Letter to the Editor

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

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Yong Jun Choi, M.D. and Min Kwang Byun, M.D., Ph.D.
Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea



**Address for correspondence**
**Min Kwang Byun, M.D., Ph.D.**
Division of Pulmonology, Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, 211 Eonju-ro, Gangnam-gu, Seoul 06273, Republic of Korea
**Phone** 82-2-2019-3454
**Fax** 82-2-3463-3882
**E-mail** littmann@yuhs.ac
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We appreciate the insightful comments from Sungurtekin et al.[1] on our study that investigated the correlation between low muscle mass and poor clinical outcomes in chronic obstructive pulmonary disease (COPD) patients[2]. They pointed out areas where our research design could be improved and raised valid concerns.

Firstly, Sungurtekin et al.[1] suggested incorporating nutritional status and exercise levels to enhance the significance of our results. We agree that these factors are important in COPD treatment and including them could strengthen the analysis[3,4]. Unfortunately, due to the retrospective nature of our study, we did not have access to relevant data on nutritional status and exercise levels. While there may be some controversy, serum albumin levels can be used as an indicator of recent nutritional status[5,6]. In our study, we found a correlation between serum albumin level and skeletal muscle mass index (coefficient [r]=0.1614). However, serum albumin was not identified as a risk factor for exacerbation in the Cox regression analysis (hazard ratio, 0.724; p=0.139 in Table 4)[2]. It is known that albumin, affected by inflammation and underlying diseases, may not accurately reflect nutritional status alone[6,7]. Therefore, future studies should consider including nutritional status and exercise in their investigations to provide a more comprehensive analysis.

The second comment raised the question of whether increasing the sample size would improve the statistical significance in female COPD patients. Sex is also a significant variable associated with muscle mass. To account for sex in the analysis, subgroup analysis was conducted during the univariate analysis (Table 3)[2]. In the results, total skeletal muscle mass index, truncal skeletal muscle mass index, and appendicular skeletal muscle mass index consistently exhibited a 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 explain the absence of statistical significance in female patients. Regarding the question of 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. Since the Pearson correlation coefficient between muscle mass and exacerbation is 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 pointed out the limitations of using bioelectrical impedance analysis (BIA) for measuring muscle mass. Body composition metrics can vary significantly based on age, sex, and race, especially in the presence of COPD, which could potentially result in an overestimation of fat mass[8]. To address these complexities in a comprehensive manner, it is important to gather BIA data from a large-scale prospective study involving patients with COPD. Taking these factors into account, our study, as mentioned by Sungurtekin et al.[1], could help in accumulating regional data.

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

## Authors' Contributions

Conceptualization: all authors. Methodology: all authors. Formal analysis: all authors. Data curation: all authors. Software: all authors. Validation: all authors. Investigation: all authors. Writing - original draft preparation: all authors. Writing - review and editing: all authors. Approval of final manuscript: all authors.

## Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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