

## Peer Review File

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### Reviewer A:

#### Comment 1: F-V curve patterns

Reviewer thinks that the definition of break point, sharp angle, or blunt angle are unclear. Reviewer wonders if it is possible to make a clear distinction between biphasic with blunt angle and curvilinear.

**Reply 1:** It was a visual judgement indeed, but as was depicted in figure 3, so called sharp point appeared abruptly with approximately right angle but the blunt point formed gradually with smooth curvature. There were two distinct different slopes on biphasic curve with blunt angle, and in contrast, there was usually gradually and continuously changing slopes on curvilinear. We have already illustrated the definition of the angle in full detail in this manuscript, and we have added image information, which are shown with a yellow background.

**Comment 2:** Are authors able to propose some mathematical indices for these classifications? Or were these classifications determined by a consensus of several doctor's decisions?

**Reply 2:** These classifications were based on previous studies and we have made further explanation in this manuscript. In our study, all the determination was based on the agreement of at least two doctors.

**Comment 3:** Abstract, Method, line 9 “proformed” should be “performed”

**Reply 3:** We have made the modification, which are shown with a yellow background.

**Comment 4:** Table2,3 “Crosstabulation” may be “cross tabulation”

**Reply 4:** We have made the modification, which are shown with a yellow background.

### Reviewer B:

**Comment 1:** Section ‘Introduction’, page 3: In the sentence “.....was used to be an uncommon event and more variable in the configuration of flow-volume curve”. The authors are requested to add the abbreviation “F-V curve” in parenthesis, as this is the first instance of mentioning this word.

**Reply 1:** We have made the modification, which are shown with a yellow background.

**Comment 2:** Section ‘Introduction’, page 3: The authors are requested to provide references for this sentence: “There is only morphological description of biphasic F-V curve pattern, a lack of

comparison with normal subjects and patients with small airway diseases, and a small sample size in previous studies”. Further, this sentence presents a lot of information, and the authors are requested to consider breaking this sentence into two or more sentences to make it easy to understand for the reader.

**Reply 2:** We have made the modification, which are shown with a yellow background and the reference was provided

**Comment 3:** Section ‘Methods’, page 3: The authors mention that the study was retrospective, and patients were diagnosed between October 2006 and December 2019. The authors are requested to specify what steps were taken to identify these patients. Were these patients identified from an electronic database/electronic medical records/disease registry? Also, why was a cutoff of October 2006 used? Were the authors looking for patients with a sample size in mind?

**Reply 3:** We identified our patients with unilateral bronchus obstruction in our electronic databases in bronchoscopy record, which has been available in our hospital since 2006. Those with bronchoscopy and/or CT scan of the chest, as well as spirometry were recruited. We have made the modification, which are shown with a yellow background.

**Comment 4:** Section ‘Methods’, subsection ‘Statistical analysis’, page 6: The authors are requested elaborate on the logistic regression analyses such as the variables in the analyses and whether it was unadjusted or multivariable.

**Reply 4:** The binary logistic regression analyses was performed after adjustment for age and gender. It’s univariable and bivariable logistic regression for differentiation of COPD and UMBO because of the relatively small sample size. And we have already explained the results of logistic regression in the part of differentiation between UMBO and COPD.

**Comment 5:** Section ‘Results’: The authors are requested to re-number the tables to match the sequence in which it is mentioned in the manuscript. Table 4 is mentioned after Table 1b and before Table 2 in the manuscript. Hence changing the number assigned to the tables would be easier for the reader to follow.

**Reply 5:** We have made the modification, which are shown with a yellow background.

**Comment 6:** Section ‘Results’, sentences: “.....UMBO group and the other two groups, but correlation was only marginal”, and “A strong correlation was shown in location and in angle with different groups”. These sentences are based on Chi-squared tests and not based on correlation tests. Hence the authors are requested not to use the word ‘correlation’.

**Reply 6:** We have made the modification, which are shown with a yellow background.

**Comment 7:** Section ‘Results’, subsection ‘Differentiation between UMBO and COPD’, page 8: The authors are requested to elaborate on whether there were 24 patients with UMBO and 24 patients with COPD, or were there a total of 24 patients which included both UMBO and COPD. The authors are requested to provide details about other variables in the logistic regression analysis. Also, the authors are requested to include a table with the odds ratio of all variables included in the logistic regression analysis.

**Reply 7:** We have made the modification, which are shown with a yellow background.

**Comment 8:** Section ‘Discussion’, sentence “In terms of this study, an earlier breakpoint, almost sited ahead of MEF50 or even MEF75, although just a minority, was usually depicted in grade I or grade III, which was inconsistent with the previous study, but the reason was unknown and remained to be answered”. The authors are requested to simplify this sentence and consider breaking it down into two or more sentences.

**Reply 8:** We have made the modification, which are shown with a yellow background.

**Comment 9:** Figure 1, page 16: The authors are requested to modify this flowchart. All patients, including normal patients should start at the top of the graph.

**Reply 9:** We have made the modification, which are shown with a yellow background.

**Comment 10:** The authors are requested to correct the following sentences for grammar:

“All those with breakpoints located after MEF50, were turned out to be grade II stenosis .....

“Meanwhile, the sharp inflections were appeared in over 50%....”

“On the other hand, it is more probable to be COPD for who with sharp breakpoint located ahead of MEF75”.

**Reply 10:** We have made the modification, which are shown with a yellow background.

#### **Reviewer C:**

The authors address the usefulness of flow-volume curves in the detection of unilateral main bronchus obstruction (UMBO). Certainly, it is interesting to get clues on the existence of UMBO from spirometry prior to the use of more advance procedures. In my view, the ms. could be improved in some points.

**Comment 1.** More explanation is needed on how breakpoints and angles were identified. Visually? By several observers?

**Reply 1:** These tests were conducted by well-trained technicians based on the statement of the ATS/ERS guideline. The patterns of the F-V curves were visually evaluated by at least 3 respiratory physicians reaching a consensus, and we made a double check after a few days. We have already illustrated the definition of the site and angle in detail in this manuscript, and we have added image information, which are shown with a yellow background.

**Comment 2.** The propensity score analysis should be described in detail, or omitted. SPSS has only very limited options regarding this. Which type of matching was used etc? The case numbers are low, compared to the instances in which I know propensity score matching to be useful, thus matching might run into difficulties. Was simple fully adjusted logistic regression not sufficient, particularly as the matching included only two variables?

**Reply 2:** Due to the small cases of this manuscript even in unmatched groups, PSM was necessary and bivariable logistic regression was used We have made the modification and the detail of PSM was described in this manuscript, which are shown with a yellow background.

**Comment 3.** BMI should be included in table 1a, as obesity might affect flow-volume curves.

**Reply 3:** There was no statistically significant difference in BMI among three groups. We have made the modification, which are shown with a yellow background.

**Comment 4.**The order of tables should be as cited in the text (table 4).

**Reply 4:** We have made the modification, which are shown with a yellow background.

**Comment 5.**In my view, the relevant comparisons are not those between the three groups but between UMBO and COPD. Please give the respective p-values (post hoc or otherwise).

**Reply 5:** We have added all of the respective p-values in relevant tables shown with a yellow background.

**Comment 6.**I think, from a practical point of view, a decision algorithm derived from the spirometric and other data might be more useful than logistic regression that cannot be really used by the reader. For example, the authors might try decision trees (available in SPSS).

**Reply 6:** We have made the modification, which are shown with a yellow background.

**Comment 7.**Tables 3 and 5: Formally, the chi-square statistics is not valid if one of the cells of the tables has zero events. That should be noted, although it probably had no effect.

**Reply 7:** We have made the modification, which are shown with a yellow background.

**Comment 8.**How was the diagnosis of COPD established? Were there patients with concomitant asthma among COPD patients?

**Reply 8:** The diagnosis of COPD was established on the newest Gold report. Post-bronchodilator FEV1 were used in this study. Other small airway diseases including asthma or concomitant asthma were excluded.