

**Peer Review File**

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**Reviewer A**

This study evaluated PA dilatation in patients with BE. This is an interesting and enrolled relatively a large number of patients. However, this study had negative results.

1. In background of this study, was there any previous report about the relationship between pulmonary hypertension and NTM infection (or NTM-PD) or the clinical importance of PTH in these patients?

REVIEWER A REPLY 1: Reference 14 is the largest study that reported the prevalence of pulmonary hypertension in patients with NTM pulmonary disease. This study found that in NTM patients, pulmonary hypertension was associated with an increased risk of all-cause mortality. Pulmonary hypertension was determined from the medical record. This has been added to the introduction.

CHANGES IN TEXT:

Lines 85-89 discuss Reference 14

2. NTM infection and NTM-PD which should meet the diagnostic criteria by ATS/IDSA guidelines are different in definitions and have different clinical significances. How many patients were NTM infection and NTM-PD?

REVIEWER A REPLY 2: The Bronchiectasis Research Registry does not differentiate those with NTM infections versus those that meet ATS/IDSA criteria for NTM pulmonary disease. This is clarified in the manuscript.

CHANGES IN TEXT:

Lines 81-83

3. Was there any correlation between PA dilation and PFT including FEV1 and FEV1/FVC?

REVIEWER A REPLY 3: We performed a post hoc analysis and found that PA:Ao was negatively correlated with FEV1 (L), FEV1% and FEV1/FVC. These data make sense as we would expect a higher PA:Ao in those with more severe lung disease.

CHANGES IN TEXT:

Lines 156-160; Supplemental Table 1.

4. Is there any data about relationship between PA diameter and clinical outcomes including acute exacerbation of BE, progression of NTM-PD, and mortality?

REVIEWER A REPLY 4: We have included data on PA:Ao and acute exacerbations of

bronchiectasis in the supplement. However, we do not have any data on progression of disease or mortality because we collected data from the initial enrollment into the Bronchiectasis Research Registry. Longitudinal data were not collected for this study.

CHANGES IN TEXT:

Lines 160-161; Supplemental Table 2.

**Reviewer B**

In this article the authors address the study of pulmonary artery dilation and its association with NTM infections amongst other factors.

The article is interesting and informative as well as being well written.

I only have a few small nitpicks;

1) With regard to the methodology, were there any attempts at seeing how good the inter-reader correlation was? I see that the measurement methodology was agreed upon beforehand but perhaps it would have been a good idea to check a sample to verify that the radiologists were indeed reproducible as would be expected.

REVIEWER B REPLY 1: There was no formal measurement of inter-reader correlation. However, the measurement methodology was agreed upon prior to study initiation and the three interpreting radiologists work at one institution.

CHANGES IN TEXT:

Line 112, we added that all 3 radiologists were at OHSU.

2) Small grammar correction in line 169, there is no need for the extra commas around “and therefore”.

REVIEWER B REPLY 2: Thank you for the identifying this error. The commas have been removed.

CHANGES IN TEXT:

Line 200, the commas around “and therefore” have been removed

3) The conclusion could be better demarcated. The fact that it is merged with the limitations is a little off-putting.

REVIEWER B REPLY 3: we have separated the limitations from the concluding paragraph. This should provide an improved flow the discussion.

CHANGES IN TEXT:

The concluding paragraph now starts at line 225

**Reviewer C**

Nice study

A clinically relevant study --- should be accepted.

REVIEWER C REPLY 1: We thank the reviewer for their comments.

#### **Reviewer D**

This is a thoughtful evaluation and well written observational study. Could the authors describe how FEV1 is associated with PA dimensions?

REVIEWER D REPLY 1: As noted above, we have now included a post hoc analysis of PA: Ao and pulmonary function tests. We found that PA: Ao was negatively correlated with FEV1 (L), FEV1% and FEV1/FVC.

CHANGES IN TEXT:

Lines 156-160; Supplemental Table 1.

Could they also report what percentage of patients have coexistent pulmonary (COPD/OSA/PHTN) and cardiac disease (CHF), both in their table 1 and in the subgroups?

REVIEWER D REPLY 2: The Bronchiectasis Research Registry collects data on the diagnosis of COPD but it does not collect data on OSA, pulmonary hypertension or CHF. We found 55 patients in our cohort carried a diagnosis of COPD. This has been referenced in the text and Table 1.

CHANGES IN TEXT:

Line 137 and Table 1

As for patients with supplemental oxygen, it seems a limitation of this observational study is that patients who have ambulatory or nocturnal hypoxia may not be identified. Is there a protocol for assessing these patients at intervals that may help understand this better?

REVIEWER D REPLY 3: The use of supplemental oxygen in our study includes ambulatory oxygen use and nocturnal oxygen use. We did not distinguish between different forms of oxygen use. We have clarified this in the text.

CHANGES IN TEXT:

Lines 138-139

Could the authors expand on the statement that just elevated PA diameter portends a poor outcome? What is this a marker of?

REVIEWER D REPLY 4: elevated PA diameter is potential surrogate for underlying pulmonary hypertension, and pulmonary hypertension is associated with increased mortality in patients with NTM pulmonary disease [ref 14]. Furthermore, an elevated PA diameter has been associated with mortality and exacerbation frequency in COPD [references 6-8].

CHANGES IN TEXT:

We have reiterated the importance of PA dilation in the discussion, lines 188-189

**Reviewer E**

The authors provide a well written retrospective analysis of CT chest imaging obtained from patients with NTM pulmonary disease followed at a single center. The study sought to identify frequency of abnormal PA/Ao diameter ratio in this unique patient cohort. The authors identified a high rate (roughly 13%) of elevated ratios among the study cohort supporting the concern that PH is a prevalent comorbidity however these findings have not previously been published specific to NTM-PD. The authors utilize appropriate statistical approaches and identified a correlation w/ need for supplemental oxygen. The authors provide bronchiectasis scoring using the Reiff scoring tool however a significant portion of the patient cohort was excluded due to prior lobectomy. In my opinion this is the most important weakness of this study and needs to be addressed- these patients were excluded from the analysis but they likely had the most severe parenchymal destruction/disease severity - hence the need for lobectomy. These lobes should be scored empirically using a score of three for the lobes that were excised and then the remaining lung should be scored accordingly. The statistical approach should then be repeated using the full cohort- since these patients likely had the most severe parenchymal destruction (thus necessitating surgery) they are more likely to have PA/Ao abnormalities. Nevertheless- this article provides new insight to the use of cross sectional imaging in this population as well as the risk for occult pulmonary hypertension- I suspect that once the additional patients are included in the analysis the findings will be more robust and more accurately descriptive of the broad heterogeneity of disease -excluding these severely diseased patients likely de-emphasized the rates of these imaging findings.

REVIEWER E REPLY 1: We thank the reviewer for this comment. The approach to managing absent data from 1 or more lobes is an important consideration for future studies. We re-analyzed the data by including the 27 patients who had 1 or more lobe that could not be scored. There were 31 lobes that could not be scored and were assigned a score of 3. Five of the 27 had a PA/Ao >0.9 (18.5%). We have included the new analysis as a supplemental piece of data because our a priori statistical plan was to exclude those who had a lobe that could not be scored. However, we have highlighted in the discussion that had these patients been included, the modified Reiff score would have been associated with higher PA/Ao.

CHANGES IN TEXT:

Lines 163-177, lines 217-223. Data in Supplemental Table 3 and Supplemental Table 4.