Brief Report

Prevalence of pulmonary artery dilation in non-cystic fibrosis bronchiectasis: a computed tomography analysis from a cohort of the US Bronchiectasis and Nontuberculous Mycobacteria Research Registry

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Abstract: Although pulmonary artery (PA) dilation is independently associated with significant morbidity and mortality in patients with pulmonary diseases irrespective of diagnosed pulmonary hypertension, its relationship with nontuberculous mycobacteria (NTM) is unknown. The Bronchiectasis and NTM Research Registry is a multicenter registry created to foster research in non-cystic fibrosis (CF) bronchiectasis and NTM lung disease. The majority of patients with non-CF bronchiectasis at Oregon Health & Science University have NTM infections. To determine the prevalence of PA dilation in these patients and its association with supplemental oxygen use, severity of bronchiectasis, tobacco use, and NTM in the sputum culture, we evaluated the chest computed tomography (CT) scans from 321 patients in a cross-sectional analysis. We measured the severity of bronchiectasis by applying modified Reiff criteria and measured the diameters of the PA and aorta (Ao), with PA dilation defined as a PA:Ao ratio >0.9. In our cohort, the mean age was 67.3 years and 83.2% were female. The mean modified Reiff score was 7.1, indicating moderate disease severity. Forty-two patients (13.1%) were found to have PA dilation. PA dilation was positively associated with the use of supplemental oxygen (P<0.001), but there was no association between PA dilation and NTM infection.

Keywords: Bronchial diseases; nontuberculous mycobacteria (NTM); pulmonary artery (PA); hypoxemia

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Introduction

Bronchiectasis is defined on imaging as bronchial dilation greater than 1.5× the adjacent artery (1). Chronic inflammation and infection can lead to subsequent parenchymal destruction (2). Destruction of alveolar units causes hypoxia, which results in pulmonary vasoconstriction and eventually pulmonary hypertension (3). Pulmonary hypertension can manifest as pulmonary artery (PA) dilation, and PA dilation can be identified on chest computed tomography (CT) by the presence of a PA ≥29 mm in diameter in men and ≥27 mm in diameter in women or a ratio of the PA to aorta (Ao) >0.9 (4). The clinical relevance of PA dilation has been well established. For example, in severe chronic obstructive pulmonary

disease (COPD), the prevalence of PA dilation ranges from 20–24% (5,6), is positively associated with exacerbations and mortality (6-8), and the presence of a PA:Ao ratio >1 on chest CT outperformed echocardiography in predicting elevated mean PA pressure (9). In a study of 91 patients with bronchiectasis, the majority of whom had idiopathic bronchiectasis, an average diameter of the right and left main PAs >18 mm was a predictor of increased mortality with a hazard ratio of 1.24 (10). Thus far, there have been no studies examining the prevalence of PA dilation in nontuberculous mycobacteria (NTM) predominant non-cystic fibrosis (CF) bronchiectasis.

The Bronchiectasis and NTM Research Registry was created by the COPD Foundation to foster research in non-CF bronchiectasis and NTM lung disease (11). The registry does not distinguish between NTM infection and American Thoracic Society criteria for NTM pulmonary disease. The majority of patients with non-CF bronchiectasis at Oregon Health & Science University have NTM infections. NTM infection is associated with increased mortality (12,13). One retrospective study of 106 patients with NTM pulmonary disease found that pulmonary hypertension was present in 11% of patients and it was associated with increased all-cause mortality (14). In that study, pulmonary hypertension was determined from the medical record. However, there have been no studies on the prevalence of PA dilation in NTM patients. The objective of this study was to measure the prevalence of PA dilation in a large cohort with non-CF bronchiectasis predominantly due to NTM and to determine the association of PA dilation with important clinical factors. The following clinical factors were evaluated: supplemental oxygen use, severity of bronchiectasis, tobacco use, and NTM in the sputum culture. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1316/rc).

Methods

Study population

We identified 380 patients at Oregon Health & Science University participating in the Bronchiectasis and NTM Research Registry from 2010–2019. We excluded six patients with duplicate records, 17 patients without CT scans available for review, and one patient who had not completed enrollment in the Bronchiectasis and NTM Research Registry. Of the remaining 356 patients, CT chest performed in closest proximity to enrollment date in the Bronchiectasis and NTM Research Registry was reviewed for each patient. An additional 35 patients were excluded due to poor quality CT scans limiting evaluation (n=2), presence of traction bronchiectasis as a result of idiopathic interstitial pneumonia-related pulmonary fibrosis (n=3), diagnosis of CF after enrollment (n=3), and an inability to score one or more lobes due to lobectomy/resection or significant atelectasis/scarring that precluded scoring (n=27). This left a total of 321 patients in the cross-sectional analysis. The clinical variables of supplemental oxygen use, tobacco use, and results of the sputum culture were collected from the Bronchiectasis and NTM Research Registry and electronic medical record. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The institutional review board of Oregon Health & Science University approved the Bronchiectasis and NTM Research Registry and the current study (IRB ID: IRB00005864, MOD ID: MODCR00010417). All patients provided written informed consent prior to enrollment in the Bronchiectasis and NTM Research Registry.

Modified Reiff score and PA:Ao

One of three fellowship-trained thoracic radiologists working at Oregon Health & Science University reviewed and scored every CT scan of the chest using modified Reiff criteria (15,16), with agreement on how to obtain the PA and Ao measurements made amongst the three radiologists prior to performance of all measurements. The main PA and Ao diameter were measured on axial soft tissue images with electronic calipers at the level of the bifurcation of the right main PA (4), with elevation defined as PA:Ao >0.9. The radiologists were blinded to all clinical data and CT scans were reviewed in batches. Each lobe, including the lingula, was scored based on the highest severity of airway dilation: no bronchiectasis (score =0), <2× diameter of adjacent PA (score =1), 2–3× diameter of adjacent PA (score =2), >3× diameter of adjacent PA (score =3). A total score of 0 is normal, 1–6 is mild bronchiectasis, 7–12 is moderate bronchiectasis and 13–18 is severe bronchiectasis.

Statistical analysis

We used analysis of variance (ANOVA) for categorical independent variables, *t*-tests for binary independent variables, and linear regression to determine the association

Table 1 Baseline demographics and clinical characteristics

Factors	Values
Age (years), mean (SD), n=321	67.3 (13.2)
Gender, n (%), n=321	
Female	267 (83.2)
Male	54 (16.8)
Diagnosis of COPD, n (%), n=321	55 (17.1)
Number of exacerbations in the last 2 years, n=261	
Mean (SD)	1.1 (1.5)
0, n (%)	138 (52.9)
1–2, n (%)	81 (31.0)
3+, n (%)	42 (16.1)
Tobacco use, n (%), n=312	
Non-user	175 (56.1)
Former user	125 (40.1)
Current user	12 (3.8)
Oxygen use, n (%), n=310	
No	282 (91.0)
Yes	28 (9.0)
FEV1 (L), mean (SD), n=184	1.91 (0.72)
FEV1%, mean (SD), n=182	73.5 (23.2)
FEV1/FVC%, mean (SD), n=182	66.8 (11.1)
Bacterial culture, n (%), n=184	
NTM	106 (57.6)
Pseudomonas	23 (12.5)
NTM & pseudomonas	31 (16.8)
Neither NTM nor pseudomonas	24 (13.0)

SD, standard deviation; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; NTM, nontuberculous mycobacteria.

between PA:Ao ratio and modified Reiff score. Post-hoc, pairwise differences were estimated to determine which categorical factor means were different from each other; multiple comparisons were adjusted for using the Tukey-Kramer method. All model assumptions were assessed. All analyses were performed in STATA/SE 15.1 (StataCorp, College Station, TX, USA).

Table 2 CT measurements of pulmonary artery, aorta and bronchiectasis severity (n=321)

Factors	Values
Modified Reiff score[†]	
Mean (SD)	7.1 (3.8)
Normal (score =0), n (%)	7 (2.2)
Mild (score =1–6), n (%)	143 (44.5)
Moderate (score =7–12), n (%)	143 (44.5)
Severe (score =13–18), n (%)	28 (8.7)
Ao diameter (mm), mean (SD)	31.5 (4.0)
PA diameter (mm), mean (SD)[‡]	24.6 (3.5)
PA/Ao, mean (SD)	0.79 (0.11)

[†], 27 CT scans had 1 or more lobes that could not be scored because of lobectomy/resection, atelectasis, or scarring. Those scans were not included this analysis; [‡], 66 CT scans were contrast enhanced. CT, computed tomography; SD, standard deviation; Ao, aorta; PA, pulmonary artery.

Results

A total of 321 patients were included in the final analysis (*Table 1*). The mean age was 67.3 years and 83.2% were female. Pulmonary function testing revealed moderate obstructive lung disease based on GOLD criteria, with a mean forced expiratory volume in 1 s percentage (FEV1%) of 73.5% and 17.1% of patients carried a formal diagnosis of COPD. In our cohort, 9.0% of patients required the use of supplemental oxygen (defined as use of continuous, ambulatory or nocturnal supplemental oxygen) and <4% of patients were active smokers. Sputum culture data were available for 184 patients. Sputum cultures were positive for NTM in 75% of the registry patients (58% were only positive for NTM and 17% were positive for NTM and *Pseudomonas aeruginosa*). Measurements of bronchiectasis severity showed that 89% had mild to moderate disease (*Table 2*). PA measurements revealed a mean PA diameter of 24.6 mm [standard deviation (SD): 3.5 mm] with a mean PA:Ao ratio of 0.79 (SD: 0.11). A total of 42 out of 321 patients (13.1%) demonstrated PA dilation as defined by PA:Ao ratio >0.9.

Prespecified factors were evaluated to identify associations with PA dilation. The factors evaluated were use of supplemental oxygen, severity of bronchiectasis,

Table 3 Clinical factors associated with pulmonary artery dilation[†]

Clinical factors	Mean PA/Ao (95% CI)	β-coefficient (95% CI)[‡]	P value[§]
Oxygen use			<0.001
No (n=282)	0.78 (0.77, 0.79)	Reference	
Yes (n=28)	0.87 (0.83, 0.91)	0.086 (0.045, 0.127)	
Severity of bronchiectasis[¶]	0.79 (0.78, 0.80)	0.003 (–0.000, 0.006)	0.07
Tobacco use			0.12
Non-user (n=175)	0.78 (0.76, 0.79)	Reference	
Former user (n=125)	0.80 (0.78, 0.82)	0.025 (–0.000, 0.050)	
Current user (n=12)	0.81 (0.75, 0.87)	0.034 (–0.030, 0.097)	
Sputum culture			0.55
Neither NTM nor pseudomonas (n=24)	0.79 (0.74, 0.83)	Reference	
NTM (n=106)	0.79 (0.77, 0.81)	0.002 (–0.046, 0.051)	
Pseudomonas (n=23)	0.82 (0.77, 0.86)	0.030 (–0.033, 0.093)	
NTM and pseudomonas (n=31)	0.81 (0.77, 0.85)	0.025 (–0.033, 0.084)	

[†], means and β-coefficients were estimated from a series of simple linear regression models in which each clinical factor was the single explanatory variable; [‡], β-coefficients for categorical variables can be interpreted as "the difference between category k and the reference category". For continuous variables, the β-coefficient can be interpreted as "for every unit increase in X, PA/Ao increases by β"; [§], P values for categorical variables with 3 or more categories are type III P values for the overall association of that variable and PA/Ao; [¶], severity of bronchiectasis was measured using the modified Reiff score. PA, pulmonary artery; Ao, aorta; CI, confidence interval; NTM, nontuberculous mycobacteria.

tobacco use, and microbial composition of sputum culture. There was a statistically significant association between PA dilation and use of supplemental oxygen compared to non-users: the mean PA:Ao was 0.87 (SD: ±0.11) for those using supplemental oxygen compared to mean PA:Ao of 0.78 (SD: ±0.11) among non-users (P<0.001) (*Table 3*). There was no statistically significant association between presence or absence of PA dilation and severity of bronchiectasis, tobacco use, or NTM infection. Additional post-hoc analyses were done to understand the association between PA:Ao and pulmonary function tests and exacerbation frequency. We found that the PA:Ao was negatively correlated with FEV1 (L), FEV1% and the ratio of the FEV1 to forced vital capacity (FVC), indicating that worsening pulmonary function was associated with higher PA:Ao (Table S1). On the other hand, exacerbation frequency was not consistently associated with PA:Ao (Table S2).

A priori, we designed the study to exclude patients who had one or more lobes that could not be scored by modified Reiff criteria. However, these lobes represent the most severe stages of bronchiectasis, where the lobe is either heavily scarred or has been surgically removed. Therefore, by excluding these patients, we were excluding the most severe patients in our cohort. In order to understand what effect this exclusion had on our results, we performed a post-hoc analysis that included the 27 patients who had 1 or more lobes that could not be scored by modified Reiff criteria. Each lobe that could not be scored by was empirically given a score of 3 (maximum score for a lobe). Among these 27 patients there were 31 lobes that could not be scored radiographically. Five of the 27 patients had a PA:Ao >0.9. However, the overall change in the mean Pa:Ao of the cohort did not change (Table S3). When examining the clinical factors associated with PA:Ao dilation, we found that supplemental oxygen use continued to be a significant association (Table S4). With the inclusion of the 27 previously excluded patients, the modified Reiff score was now associated with PA:Ao dilation (Table S4).

Discussion

In this report, we analyzed CT scans from 321 patients with non-CF bronchiectasis in order to determine the prevalence

of PA dilation within this cohort and to evaluate whether prespecified factors—supplemental oxygen use, severity of bronchiectasis, tobacco use, or NTM in the sputum culture—were associated with PA dilation. These factors were chosen based on their association with hypoxemia and/or parenchymal destruction and therefore their ability to induce PA dilation. PA dilation has been associated with exacerbations and mortality in patients with COPD (6-8). Overall, we found that 13.1% of the cohort met criteria for PA dilation. Of the factors examined, only use of supplemental oxygen was associated with PA dilation. This result is consistent with studies showing an association between hypoxemia and pulmonary hypertension in patients with bronchiectasis (17,18). We used descriptive statistics in our study and we did not find any association between NTM and PA dilation; prospective studies are needed to better delineate contributions from various factors to the PA dilation in patients with NTM and non-CF bronchiectasis.

The prevalence of PA dilation in our cohort is lower than the prevalence reported in patients with moderate-severe COPD (5,6). One explanation for this is that our cohort had mild-moderate bronchiectasis and therefore had less parenchymal and vascular destruction. A lower level of parenchymal and vascular destruction is less likely to lead to PA dilation and this is supported by the modest prevalence of hypoxemia in the cohort, with 9.0% using supplemental oxygen. To measure the severity of bronchiectasis, we used the modified Reiff score because of its ease of use despite differences in CT techniques. In our cohort, the modified Reiff score found higher scores in the middle lobe and lingula (data not shown), which is a distribution of disease that is consistent with the overall Bronchiectasis and NTM Research Registry data (11). This consistency supports the accuracy of the modified Reiff scoring in our study.

Limitations of this study include the single center design. This was necessary because the Bronchiectasis and NTM Research Registry does not have a central imaging repository. Also, the Bronchiectasis and NTM Research Registry does not include right heart catheterization data and very few patients have echocardiograms, making it difficult to determine the correlation between PA dilation and mean PA pressure. However, previous work in COPD found PA dilation outperformed echocardiography in detecting pulmonary hypertension (9). An additional limitation is that follow-up CT scans were not included in this analysis and thus data are lacking regarding the development of PA dilation over time. A final limitation is that our *a priori* study design was to exclude patients who had 1 or more lobes that could not be scored by modified Reiff criteria due to surgical resection or severe scarring and atelectasis. However, it is important to note that these lobes represent the most severe forms of disease and our post-hoc analysis determined that inclusion of these patients by assigning the highest score possible to the unscored lobes resulted in a slight association between the modified Reiff score and the PA:Ao.

Despite these limitations, our analysis included a large number of patients and our study provides important additional data on the low prevalence of PA dilation in a cohort of patients with NTM predominant infection and mild-moderate non-CF bronchiectasis. Furthermore, PA dilation in this cohort was associated only with use of supplemental oxygen. This suggests that further work-up for underlying pulmonary hypertension should be implemented in patients non-CF bronchiectasis who require supplemental oxygen.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1316/rc

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1316/prf

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The institutional review board of Oregon Health & Science University approved the Bronchiectasis and NTM Research Registry and the current study (IRB ID: IRB00005864, MOD ID: MODCR00010417). All patients provided written informed consent prior to enrollment in the Bronchiectasis and NTM Research Registry.

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