Reviewer's report

Title: Lung diffusing capacity for nitric oxide and carbon monoxide in relation to morphological changes as assessed by computed tomography in patients with cystic fibrosis

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Reviewer: Ivo van der Lee

Reviewer's report:

This article reflects the disharmony that exists in pulmonary medicine between imaging on the one hand and functional testing on the other hand. These two different pathophysiological aspects are coming together in this manuscript: function meets imaging. Therefore, the main question of this small but fine study is challenging.

Because NO is not influenced by capillary blood volume, the DLNO is a true measure for the diffusive properties of the alveolo capillary membrane. In fact, CO is much less classified for this measure. The fact that DLNO is not widely accepted, is pure technical: only since short time DLNO equipment is available. It is logical to search for correlations between this new measure (DLNO) with well known measures like the CT for parenchymal destruction evaluation. This leads directly to one of the weaker point of this study: the Brody score consists mainly of scoring airway disease. Only parenchymal destruction will influence the DLNO. The reason that a strong correlation was found between the DLNO and Kno and the Brody CT score, could be based on the fact that the parenchymal disease is correlated with the Brody score, but not based on loss of surface of the membrane, but on other factors. In that case, the good correlation between DLNO and Brody score should not be causal connected. This possibility should be explored in the discussion section.

In the methods section, no mention is made that [Hb] is measured, I trust that were is stated that "dlco is corrected to the standard Hb", indeed Hb of the subjects is measured. This is of course essential. Please more detailed description here.

Table 4 showes a 5 * 16 matrix of correlation coefficients. This leads to 80 parameters, in which no one will surprised that some significant relation will be found. Furthermore, many parameters on the vertical axis are intercorrelated, for example Raw and FEV1. Some parameters like DLNO and Dm have of course exactly the same correlation coefficients, therefore this table has too abundant data in it, to my opinion. If data is shown, odd correlations need to be explained: eg. how can anyone explain the significant correlation between Vcap and peribronchial thickening. I can't. Therefore, leave some irrelevant data out please.
In conclusion, the main results that the DLNO has significant correlation with the Brody score in CF patients is worthy of publication. Whether this proves that DLNO in this study reflects the parenchymal destruction is open for discussion. This subtle distinction should be more specified in the discussion section.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests