Sarcopenia in Outcome in Chronic Obstructive Pulmonary Disease: Is the Tip of the Iceberg?: Authors’ Reply

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We appreciate the insightful comments from Hulya et al.\textsuperscript{1} on our study investigating the correlation between low muscle mass and poor clinical outcomes in COPD patients\textsuperscript{2}. They highlighted areas for potential improvement in our research design and raised valid concerns.

Firstly, Hulya et al. suggested incorporating nutritional status and exercise levels to enhance the significance of our results. Acknowledging the importance of these factors in COPD treatment, we agree that their inclusion could strengthen the analysis\textsuperscript{3,4}. Unfortunately, due to the retrospective nature of our study, relevant data on nutritional status and exercise levels were unavailable. While there may be some controversy, serum albumin levels can serve as one of the indicators reflecting recent nutritional status\textsuperscript{5,6}. In our study, serum albumin level was correlated with skeletal muscle mass index (coefficient [r]=0.1614). However, it was not identified as a risk factor for exacerbation in the Cox regression analysis (hazard ratio; 0.724, P=0.139, Table 4). As is known, albumin, affected by inflammation and underlying diseases, may not precisely reflect nutritional status alone\textsuperscript{5,7}. Therefore, future studies should consider the inclusion of nutritional status and exercise in their investigations to provide a more comprehensive analysis.

The second comment raised the question of whether an enlarged sample size would improve statistical significance in female COPD patients. Sex is also a significant variable associated with muscle mass. To adjust for sex in the analysis, subgroup analysis was conducted during univariate analysis (Table 3)\textsuperscript{2}. In the results, total skeletal muscle mass index, truncal skeletal muscle mass index, and appendicular skeletal muscle mass index exhibited a consistent negative correlation with exacerbation. However, statistical significance was not observed in
females. We discussed that the limited number of female patients (64 individuals) in our study might account for the absence of statistical significance in female patients. Regarding question about whether increasing the sample size would lead to statistical significance, we could respond that there is a high likelihood of achieving significance. The required sample size for reaching statistical significance can be calculated based on our study, although it may vary depending on the specific study design. Assuming an effect size of 0.2, a one-tail test would require 153 individuals in the female group, while a two-sided test would necessitate 193 individuals. Pearson correlation coefficient between muscle mass and exacerbation are currently negative, it is expected that a one-tail test would be sufficient. They also raised additional concerns about the potential adverse association between nutritional status and dementia, especially considering the higher prevalence in females. We share this concern and believe that either excluding dementia patients or incorporating dementia into the multivariate analysis could have yielded more meaningful results.

The third comment highlighted limitations of bioelectrical impedance analysis (BIA) for muscle mass measurements. Body composition metrics vary significantly with age, sex, and race, particularly when COPD is present, potentially leading to fat mass overestimation. To address these complexities comprehensively, it is crucial to accumulate BIA data in the COPD patient population through large-scale prospective studies. Given these considerations, our study, as Hulya et al. have pointed out, could contribute to the accumulation of regional data.

Our retrospective study lacks a standardized protocol, introducing potential biases. Therefore, a well-designed prospective study is warranted. This future research should consider factors such as nutritional status, exercise capacity, and technical methods for measuring muscle mass to further explore the relationship with clinical outcomes in COPD patients.


