Factors limiting the utility of bronchoalveolar lavage in the diagnosis of COVID-19

Reply to D. Aggarwal and V. Saini:

We thank D. Aggarwal and V. Saini for their comments on our research letter [1], as they allow us to better highlight the main key points of our study, dismissing possible misinterpretation of its results.

D. Aggarwal and V. Saini misreported that bronchoalveolar lavage (BAL) was negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rRT-PCR in a majority of cases, including 38 patients with "strong clinical and radiological suspicion for COVID-19". Indeed, we reported that, among those patients who underwent chest computed tomography (CT) scan, 38 revealed radiological signs compatible with an ongoing viral infection but not necessarily typical features of coronavirus disease 2019 (COVID-19). On the contrary, in the only two cases of our series in which CT scan showed typical signs of COVID-19 infection according to a recently published international consensus statement [2], BAL was positive for SARS-CoV-2, despite previous negative upper respiratory tract swabs. Moreover, we reported that, when chest CT scan was normal, then both upper respiratory tract swabs and BAL were rRT-PCR-negative for SARS-CoV-2.

These findings support our main observation that BAL is likely to be negative if one or more upper respiratory tract specimens and thoracic imaging are concordantly negative; therefore, it should be only reserved for those cases in which a high clinical and radiological suspicion for COVID-19 stands despite negative upper respiratory tract swabs.

D. Aggarwal and V. Saini also deem that our results might imply a high false-negative rate of rRT-PCR for SARS-CoV-2 in BAL samples. However, our study aimed at evaluating not the diagnostic yield of BAL in COVID-19, but the agreement (test concordance) between negative upper respiratory tract swabs and BAL to exclude COVID-19. This is a fundamental concept that we believe may be of valuable support to clinical practice in times of pandemics, when excessive demands for BAL confirmation of repeatedly negative upper respiratory swabs expose operators to a high infectious risk while being clinically futile. In fact, BAL has an unquestioned role in the diagnosis of pneumonia when non-invasive methods are not sufficient for an aetiologic characterisation; however, concerning SARS-CoV-2, we showed that BAL has a limited role in excluding COVID-19 if both upper respiratory swabs and chest CT are negative. We obviously agree with D. Aggarwal and V. Saini that clinical performance of a diagnostic test varies not only in light of its sensitivity but also of pretest probability, which is affected by several factors, one of which is disease prevalence. Nevertheless, it is not possible to calculate a true pretest probability for COVID-19 at the moment, as the actual prevalence of SARS-CoV-2 infection is still not known [3].

Finally, D. Aggarwal and V. Saini request detailed insight of our study population with regard to alternate diagnoses, clinical outcomes and their correlation with rRT-PCR test performance on upper and lower respiratory tract. Unfortunately, this is out of the main focus of this study and it would need much more space than allowed by the journal for this manuscript format to be elucidated.

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References

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2 Simpson S, Kay FU, Abbara S, *et al.* Radiological Society of North America expert consensus statement on reporting chest CT findings related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA. *Radiol Cardiothorac Imaging* 2020; 2: e200152.

3 Woloshin S, Patel N, Kesselheim AS. False negative tests for SARS-CoV-2 infection – challenges and implications. *N Engl J Med* 2020; 383: e38.