

### General comments

The manuscript presented entitled “Factors Associated with Bronchiectasis in Korea: A National Database Study” is a relevant and interesting study. The study design was properly described and is able to answer the study question. The results are presented clearly and summarized in tables and figures. The conclusion answers the study question and is well written. I have some suggestions for improving the text bellow.

**Response.** We appreciate the reviewer’s encouragement and helpful comments that have substantially improved the quality of our paper. We are submitting a revised manuscript that addresses the concerns raised. A detailed, point-by-point response to these concerns is attached.

### Specific comments

**Comment 1 (C1).** Key Words: the key words used, except “bronchiectasis” are not registered in the search engines. Use key words previously described in MeSH (NCBI).

**Response 1 (R1).** We have modified the keywords as recommended (page 3, lines 51–52).

**C2.** Line 41: remove “In recent studies”

**R2.** We have removed the phrase as recommended (page 4, line 54).

**C3.** Insert the aim of the study.

**R3.** We have added the aim of the study in the Abstract of the revised manuscript (page 4, lines 56–58).

*“The aim of this study was to evaluate the factors associated with bronchiectasis using a national representative database.”*

**C4.** Lines 46-48: the writing of the text needs to be improved (eg: "..., was performed").

**R4.** To address your concern, we have revised the Abstract (page 4, lines 59–62).

*“We conducted a cross-sectional study using data from the Korean National Health and Nutrition Examination Survey 2007–2009. To evaluate factors associated with bronchiectasis, a multivariate logistic analysis was used with adjustment for demographic and socioeconomic factors.”*

## **Introduction**

**C5.** Provide a better justification for the study. What benefits will the study provide? What are the expected impacts?

**R5.** Thank you for your helpful comments. To address your concern, we have emphasized the expected impact in the Introduction section of the revised manuscript (pages 6–7, lines 106–108).

*“This information could be helpful to provide doctors with clinical clues that can help diagnose bronchiectasis early and manage patients suffering from chronic respiratory symptoms properly.”*

## **Methods**

**C6.** Why only the years 2007 and 2009 was evaluated? Wouldn't it be more appropriate to analyze updated data?

**R6.** Thank you for the pertinent response. Unfortunately, the Korean NHANES has questionnaires for physician-diagnosed bronchiectasis from 2007–2009 only. Hence, we assessed the 2007–2009 Korean NHANES dataset.

**C7.** Inform if the study was approved by the research ethics committee

**R7.** Thank you for pointing this out. This is not clearly stated in our manuscript. The Korean NHANES study protocols were approved by the Institutional Review Board of the Korean Centers for Disease Control and Prevention. Written informed consent was obtained from all participants. We have clarified this issue in the revised manuscript (page 7, lines 123–125 and page 16, lines 328–330).

*“The Korea NHANES study protocols were approved by the Institutional Review Boards of the Korean Centers for Disease Control and Prevention. Written informed consent was obtained from all participants.”*

**C8.** Insert the reference of EQ-5D questionnaire.

**R8.** We have added the reference for the EQ-5D index in the Methods section of the revised manuscript (page 7, line 131).

### **Statistical analysis**

**C9.** Only univariable and multivariable logistic regression analyses were reported. Inform the other analyses used.

**R9.** Thank you for your comment. We have provided more detailed information on statistical analyses in the Methods section of the revised manuscript (pages 7–8, lines 138–145).

*“All statistical analyses were performed using NHANES weights and survey (svy) commands in STATA (release 13.1; StataCorp LP, College Station, TX, USA) to account for the complex multistage probability sampling design. The prevalence and 95% confidence interval (CI) for each variable were calculated for both groups. Intergroup comparisons of continuous variables and categorical variables between the two groups were performed using t-test and chi-squared test, respectively. To evaluate factors associated with bronchiectasis, both univariable and multivariable logistic regression analyses were performed. Model 1 was adjusted for age, sex, BMI, and factors with p-values < 0.2 in univariable analysis. Model 2 was additionally adjusted for presence of airflow limitation. Subjects with missing values in the pulmonary function test were not included in Model 2. Two-tailed analyses were conducted, and p-values <0.05 were considered significant.”*

**C10.** How were subjects without bronchiectasis and Subjects with bronchiectasis compared?

**R10.** Intergroup comparisons of continuous variables and categorical variables between the two groups were performed using t-tests and Chi-square tests, respectively. We have revised the Methods section accordingly (page 8, lines 153–155).

**C11.** Which p value was considered statistically significant?

**R11.** Thank you for your comment. Two-tailed analyses were conducted, and p-values < 0.05

were considered significant. We have revised the Methods section accordingly (page 9, lines 159–160).

## **Results**

**C12.** Table 1. Inform the p value in the spirometric pattern variables

**R12.** The variables for the “spirometric pattern” are normal, restrictive, and obstructive. Hence, we decided to provide a current p-value  $< 0.001$  in the Table 1 of our original manuscript.

**C13.** Line 175: Refer to Table 2

**R13.** We appreciate your careful review of our manuscript. We have referred to Table 2 in the Results section of the revised manuscript (page 10, line 196 and page 10, line 205).

**C14.** Table 2. Keep in the table, in the column of the multivariate analysis, only the variables that are inserted in the model.

**R14.** We have modified Table 2 to keep the variables that were inserted in the models, as you have recommended (pages 23–24).

**C15.** Table 2. Put the titles “univariate analyze” and “multivariate analysis”

**R15.** We have inserted the titles of univariate and multivariate analyses in Table 2, as you have recommended (page 23).

**C16.** Figure 1: I suggest inserting the figure in the article and not in the supplementary material.

**R16.** Thank you for your comment. We have provided the figure as Figure 2 instead of Supplementary Figure 1, as you have recommended (page 11, line 211 and page 25, lines 450–453).

**C17.** Inform the  $r^2$  value of the analysis of models 1 and 2.

**R17.** We appreciate your valuable comments. Since we used logistic regression analysis, we have provided Pseudo  $R^2$  values of Models 1 and 2 in the Results section of the revised manuscript (page 9, line 201, and line 205).

**C18.** The values presented in the text and in the tables and figure are repeated. Avoid

duplication in the presentation of results. Remove the data that is already shown in the tables.

**R18.** Thank you for your comment. We have removed duplications shown in the tables in the Results section of the revised manuscript, as you have recommended (pages 9–10, lines 166–188).

## **Discussion**

**C19.** Lines 2445-254: This paragraph repeats information previously presented. Avoid these repetitions and better discuss the impacts of the study.

**R19.** We agree with your opinion. Accordingly, we have modified the Discussion section of the revised manuscript (page 11, lines 218–223).

*“Factors associated with bronchiectasis included respiratory symptoms such as airflow limitation, pulmonary TB, a lower family income/educational level, and poorer quality of life, compared with subjects without bronchiectasis. Considering that bronchiectasis is still under-recognized, it is important to elucidate factors associated with bronchiectasis, which would help clinicians diagnose and manage bronchiectasis early in patients with chronic respiratory symptoms.”*

**C20.** Bronchiectasis is often underreported, undiagnosed, or diagnosed as another chronic respiratory disease. Discuss this fact and the impacts that this underreporting has on the study results.

**R20.** We appreciate your valuable comments, which have substantially improved the quality of our paper. We have modified the Discussion section of the manuscript (page 13, lines 261–273).

*“Bronchiectasis is often underreported or underdiagnosed although it is associated with a significantly increased health burden worldwide, an annual exacerbation frequency of up to 3 per patient per year, and a clear attributable mortality. From this point of view, revealing factors associated with bronchiectasis would be very helpful in reducing the bronchiectasis-related health burden through early diagnosis and management of this disease. Our study showed that asthma and the presence of airflow limitation are associated with bronchiectasis. As comorbid bronchiectasis results in a poorer disease control and more frequent exacerbation in patients with COPD or asthma, our results strongly suggest that clinicians should suspect the presence of bronchiectasis when they encounter patients with poorly*

*controlled airway diseases. Consistent with a previous report, this study also emphasizes that bronchiectasis is significantly associated with a previous history of pulmonary TB. Thus, bronchiectasis should be considered as a differential diagnosis when patients have persistent respiratory symptoms even after completion of TB treatment.”*

**C21.** It is interesting that patients with bronchiectasis have lower family income and lower educational level. However, these findings have not been discussed. I suggest to discuss these findings.

**R21.** Thank you for your comments. We have discussed this issue in the Discussion section of the revised manuscript (pages 13–14, lines 272–285).

*“Another interesting finding is that subjects with bronchiectasis showed a lower family income and lower educational level. Due to the cross-sectional design, we could not fully explain the causal relationship between bronchiectasis and socioeconomic status. One possible explanation is that a low socioeconomic status could contribute to the development of bronchiectasis. Many studies have shown that a lower socioeconomic family is associated with respiratory infection, including TB, which is a well-known risk factor for bronchiectasis. In contrast, bronchiectasis could contribute to a low socioeconomic status in these patients. Patients with bronchiectasis could be at risk of disability and low work productivity (work loss, reduced work hours, absenteeism, and early retirement) due to substantial symptomatic burden, as shown in studies evaluating disability and job status in subjects with COPD. An increased medical burden in subjects with bronchiectasis could also contribute to their low socioeconomic status. Thus, long-term and large-scale prospective cohort studies are warranted to elucidate the causal inference of this phenomenon in the future.”*