Comment on: Bronchoalveolar lavage fluid lymphocytosis in chronic hypersensitivity pneumonitis: a systematic review and meta-analysis

To the Editor:

We commend Adderley *et al.* [1] for their meta-analysis assessing bronchoalveolar lavage fluid (BALF) lymphocytosis in the diagnosis of chronic hypersensitivity pneumonitis. Distinguishing chronic hypersensitivity pneumonitis (cHP) from idiopathic pulmonary fibrosis (IPF) has prognostic and therapeutic implications. Since there are no studies using lung biopsy as the gold standard to answer this question, the authors had to rely on observational studies, some of which used BALF lymphocytosis as a criterion to diagnose cHP. The authors acknowledge that this can cause diagnostic test incorporation bias. Incorporation bias can result in falsely increased estimates of the association between BALF lymphocytosis and cHP, or in biased conclusions that a bronchoalveolar lavage (BAL) lymphocyte count can rule in or rule out cHP. This is because specificity and sensitivity can be affected when the test under study is used as part of the gold standard to diagnose the condition of interest [2].

To avoid this bias, it is essential to exclude from a systematic review studies that used BALF lymphocytosis as a criterion to diagnose cHP, or to eliminate them from the analysis.

Yang *et al.* [3] reported that, after excluding studies that used BALF lymphocytosis as a criterion to diagnose cHP, the mean BALF lymphocyte count in patients with cHP was 32.7%, significantly lower than that reported by Adderley *et al.* [1] (42.8%), suggesting the presence of incorporation bias in the latter study. Patolia *et al.* [4] reported in their meta-analysis a 20.8% mean difference in the percentage of BALF lymphocytes between fibrotic hypersensitivity pneumonitis and IPF, compared to a 32.8% difference in BALF lymphocytes between cHP and IPF in the study reported by Adderley *et al.* [1].

To obtain unbiased estimates of BALF lymphocytosis to differentiate cHP from IPF, we suggest that Adderley *et al.* [1] re-analyse the BALF lymphocyte count after excluding studies that used BALF lymphocytosis as a criterion to diagnose cHP. This will provide a more reliable estimate of the role of BALF lymphocytosis in diagnosing cHP.

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Bronchoalveolar lavage fluid lymphocytosis may be useful in the diagnosis of chronic hypersensitivity pneumonitis. However, reanalysis after eliminating studies that used bronchoalveolar lavage lymphocytosis as part of the diagnostic criteria is needed. https://bit.ly/34AmHmm

Cite this article as: Moran-Mendoza O, Khalil M. Comment on: Bronchoalveolar lavage fluid lymphocytosis in chronic hypersensitivity pneumonitis: a systematic review and meta-analysis. *Eur Respir J* 2021; 57: 2004347 [https://doi.org/10.1183/13993003.04347-2020].

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Received: 27 Nov 2020 | Accepted: 13 Dec 2020

Conflict of interest: O. Moran-Mendoza has nothing to disclose. M. Khalil has nothing to disclose.

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