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RESPONSE TO LETTER

Letter to the Editor, International Journal of COPD [Response to Letter]

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Dear editor

We appreciate the observations of Prof. Miller and colleagues about our article recently published in the International Journal of COPD.[1] The authors feel that our conclusions are not supported by data, based on two main arguments.

The first is that concordant and discordant patients are different. This is obvious, and in fact, extensively detailed in our study. It seems that the authors erroneously suggest that our study is penalized by selection bias since concordant and discordant groups are quite dissimilar. In fact, we just compared two different ways of defining airway obstruction in the same prospective cohort, in a similar approach to that used by Prof. Miller et al in a previous publication.[2] Regrettably, in their study, the lack of longitudinal follow-up prevented drawing valid conclusions about the evolution of the patients. Our data suggest that LLN is usually a more restrictive criterion and may misclassify patients with less severe disease. This explains the differences observed during the follow-up in hospitalizations and the COPD mortality after age-adjustment. Our results and those of several previous articles confirm that some patients classified as non-obstructive and therefore without COPD by LLN in fact present severe exacerbations and COPD mortality during follow-up.[3,4]

The second argument is that in patients with advanced COPD, the FEV1/FVC ratio can become artificially increased by premature distal airway closure in the spirometric evaluation of vital capacity with forced spirometry. However, the statement that in our study deterioration of pulmonary function was analyzed by the decline of FEV1/FVC ratio is incorrect. The loss of pulmonary function was measured with FEV1 (see Figure 3). It is true that the annualized FEV1/FVC ratio decreased more in discordant patients during follow-up. Nevertheless, the most relevant data concerning this argument—and not mentioned by the authors of the letter—is that 81% of discordant patients in the initial spirometry became concordant during follow-up. Since the two spirometric measures were performed in a similar manner, the fact that a considerable proportion of initially discordant patients developed obstruction by both criteria during the follow-up suggests that the exclusive use of LLN delayed the diagnosis. In our opinion, this is independent of the premature distal airway closure, which in any case should be similar in the two spirometric measurements.

Finally, a few additional considerations. FR and LLN are two ways to artificially divide a continuous variable (FEV1/FVC), and therefore rather than two different diagnostic criteria, FR and LLN represent two different points to dichotomize the

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same variable. Since COPD is a progressive disease, before reaching the formal threshold of airway obstruction, either by FR or LLN, FEV1/FVC must decline progressively. It is well-known that many non-obstructive patients had radiological involvement on CT preceding by years the accepted definition of airway obstruction, in what some authors have labelled "pre-COPD".[5,6] In other words, in the absence of a biomarker, COPD is diagnosed when functional (airway obstruction) or radiological involvement becomes evident. For this reason, we compare two different cutoffs for the same variable, our conclusions are prudent - LLN seems to be less useful for COPD diagnosis in primary care - and we do not state at any point that our data "clearly demonstrate" that FR is superior to LLN, as the authors of the letter suggest.

Disclosure

Pere Almagro reports grants from AstraZeneca and SEPAR, personal fees from Chiesi, Boehringer Ingelheim, and GlaxoSmithKline, travel support from Rovi and Esteve, unrelated to the submitted study. Montse Llordés reports speaker fees from Boehringer-Ingelheim, Glaxo, and Gebro, outside the submitted work. The authors report no other conflicts of interest in this communication.

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