} were confirmed at the arrival of BAL_{CX} in 81.6% of cases (confirmation of prescribed antibiotics in 57.2% of cases; confirmation of antibiotics withheld in 24.5% of cases) (Figure 1).
3. *Limitation #1*: *be aware of what is missing*.
   As the authors stated, an intrinsic limitation of mPCR-based tests is the (relatively) limited number of targets. In the CoV-AP study, BAL_{FAPPP} was not able to microbiologically characterize VAP caused by Corynebacterium spp and Aspergillus spp (12.2%

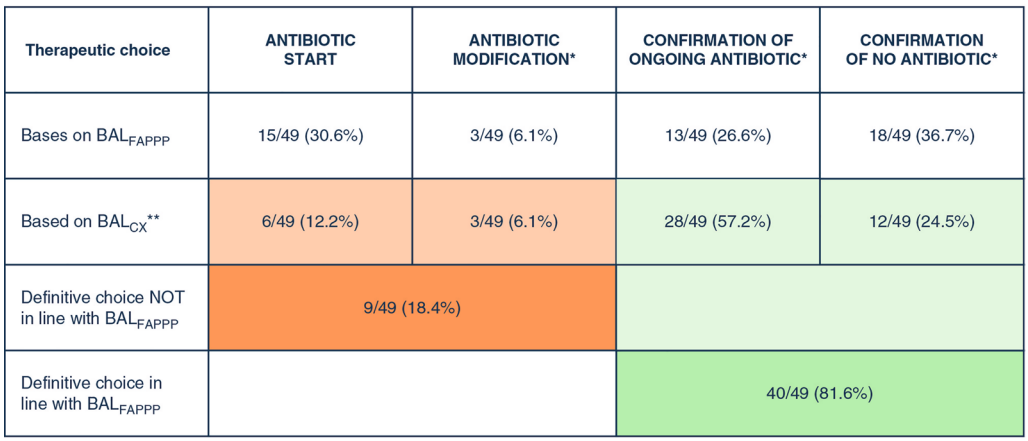

Fig. 1 Therapeutic choices based on BAL_{FAPPP} and BAL_{CX} in patients with suspected VAP of the CoV-AP study. *16/49 patients (32.6%) were already on antimicrobial therapy at the time of BAL acquisition. **Therapeutic choices based on BAL_{CX} considered decisions guided by BAL_{FAPPP} as baseline

of total cases) [4]. Beyond COVID-19, in our clinical practice, the main limitation of BAL_{FAPPP} is the absence of detection of uncommon Enterobacterales and non-fermenting gram-negative bacteria (*i.e.*, *Stenotrophomonas maltophilia*), which are a rare but possible cause of LRTIs in patients with long ICU stay or immunocompromised hosts such as solid organ transplant.

4. *Limitation #2*: *all that glitters is not gold*.
   In the CoV-AP cohort, the prevalence of VAP caused by multidrug-resistant organisms was low (7% with BAL_{FAPPP} and 3% with BAL_{CX}). Interestingly, of the three cases with resistance mechanisms detected in BAL_{FAPPP}, only one was confirmed by BAL_{CX}. Although uncommon, discrepant results between BAL_{FAPPP} and standard cultures or other molecular methods have been reported [5].

Most likely, mPCR-based tests will change the management of VA-LRTIs, if is not already happening. While waiting for further trials to assess their impact on antibiotic consumption and clinical outcomes, physicians should be aware of their strengths and limitations.

Author details
[1] Infectious Diseases Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy. [2] Department of Pathophysiology and Transplantation, University of Milano, Milan, Italy. [3] Department of Anaesthesia, Critical Care and Emergency, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy. [4] Microbiology Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.

Funding
This study was partially funded by the MSD Investigator Initiated Studies Program (MISP) 2020, by the Italian Ministry of Health—Current Research IRCCS, and by the project STOP COVID financed by COVID-19 emergency donations.

Declarations

Conflicts of interest
MT declared there are no conflicts of interest; DM received speaker's honoraria from Pfizer and MSD and received travel grants from Pfizer; MP declared there are no conflicts of interest; CM declared there are no conflicts of interest; and AB received speaker's honoraria and fees for attending advisory boards from AstraZeneca, bioMérieux, Janssen-Cilag, Nordic Pharma, Pfizer, QIAGEN, Sobi, and ViiV and received research grants from Gilead.

Ethical approval and consent to participate
This clinical study was approved by the Milan Area 2 Ethical Committee (#97_2021). We received informed consent from participants or their proxies. All data processing was performed according to the Declaration of Helsinki.

Publisher's Note

Accepted: 24 February 2024
Published: 18 March 2024

References

1. Kreitmann L, Helms J, Martin-Loeches I, Salluh J, Poulakou G, Pène F, Nseir S (2024) ICU-acquired infections in immunocompromised patients. Intensive Care Med. https://doi.org/10.1007/s00134-023-07295-2
2. Martin-Loeches I, Torres A, Nagavci B, Aliberti S, Antonelli M, Bassetti M, Bos LD, Chalmers JD, Derde L, de Waele J, Garnacho-Montero J, Kollef

M, Luna CM, Menendez R, Niederman MS, Ponomarev D, Restrepo MI, Rigau D, Schultz MJ, Weiss E, Wunderink R (2023) ERS/ESICM/ESCMID/ALAT guidelines for the management of severe community-acquired pneumonia. Intensive Care Med 49(6):615–632. https://doi.org/10.1007/s00134-023-07033-8

3. Darie AM, Khanna N, Jahn K, Osthoff M, Bassetti S, Osthoff M, Schumann DM, Albrich WC, Hirsch H, Brutsche M, Grize L, Tamm M, Stolz D (2022) Fast multiplex bacterial PCR of bronchoalveolar lavage for antibiotic stewardship in hospitalised patients with pneumonia at risk of Gram-negative bacterial infection (Flagship II): a multicentre, randomised controlled trial. Lancet Respir Med 10(9):877–887. https://doi.org/10.1016/S2213-2600(22)00086-8
4. Mangioni D, Panigada M, Palomba E, Bobbio C, Chatenoud L, Alagna L, Fumagalli J, Gori A, Grancini A, Guzzardella A, Lombardi A, Matinato C, Meli A, Muscatello A, Porretti L, Tomasello M, Trombetta E, Valenti L, Bandera A, Grasselli G (2023) Incidence, microbiological and immunological characteristics of ventilator-associated pneumonia assessed by bronchoalveolar lavage and endotracheal aspirate in a prospective cohort of COVID-19 patients: CoV-AP study. Crit Care (Lond, Engl) 27(1):369. https://doi.org/10.1186/s13054-023-04658-5
5. Murphy CN, Fowler R, Balada-Llasat JM, Carroll A, Stone H, Akerele O, Buchan B, Windham S, Hopp A, Ronen S, Relich RF, Buckner R, Warren DA, Humphries R, Campeau S, Huse H, Chandrasekaran S, Leber A, Everhart K, Harrington A, Bourzac KM (2020) Multicenter evaluation of the BioFire FilmArray pneumonia/pneumonia plus panel for detection and quantification of agents of lower respiratory tract infection. J Clin Microbiol 58(7):e00128-e220. https://doi.org/10.1128/JCM.00128-20