[15] Female Reproductive Factors and Incidence of Nontuberculous Mycobacterial Pulmonary Disease Among Postmenopausal Women in Korea

Hayoung Choi[1,2]; Lee Hyun[3]

[1]*University of Dundee, Dundee, United Kingdom;* [2]*Hallym University College of Medicine, Seoul, Korea (Republic of);* [3]*Hanyang University College of Medicine, Seoul, Korea (Republic of)*

Background/Aims:
There are conflicting results regarding endogenous estrogen exposure and risk of incident nontuberculous mycobacterial pulmonary disease (NTM-PD). In addition, evidence on impact of hormone replacement therapy (HRT) on risk of NTM-PD is lacking. This study aimed to evaluate the impacts of endogenous estrogen exposure and HRT on risk of NTM-PD in postmenopausal women.

Methods:
This population-based cohort study comprised 1 400 095 postmenopausal women without previous NTM-PD who participated in the 2009 national health screening exam in South Korea. The cohort was followed until the date of incident NTM-PD, death, or December 2018. We evaluated whether lifetime endogenous estrogen exposure and HRT were associated with incident NTM-PD. Endogenous estrogen exposure was evaluated using age at menarche and menopause and reproductive period (duration between age at menarche and age at menopause).

Results:
During a median of 8.4 (interquartile range, 8.2–8.7) years of follow-up, 0.1% of participants (1818/1 400 095) developed NTM-PD, with an incidence rate of 0.15/1000 person-years. Multivariable Cox regression analyses showed no significant relationship between endogenous estrogen exposure (age at menarche, age at menopause, and reproductive period) and risk of NTM-PD. In contrast, duration of HRT showed a significant dose–response relationship with incident NTM-PD even after adjustment for demographics and reproductive factors (adjusted hazard ratio [95% CI]: 1.30 [1.12–1.51] in HRT for <2 years; 1.28 [1.03–1.59] in 2–5 years; and 1.65 [1.33–2.05] in ≥5 years).

Conclusion:
While there was no significant association with endogenous estrogen exposure, HRT was monotonically associated with increased risk of NTM-PD in postmenopausal women.

Conflict of interest(s):

This work was supported by National Research Foundation of Korea (NRF) grants funded by the Ministry of Science, Information, and Communications Technologies (nos. 2020R1F1A1070468 and 2021M3E5D1A0101517621 to H. L.; no. 2019R1G1A1008692 to H. C.) and the Korean Ministry of Education (no. 2021R1I1A3052416 to H. C.).

[16] Gastroesophageal Reflux Disease Increases Susceptibility to Nontuberculous Mycobacterial Pulmonary Disease

Hayoung Choi[1,2]; Lee Hyun[3]

[1]*University of Dundee, Dundee, United Kingdom;* [2]*Hallym University College of Medicine, Seoul, Korea (Republic of);* [3]*Hanyang University College of Medicine, Seoul, Korea (Republic of)*

Background/Aims:
Gastroesophageal reflux disease (GERD) is a common comorbidity of nontuberculous mycobacteria (NTM) pulmonary disease (PD). Although GERD is associated with more symptoms and severe disease in patients with NTM PD, whether GERD is associated with an increased risk of NTM PD developing is unknown. This study aimed to answer three research questions: Is GERD associated with an increased risk of NTM PD? If so, which factors are associated with an increased risk of NTM PD in patients with GERD? What are the effects of NTM PD on healthcare use in patients with GERD?

Methods:
Data from the Korean National Health Insurance Service National Sample Cohort between 2002 and 2015 were used. The incidence and risk of NTM PD were compared between patients with GERD (GERD cohort; n = 17,424) and patients matched for age, sex, type of insurance, and Charlson Comorbidity Index (matched cohort; n = 69,696). Using the GERD cohort, the factors associated with incident NTM-PD also were evaluated.

Results:
During a median follow-up duration of 5.1 years, the age- and sex-adjusted incidence of NTM PD was significantly higher in the GERD cohort (34.8 per 100,000 person-years [PY]) than in the matched cohort (10.5 per 100,000 PY; $P < .001$), with a subdistribution hazard ratio (HR) of 3.36 (95% CI, 2.10-5.37). Regarding risk factors associated with NTM PD, age of 60 years or older (adjusted HR, 3.57; 95% CI, 1.58-8.07) and bronchiectasis (adjusted HR, 18.69; 95% CI, 6.68-52.28) were associated with an increased risk of incident NTM PD in the GERD cohort. Compared with patients with GERD who did not demonstrate NTM PD, those with NTM PD showed higher all-cause (13,321 PY vs 5,932 PY; $P = .049$) and respiratory disease-related (5,403 vs 801; $P = .011$) ED visits or hospitalizations.

Conclusion:
GERD is associated with an increased incidence of NTM PD. Older age and bronchiectasis are risk factors for NTM PD in patients with GERD. NTM PD in patients with GERD is associated with increased healthcare use.

Conflict of interest(s):

This work was supported by the National Research Foundation of Korea (NRF), funded by the Ministry of Science, Information and Communications Technologies (Grants 2020R1F1A1070468 and 2021M3E5D1A01015176 to H. L.) and the Korean Ministry of Education (Grant 2021R1I1A3052416 to H. C.).

[17] The role of FDG-PET in non-tuberculous mycobacterial disease: a large case series and review of the literature

Alberto Gaviraghi[1]; Giacomo Stroffolini[2]; Daniele Penna[3]; Pavilio Piccioni[4]; Francesco Venuti[1]; Carlotta Botto[4]; Michele Trezzi[5]; Margherita Betti[6]; Paola Anna Erba[7]; Tommaso Lupia[8]; Giovanni Di Perri[1]; Stefano Aliberti[9]; Andrea Calcagno[1]

[1]*Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, c/o Amedeo di Savoia Hospital, ASL Città di Torino, Turin, Italy;* [2]*Department of Infectious-Tropical Diseases and Microbiology, IRCCS Sacro Cuore Don Calabria Hospital;, Negrar di Valpolicella, Italy;* [3]*Nuclear Medicine, Affidea IRMET, Turin, Italy;* [4]*Unit of Pneumology, 'Amedeo di Savoia' Hospital, ASL 'Città di Torino', Turin, Italy;* [5]*U.O.C. Malattie Infettive e Tropicali, Azienda Ospedaliero-Universitaria Senese, Siena, Italy;* [6]*Medical Physics Unit, Azienda USL Toscana Centro, Prato, Italy;* [7]*Regional Center of Nuclear Medicine, Department of Translational Research and Advanced, Technologies in Medicine, University of Pisa, Pisa, Italy;* [8]*Infectious Diseases Unit, Cardinal Massaia Hospital, Asti, Italy;* [9]*IRCCS Humanitas Research Hospital, Respiratory Unit, Rozzano (MI), Italy*

Background/Aims:
Non-tuberculous mycobacteria (NTM) are associated with a large *spectrum* of pathological manifestation; pulmonary localization is the commonest one characterizing NTM lung disease (NTM-LD). Despite specific guidelines based on clinical, radiological and microbiological criteria, symptoms are poorly specific and late diagnosis is common. 18-Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) is performed in the diagnostic and follow-up process of oncological, autoimmune and infectious diseases and has shown promising results in the assessment of patients with pulmonary tuberculosis. This work aims to describe the features of patients with NTM-LD who underwent FDG/PET for any clinical indication.

Methods:
We performed a secondary analysis of a prospective observational cohort study including adult patients with NTM-LD who underwent a FDG-PET/CT. We evaluated demographic, clinic, radiological and therapeutic characteristics of our population. An experienced radiologist in nuclear medicine evaluated radiotracer uptake. Data are described as number (percentage) and median (interquartile range) and non-parametric tests were used for comparisons (Mann-Whitney and Spearman).

Results:
A total of 20 patients with NTM-LD were identified: clinical, demographic, microbiological and radiological features of the study population are reported in **Table 1.** The main reason to perform a PET/CT scan was differential diagnosis with malignancy (75%). FDG/PET showed a median of 2 (2-3) positive pulmonary lesions with a diameter of 8 (5.8-10.3) mm. SUV max was 4.2 (3.6-5.3). We found no difference in SUV max according to demographic, radiological and clinical patients' variables nor according to different NTM species (MAC vs. Non-MAC). At univariate regression model, only asthma (p=0.035) and

HIV co-infection (p=0.023) were independently associated with a significantly increased number of FDG-PET positive pulmonary lesions. Clinical, radiological and microbiological features on the study participants did not differ from what has been reported in other case series (32 identified cases, patients' characteristics shown in **Table.1**) with similar number of lesions (1 to numerous), diameter (2.5, 1.63-2.5) and SUVmax (4.8, 3.00- 7.23).

Conclusion:

We describe the largest case series of patient with NTM-LD with available PET/CT results. In accordance with the available literature we showed the potential role of this nuclear medicine test in for differential diagnosis, staging and, potentially, prognosis. Prospective studies are warranted in order to investigate the role of FDG-PET in the management of complex patients with NTM-LD

Conflict of interest(s) (if any – not included in the 500 words):

A.C., M.T., S.A. have received consunltancy fees by INSMED

[20] Factors associated with frequent exacerbations in subjects with bronchiectasis: A one-year follow-up data from KMBARC

Bumhee Yang[1]; Hayoung Choi[2]; Hyun Lee[3]; Yeon Mok Oh[4]; Seung Won Ra[5]

[1]*Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Chungbuk National University Hospital, College of Medicine, Chungbuk National University, Cheongju, Korea (Republic of);* [2]*Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Internal Medicine, Hallym University Kangnam Sacred Heart Hospital, Seoul, Korea (Republic of);* [3]*Department of Internal Medicine, Hayang University College of Medicine, Seoul, Korea (Republic of);* [4]*Department of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea (Republic of);* [5]*Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, Korea (Republic of)*

Background/Aims: Frequent exacerbations are associated with poor outcomes in patients with non-cystic fibrosis bronchiectasis. However, information about risk factors associated with frequent exacerbations of bronchiectasis is scarce. Using prospectively collected data from adult patients with bronchiectasis, we determined the factors to predict frequent exacerbators.

Methods: A total of 697 subjects with bronchiectasis who were followed up for 1 year in the Korean multicenter bronchiectasis audit and Research Collaboration (KMBARC) registry were evaluated between April 2018 and Dec 2021. Multivariable logistic regression analysis was performed to evaluate factors associated with frequent exacerbations in subjects with bronchiectasis. Frequent exacerbations were defined as 3 or more exacerbations for 1-year follow-up. In addition to age, sex, and body mass index (BMI), variables with p values < 0.1 in univariable analyses were included in multivariable analysis.

Results: Compared to non-frequent exacerbators, frequent exacerbators were younger (63.4±9.3 vs. 64.8±8.9 years; p=0.043), had lower BMI (22.4±3.7 vs. 23.2±3.5 kg/m^2; p = 0.044), more dyspnea (modified Medical Round Council [mMRC] dyspnea scale≥2; 86.2% vs. 24.4%; p<0.001), lower forced expiratory volume in 1 second (FEV_1) (53.5 ± 20.4 vs. 62.3 ± 18.6 %predicted; p=0.005), higher Bronchiectasis Severity Index scores (11.1±4.0 vs. 5.5±2.8; p<0.001), lower Bronchiectasis Health Questionnaire scores (60.1±12.8 vs. 67.7±10.8, p<0.001), long-term antibiotics (24.4% vs. 4.6%; p<0.001), and more exacerbations at baseline (1.8±2.7 vs. 1.1±1.8; p=0.006). Multivariable logistic regression analysis showed that mMRC dyspnea scale≥2 (adjusted OR=3.68 [95% CI=1.77–7.63]) and the number of any exacerbations during the previous year (adjusted OR=1.24, 95% CI= 1.09-1.40) were significant risk factors for frequent exacerbations.

Conclusion: Dyspnea and the frequency of exacerbation in the past year were

independent factors predicting frequent exacerbations in subjects with bronchiectasis in Korea.

Conflict of interest(s) (if any – not included in the 500 words): None

[21] Association of bronchiectasis and bronchial asthma: differential implication of eosinophilic and neutrophilic inflammatory pathways and their clinical impact

Andreas M. Matthaiou[1]; Antonia Digalaki[1]; Chrysavgi Kosti[1]; Katerina Dimakou[1]

[1]*5th Department of Respiratory Medicine, Sotiria Thoracic Diseases General Hospital of Athens, Athens, Greece*

Background: Bronchiectasis and bronchial asthma are two heterogenous airway diseases of great significance that are both characterised by chronic airway inflammation. While asthma and bronchiectasis involve well-studied pathogenetic mechanisms implicating prominent eosinophilic and neutrophilic inflammatory pathways, respectively, eosinophilia is known to dominate in 20% of bronchiectasis cases. The underlying pathophysiology in the coexistence of bronchiectasis and asthma, and how this translates into clinical phenotypes and outcomes, remains obscure.

Aims: This research proposal aims to investigate the differential implication of eosinophilic and neutrophilic inflammation in the association of bronchiectasis and asthma compared to lone asthma and lone bronchiectasis. The relative extent of the two types of inflammation, both locally in the lung and in the systemic circulation, will be determined at four hierarchical levels of the pathophysiology cascade: a) immune cell-signaling, i.e. major cytokines involved; b) immune cell-derived exocytosed substances, i.e. specific eosinophil- and neutrophil-derived granule proteins; c) immune cell type and activity, i.e. activated eosinophil subtypes and actively reprogrammed neutrophils; and d) immune cell and extracellular space interaction, i.e. formation of eosinophil and neutrophil extracellular traps (EETs/NETs).

Methods: A total of 120 individuals, including 30 patients with lone bronchiectasis, 30 with lone asthma, 30 with bronchiectasis and asthma association, and 30 healthy controls, will be enrolled. Clinical data and radiological, microbiological, and functional profiles will be recorded, while health-related quality of life (HRQoL) will be estimated via QOL-B. The experimental set-up will include: a) quantification of plasma and sputum cytokines (IL-8 and IL-13) and cell-derived granule proteins (*eosinophil peroxidase* (EPO), *major basic protein 2* (MBP-2), *myeloperoxidase* (MPO), and *neutrophil elastase* (NE)) via ELISA; b) measurement of peripheral blood and sputum eosinophil subtypes (resident Siglec-$8^{+}CD62L^{+}IL\text{-}3R^{low}$ eosinophils and inducible Siglec-$8^{+}CD62L^{low}IL\text{-}3R^{high}$ eosinophils) and reprogrammed $CD15^{+}CD16^{+}CD66b^{+}CD62L^{low}CD11b^{high}$ neutrophils via flow cytometry; c) EET/NET formation assays; and d) correlation of the findings with chronic symptoms and HRQoL, acute exacerbation rate and severity, lung functional deterioration, airway chronic infection, and parenchymal structural changes.

Expected Results: The association of bronchiectasis and asthma is expected to present with: a) predominant eosinophilic inflammation (higher levels of IL-13, EPO, MBP-2, activated eosinophil subtypes and EET formation) resembling asthma; b) predominant neutrophilic inflammation (higher levels of IL-8, MPO, NE, actively reprogrammed neutrophils and NET formation) resembling bronchiectasis; or c) mixed eosinophilic and

neutrophilic inflammation. Dominance of neutrophilic inflammation may correlate to airway bacterial infection, unfavourable lung function and chest imaging findings, frequent exacerbations, and worse HRQoL, and may predict better response to antibiotics. On the other hand, dominance of eosinophilic inflammation may also correlate to frequent exacerbations, and may predict better response to inhaled bronchodilators and corticosteroids that have no sufficient evidence for use in bronchiectasis.

Conclusion (Implications): By revealing differences regarding the pathophysiology cascade, a better understanding of the pathogenetic mechanisms of eosinophilic and neutrophilic inflammation in bronchiectasis and asthma association may contribute to the development and establishment of targeting diagnostic and therapeutic strategies for this entity.

Conflict of Interest: The authors declare no conflict of interest.

[22] Prevalence of chronic rhinosinusitis and its relating factors in patients with bronchiectasis: findings from KMBARC registry

Ji-Ho Lee[1]; Hyun Lee[2]; Yeon-Mok Oh[3]

[1]*Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea (Republic of);* [2]*Division of Pulmonary Medicine and Allergy, Department of Internal Medicine, Hanyang University Hospital, Seoul, Korea (Republic of);* [3]*Department of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea (Republic of)*

Background/Aims: Patients with bronchiectasis often present with respiratory symptoms caused by chronic rhinosinusitis (CRS). However, studies on the prevalence of CRS and its relationship with bronchiectasis are limited.

Methods: The baseline characteristics of patients with bronchiectasis recruited from the Korean Multicenter Bronchiectasis Audit and Research Collaboration were analyzed. CRS diagnosis was determined by a physician, on the basis of medical records, upper airway symptoms, and/or radiologic abnormalities. Questionnaires for quality of life, fatigue, and depression were administered when patients were stable for a minimum of 4 weeks after the bronchiectasis exacerbation

Results: The prevalence of CRS was 7.1% (66/931). Patients with CRS were significantly younger than those without CRS (60.5 ± 10.7 vs. 64.6 ± 9.3 years, $p = 0.001$). Idiopathic bronchiectasis was more common in patients with CRS compared to those without CRS (53.0% vs. 36.0%, $p = 0.006$). Lung function, inflammatory markers, exacerbations, bronchiectasis severity, and scores for quality of life, fatigue, and depression did not differ between the two groups. In a logistic regression analysis, CRS was associated with age of bronchiectasis diagnosis (OR 0.96; 95% CI 0.94–0.99; $p = 0.003$) and idiopathic bronchiectasis (1.95; 1.12–3.34; $p = 0.018$).

Conclusion: The prevalence of CRS was relatively low. CRS was not associated with the severity or clinical outcomes of bronchiectasis. Early diagnosis and idiopathic etiology were associated with CRS. Our findings reflect the low recognition of CRS in the clinical practice of bronchiectasis and highlight the need for awareness of CRS by adopting objective diagnostic criteria.

Conflict of interest(s) (if any – not included in the 500 words):

[23] Retrospective Analysis of the Clinical and Radiological Features of a Paediatric Bronchiectasis Cohort: Optimising Diagnosis and Management

Aisha Mir[1]; Stefan Unger[2,3]; Kirstin Unger[2]; Alan Quigley[2]

[1]*University of Edinburgh, Edinburgh, United Kingdom;* [2]*Royal Hospital for Children and Young People, Edinburgh, United Kingdom;* [3]*Department of Child Life & Health (UoE), Edinburgh, United Kingdom*

Background/Aims:

Paediatric non-cystic fibrosis bronchiectasis remains understudied, and delays between respiratory symptom onset and diagnosis via high-resolution CT (HRCT) scanning is common. However, controlling infection and inflammation early remains essential to halting disease progression and potentially reverse lung damage. Diagnosis of bronchiectasis is often based on radiologist opinions only. Recent ERS guidelines suggest making the diagnosis by using inner broncho-arterial ratio (BAR) with a cut off of >0.8 in paediatrics rather than 1.0 used in adults.

We aimed to investigate the association between clinical features andradiological bronchiectasis severity using broncho-arterial ratio (BAR), and to compare adult versus suggested paediatric cut-off criteria of BAR in the diagnosis of bronchiectasis.

Methods:

We retrospectively gathered data on 64 children with labelled bronchiectasis from electronic medical records in a tertiary children's hospital. 96 HRCTs were reviewed for signs of bronchiectasis by three radiologists and inter- and intra-rater reliability agreement was assessed. Inner and outer airway diameter BAR measurements were undertaken by one paediatric radiologist blinded to the patients' clinical status. BARs were correlated with clinical features including auscultation signs, wet cough, and CRP levels at the time of the HCRT. Both adult and paediatric cut-off values were used to assess BARs.

Results:

The mean age at HRCT diagnosis was 5 years (SD 3.35 years) (30 boys, 34 girls). Radiologists failed to agree with their own initial diagnoses in 8% of cases and failed to agree with each other in 27% of cases. 159 inner and 159 outer airway diameter measurements were taken after excluding patients with repeated HRCT scans and lobe measurements. 142/159 (89%) had an outer BAR>0.8 and 83/159 (52%) had an inner BAR>0.8 ($p<0.0001$). 24 (48%) additional patients were labelled with a diagnosis of

bronchiectasis using inner BAR>0.8 compared to BAR >1. Using inner compared to outer airway diameters to measure BAR, the diagnosis of bronchiectasis (BAR>0.8) was reduced by 37% (outer BAR >0.8: 89%, inner BAR>0.8: 52%). 94% (50/53) patients with HRCTs isolated pathogens at the time of the HRCT. Moraxella catarrhalis isolation, wet cough, and crackles/crepitations were significantly associated with increased outer BAR ($p<0.05$). 17 patients had repeat HRCTs. Of these, 10/17 (59%) demonstrated reduced outer and inner BARs. The mean inner BAR reduction was 0.301 (0.147) and inner BAR reduction was 0.411 (0.25).

Conclusion:
Expert radiology opinion on the diagnosis of bronchiectasis is limited by poor inter and intra observer agreement. Using a suggested BAR cut off of 0.8 compared to 1.0 significantly increased the diagnostic label of bronchiectasis and needs further evaluation in regards to sensitivity versus specificity and clinical outcome. Infection combined with clinical features present in patients with bronchodilation at HRCT implies potential bronchiectasis exacerbations. To differentiate acute (exacerbation-related) dilatation from chronic dilatation, we recommend performing HRCT upon completing exacerbation treatment

Conflict of interest(s) (if any – not included in the 500 words): None

[24] Reliability and validity of computerized adventitious respiratory sounds in people with bronchiectasis.

Beatriz Herrero-Cortina[1,2,3]; Marina Francín-Gallego[2,4]; Juan Antonio Sáez-Pérez[2]; Marta San Miguel-Pagola[2]; Laura Anoro-Abenoza[1]; Cristina Gómez-Gonzalez[5]; Jesica Montero-Marco[1,3]; Marta Charlo-Bernardos[1,3]; Elena Altarribas-Bolsa[1,3]; Alfonso Pérez-Trullén[1]; Cristina Jàcome[6]

[1]*Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain;* [2]*Universidad San Jorge, Zaragoza, Spain;* [3]*Instituto de Investigación Sanitaria (IIS) de Aragón, Zaragoza, Spain;* [4]*Research Group Movimiento Humano. Universidad de Zaragoza, Zaragoza, Spain;* [5]*Hospital General de la Defensa, Zaragoza, Spain;* [6]*CINTESIS@RISE, MEDCIDS, Faculty of Medicine of the University of Porto, Porto, Portugal*

Background Computerized adventitious respiratory sounds (ARS), such as crackles and wheezes, may be useful to monitor respiratory status of people with bronchiectasis, yet its measurement properties have been poorly explored. This study aimed to test the within-day and between-day reliability and validity of ARS in bronchiectasis.

Methods Adult outpatients with stable bronchiectasis and daily sputum expectoration were enrolled. Computerized respiratory sounds were recorded twice at 4 chest locations (right and left anterior and posterior) on two assessment sessions (7 days apart). The total number of crackles, number of wheezes and wheeze occupation rate (%) were the parameters extracted using validated algorithms.

Results A total of 28 participants (9 men; 62±12y) were included in the within-day and 25 in the between-day reliability and validity analysis. Total number of crackles and wheezes showed moderate within-day (ICC 0.87, 95%CI 0.74-0.94; ICC 0.86, 95%CI 0.71-0.93) and between-day reliability (ICC 0.70, 95%CI 0.43-0.86; ICC 0.78, 95%CI 0.56-0.90) considering all chest locations and both respiratory phases; however, wheeze occupation rate only showed moderate reliability in the within-day analysis (ICC 0.86, 95%CI 0.71-0.93). Bland-Altman plots revealed no systematic bias, but wide limits of agreement, particularly in the between-days analysis. All parameters correlated moderately with the amount of daily sputum expectoration ($r>0.4$; $p<0.05$).

Conclusion ARS presented moderate reliability and were correlated with the daily sputum expectoration in people with stable bronchiectasis. The use of sequential measurements may be an option to achieve greater accuracy of the ARS findings.

Authors declare no conflict of interest.

[25] Heart rate recovery after the 6-min walk test in people with bronchiectasis

Juan Antonio Sáez-Pérez[2]; Beatriz Herrero-Cortina[1,2,3]; Victoria Alcaraz-Serrano[4,6,9]; Elena Gimeno-Santos[5,6]; Antoni Torres[7]; Ane Arbillaga-Etxarri[8]

[1]*Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain;* [2]*Universidad San Jorge, Zaragoza, Spain;* [3]*Instituto de Investigación Sanitaria (IIS) de Aragón, Zaragoza, Spain;* [4]*Fundació Clínic per la Recerca Biomèdica (FCRB), CIBERES, Hospital Clinic de Barcelona, Barcelona, Spain;* [5]*Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Hospital Clinic de Barcelona, Barcelona, Spain;* [6]*Barcelona Institute for Global Health (ISGlobal), Barcelona, Spain;* [7]*Institut Clínic Respiratori, Hospital Clínic de Barcelona, Barcelona, Spain;* [8]*University of Deusto, Donosti, Spain;* [9]*Facultad de Ciencias de la Salud, Blanquerna, Barcelona, Spain*

Background The presence of cardiac autonomic dysfunction is considered a predictor of lower exercise capacity and future exacerbations in people with COPD. However, the cardiac autonomic function has rarely been explored in people with bronchiectasis.

Aims (i) describe the cardiac autonomic function (heart rate recovery, HRR) of people with bronchiectasis during or after completion a submaximal exercise test and (ii) to identify possible clinical determinants for a delayed HRR_1 in this population.

Methods Adult patients with stable bronchiectasis without unstable cardiovascular disease and use of medication that affect heart rate were recruited from a two-center study in Spain. Sociodemographic, anthropometric, clinical data and a patient-reported questionnaire evaluating the cough severity were collected. Participants performed 6MWT following international guidelines and heart rate was registered using Polar Team®. HRR was defined as the different between the HR at the end of 6MWT and at the first minute (HRR_1) and second minute (HRR_2) into the recovery phase. Multivariable linear regression models were used to identify the determinants of a HRR_1 delay.

Results A total of 104 patients with a mean (SD) age of 64 (13) years and mostly woman (67%) were included. The mean HRR_1 after the 6MWT was 20 bpm (12), the mean HRR_2 was 26 bpm (13). Thirty-eight participants (36%) were identified with a delayed HRR_1 after the 6MWT ($HRR_1 \leq 14$). In the multivariable linear regression model (adjusted for age, gender and body mass index), factors significantly associated with a HRR_1 delay were a bronchiectasis severity index > 8 points (classified as severe), a lower distance walked in the 6MWT and higher heart rate at baseline (table 1).

Conclusion A HRR_1 delay was observed in the 36% of the participants. Based on our findings, patients with severe bronchiectasis, lower exercise capacity and higher basal heart rate are more likely to present a HRR_1 delay.Authors declare no conflict of interest.

Authors declare no conflict of interest.

[26] IDENTIFICATION OF A SUBGROUP OF NON CYSTIC FIBROSIS BRONCHIECTASIS WITH ASTHMA TRAITS

ROBERTA PANCANI[1]; DAVIDE CHIMERA[1]; VALERIE WANDAEL[1]; FEDERICO L. DENTE[1]; FRANCESCO PISTELLI[1]; LAURA CARROZZI[1]

[1]*PNEUMOLOGY UNIT, CARDIO-THORACIC DEPARTMENT, UNIVERSITY HOSPITAL OF PISA, PISA, Italy*

Background: Asthma, bronchiectasis, and chronic obstructive pulmonary disease (COPD) are the three most prevalent chronic inflammatory airway diseases. They overlap with a frequency that goes beyond the mere crossing of probabilities due to their high individual prevalence in the general population. Although there is no study that clearly demonstrates a causal relationship that explains these two-by-two relationships, several authors insist that this combined-disorders exist, generating a original group of “overlap” patients. Many studies were performed in subjects with chronic asthma, mainly severe asthma, rarely asthma was investigate in bronchiectasis subjects. In the point of view of Precision Medicine, the treatment should be addressed on asthmatic traits in bronchiectasis.

Aims. To evaluate several methods to express asthma traits in bronchiectasis (subjects known for primarily severe asthma are excluded) by spirometry, and indices of airway inflammation.

Methods: A group of 208 subjects with non cystic fibrosis bronchiectasis, outpatient attending for the clinic in Pneumology Unit of Pisa, was evaluated. The subjects performed baseline spirometry and reversibility test with salbutamol and/or methacholine challenge test to evaluate indices of asthma. Moreover, subjects measured FeNO and/or induce sputum, to evaluate indices of eosinophilic inflammation of the airways.

Results: A group of 208 subjects with bronchiectasis was evaluated, mean age 68.3 yrs (SD 13.8), 62% female, 58% not smokers, 51% at least overweight. The mean time-to-diagnosis was 85.1 months (1-720). Out of 208 subjects with bronchiectasis, 51 showed reversibility test and/or methacholine challenge test positive for asthma trait. The 51 subjects did not show any significant difference with respect to 157 without positive response to salbutamol or methacholine, for age, for gender distribution, for dectection of microbes in airways. But smoke habit was more represented in ASTHMA group than in NO ASTHMA group of bronchiectasis (56% vs 28%, p=0.043). The two grous were similar for DLCO, serum IgE, blood NEU.%. In the table, some different indices are showed.

	No.	FEV1,% pred.	VR, % pred.	Sputum Neu. %	Sputum Eos. %	FeNO, ppb	Blood EOS.%
Asthma	51	77.8 (30.5)	134.0 (37.8)	58.6 (33.1)	13.3 (23.8)	30.1 (59.6)	5.7 (7.4)

No Asthma	157	85.2 (23.9)	119.7 (35.8)	72.7 (24.6)	3.0 (5.1)	24.3 (17.1)	3.1 (2.9)
p		0.048	0.02	0.011	<0.0001	0.011	0.002

Conclusion: The main indices of asthma, reversibility test and methacholine challenge test are able to identify subjects with concominat asthma and bronchiectasis. The identified group is significantly characterized with asthma traits, including probable eosinophilic trait. This fact has some implication to choice the treament in bronchiectasis with asthma traits.

Conflict of interest(s) (if any – not included in the 500 words):

[27] PULMONARY NOCARDIOSIS AS AN EMERGING INFECTION IN NON CYSTIC FIBROSIS BRONCHIECTASIS

ROBERTA PANCANI[1]; DAVIDE CHIMERA[1]; MASSIMILIANO DESIDERI[1]; MARIA PIA NICEFORO[1]; FEDERICO L. DENTE[1]; FRANCESCO PISTELLI[1]; LAURA CARROZZI[1]

[1]*PNEUMOLOGY UNIT, CARDIO-THORACIC DEPARTMENT, UNIVERSITY HOSPITAL OF PISA, PISA, Italy*

Background: Pulmonary nocardiosis is an opportunistic infection that belongs to Actinomycetaceae family and mainly affects immunocompromised patients. However, in one third of cases it can occur in immunocompetent patients. Nocardia spp. are Gram-positive, aerobic, filamentous, and partially acid-fast bacilli. Pulmonary Nocardiosis has a high mortality rate up to 38% according to some case series. Nocardiosis incidence is increasing due to the greater lon[1]gevity of population, which has a senescent immune system and higher number of chronic advanced comorbidities. Local alteration of the pulmonary defences predisposes to PN, as it occurs in COPD or lung sequestration or in bronchiectasis.

Aim: To alert against an emerging pathological entity – Pulmonary Nocardiosis - in bronchiectasis

Methods: In a bronchiectasis outpatient clinic setting, 4 subjects with pulmonary Nocardiosis were found

Results: In the last year, 4 subjects were identified as pulmonary Nocardiosis. The characteristics of everyone are reported in the table.

	Patient 1	Patient 2	Patient 3	Patients 4
Age	59	64	57	64
Gender	Female	Female	Female	Female
Smoke habit	Never	Former smoker (25 PY)	Former smoker, max 5 PY	Former smoker, max 5 PY
Lung Disease	bronchiectasis	COPD	Bronchiectasis, asthma	Bronchiectasis
Immunosoppression	None	None	None	None
Risk factors	NTM-PD in 2015	Not known	Previous vescical BCG; nurse	Pleuritis at 18 yrs

Clin. Manifest.	Cough, sputum, dyspnoea	Hemoptysis, frequent bronchitis	Cough, dyspnoea, recurrent fever	Cough, sputum, dyspnoea, frequent bronchitis
CRP (mg/L)	<0,50	0,55	1,21	2,21
Leuk. (Exp3/mcL)	3,4	7,8	8,7	12,5
Neu.%	36,2	67,4	65,6	63,7
Eos.%	6,2	1,2	3,1	0,9
CHEST RX	Bilateral opacities in lower lung fields	Bilateral opacities	Bilateral opacities	Bilateral confluent opacitis in lower fields
CT SCAN	Peri-bronchiectatic essudations and tree-in-bud in lower fields	Multiple consolidations with cavitas, diffuse tree-in-bud	Diffuse tree-in-bud, consolidations and cavitas	Tree-in-bud, bilateral consolidations, nodules
Presumptive diagn.	Infected bronchiectasis	Bronchitis	Tuberculosis	Infected bronchietasis
Hospitalization	No	Yes	No	Yes
Microorganism	Nocardia spp.	Nocardia abscessus	Nocardia spp.	Nocardia cyriacigeorgica
Diagn. Procedure	BFC with BAL	BFC with BAL	BFC with BAL	Sputum culture
Definite diagnosis	Pulmonary Nocardiosis	Pulmonary Nocardiosis	Pulmonary Nocardiosis	Pulmonary Nocardiosis
TREATMENT	TMP-SMX (po, 4 mo.)	Linezolid, 12 mo.	TMP-SMX (po, 6 mo.)	Imipenem iv and after Linezolid 12 mo
OUTCOME	Favorable	Unfavorable	Favorable	Favorable
Note	Poor adherence	Cotrimoxazole allergy	monitoring	Monitoring, Cotrimoxazole allergy

No patient had suspicion of Pulmonary Nocardiosis, to achieve definite diagnosis of nocardiosis, the isolation of the bacteria was necessary. Patients clinical manifestations were unspecific, and the most common symptom was cough. No detectable immunosoppression status was found. The most common risk factor was bronchiectasis. In this little group, all subjects are female, with a poor weight of the smoke habit. Finally, two patients ot of 4 showed allergy to TMP-SMX (cutaneous reactions) and other drugs have to use.

Conclusion: Bronchiectasis may be a risk factors also for Nocardiosis, and in case of recurrent or persistent exacerbations the suggestion of pulmonary Nocardiosis has to consider in the differential diagnosis of the causes of the exacerbations in bronchiectasis.

Conflict of interest(s) (if any – not included in the 500 words):

[29] COPD IN DEVELOPING WORLD – IMPACT OF PULMONARY TB SEQUELAE

Manu Chopra[1,2]; Meenakshi Chopra[1,2]; Shafin Babu PS[1,2]; Ritwik Chakravarty[1,2]

[1]*INDIAN ARMY MEDICAL CORPS, KOLKATA, India;* [2]*COMMAND HOSPITAL EASTERN COMMAND, KOLKATA, India*

Background/Aims:

In developing countries like India, both tuberculosis (TB) and Chronic obstructive pulmonary disease (COPD) are rampant. Though COPD patients offer significant smoking history with or without environmental and occupational exposures, a significant number of patients become symptomatic after suffering from pulmonary TB PTB). We carried out a cross sectional study at a tertiary care hospital of Indian armed forces to evaluate the impact of PTB sequelae on COPD.

Methods: All COPD patients and under follow up in our centre were included in the study. Besides demographic data patients were questioned regarding PTB in past (sputum smear status, duration of therapy, response to ATT, etc). Patients were also assessed for smoking (active or passive, frequency, duration), environmental or house hold exposure to smoke or biomass fuels and occupational exposure. Duration of onset of symptoms in relation to PTB were noted. Chest radiography and Pulmonary Function Tests (PFT) were carried out for all patients

Results:

1130 COPD patients were included in the study. 81% were males with mean age of 52 years. 28% patients developed features of COPD post PTB and were non-smokers. 36% patients were smokers and had suffered from PTB in past, 22% were smokers but had other environmental and occupational exposure. Patients with PTB with or without smoking reported development or worsening of symptoms mean two and a half years post diagnosis of PTB. Patients with significant PTB sequelae in form of traction bronchiectasis, fibrosis and volume loss involving 2 or more broncho pulmonary segments with or without other contributing factors had severe form of disease with poor response to management.

Conclusion:

In developing countries like India, there's a significant overlap between COPD and Post PTB obstructive lung disease (T-OPD) and a considerable number of patients are falsely labelled as COPD and managed for same with suboptimal response. More than COPD, it's T-OPD which likely is more prevalent in this part of world. Thus, evaluation of COPD

should include assessment of PTB in past and these patients should preferably be labelled as (T-OPD) and managed accordingly.

Conflict of interest(s) (if any – not included in the 500 words): NIL

[30] Long-Term Domiciliary High Flow Nasal Therapy in Patients with Bronchiectasis: A Preliminary Retrospective Observational Case-Control Study

Santi Nolasco[1,2]; Raffaele Campisi[2]; Mattia Nigro[3,4]; Pietro Impellizzeri[1]; Andrea Cortegiani[5,6]; Alberto Noto[7]; Andrea Gramegna[8,9]; Carlo Vancheri[1,2]; Francesco Blasi[8,9]; Nunzio Crimi[1]; Stefano Aliberti[3,10]; Annalisa Carlucci[11,12]; Claudia Crimi[1,2]

[1]*Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy;* [2]*Respiratory Medicine Unit, Policlinico "G. Rodolico - San Marco" University Hospital, Catania, Italy;* [3]*Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini 4, 20072, Pieve Emanuele, Milano, Italy;* [4]*IRCCS Humanitas Research Hospital, Via Manzoni 56, 20089, Milano, Italy;* [5]*Department of Surgical, Oncological and Oral Science (Di.Chir.On.S.), University of Palermo, Palermo, Italy;* [6]*Department of Anesthesia, Intensive Care and Emergency, Policlinico Paolo Giaccone, University of Palermo, Palermo, Italy;* [7]*Department of Human Pathology of the Adult and Evolutive Age "Gaetano Barresi", Division of Anesthesia and Intensive Care, University of Messina, Policlinico "G. Martino", Messina, Italy;* [8]*Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milano, Italy;* [9]*Internal Medicine Department, Respiratory Unit and Adult Cystic Fibrosis Center, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milano, Italy;* [10]*IRCCS Humanitas Research Hospital, Respiratory Unit, Via Manzoni 56, 20089, Milano, Italy;* [11]*Department of Medicina e Chirurgia Università Insubria, Varese, Italy;* [12]*Pulmonary Rehabilitation Unit, Istituti Clinici Scientifici Maugeri, Pavia, Italy*

Background/Aims: High-flow nasal therapy (HFNT) is a noninvasive respiratory support that delivers heated and humidified gases, eventually blended with oxygen, through special nasal prongs. HFNT yields several beneficial physiological effects, including wash-out of anatomical dead space, humidification and improved mucociliary clearance, reduced inspiratory effort, and improved respiratory mechanics. Given the strong physiological rationale and the documented clinical benefits of HFNT in muco-obstructive chronic respiratory diseases, we aimed to evaluate the effectiveness of long-term HFNT in patients with bronchiectasis (BE).

Methods: We conducted a retrospective, bicentric, case-control study. Consecutive adult patients (≥ 18 years old), who were referred to two tertiary-level outpatient clinics at the Policlinico University Hospital, Catania, Italy and the Policlinico Hospital, Milan, Italy, between September 2018 and October 2021, were enrolled if all of the following were present: i) a diagnosis of radiologically (at least one lobe on chest high-resolution computed tomography) and clinically significant BE; ii) a clinical history consistent with chronic cough, sputum production most days of the week and/or frequent respiratory infections; iii) at least one severe exacerbation of BE (defined as exacerbation requiring hospital admission) in the previous year; iv) optimized medical maintenance therapy, respiratory physiotherapy and pulmonary rehabilitation (performed by a specialized respiratory physiotherapist), including technical support for airway clearance, according to the European Respiratory Society guidelines. Patients on long-term home HFNT and

patients on optimized medical treatment alone (controls) were matched by age, sex, bronchiectasis severity index and exacerbations in the previous year. Data on BE exacerbations, hospitalizations/year, mucus features, including visual analog scale (VAS) for the difficulty of mucus expectoration, Saint George respiratory questionnaire (SGRQ) score and pulmonary function were collected.

Results: Twenty patients in the HFNT group and 20 controls were included. The average time of use of HFNT was 6.3 ± 1.8 hours per day. Significant reduction in exacerbations [-1.9 (-2.8 to -0.9), *p*=0.0005] and hospitalizations [-0.7 (-1.1 to -0.3), *p*=0.0006] was found in the HFNT group vs controls. The VAS score for the difficulty of mucus expectoration decreased by -2 (-2.7 to -1.3) points within the HFNT group (*p*=0.0028) after 12 months, with a between-groups difference of -2.2 (-3.9 to -0.5) points (*p*=0.0124). A statistically significant reduction of mucopurulent sputum in favour of mucoid expectoration [from 2/20 (10%) to 9/20 (45%), *p*=0.0233] was found only in the HFNT group. The SGRQ score improved significantly in patients treated with HFNT, with a -9.9 decrease (-12.7 to -6.8) (*p*=0.0012) (Figure 2, Panel C) resulting in a difference of -10.4 (-20.2 to -0.6) (*p*=0.0391) *vs* control group A slight improvement in pulmonary function [FEV_1% +6,1% (+1% to +11.3%) (*p*=0.0219), FVC% +4.6% (+0.8% to +8.3%) (*p*=0.0188) and FEF_{25-75}% +13.4 (+11 to +15.9) (*p*=0.0189) was also found in the HFNT group compared to controls.

Conclusion: In this preliminary study, long-term domiciliary HFNT improved the clinical course of patients with BE.

Conflict of interest(s): Prof. Blasi received financial grants from AstraZeneca, Chiesi Farmaceutici S.p.A and Insmed Inc.; he worked as a paid consultant for Menarini; and received speaker fees from AstraZeneca, Chiesi Farmaceutici S.p.A, GlaxoSmithKline, Guidotti, Grifols, Insmed Inc., Menarini, Novartis AG, OM Pharma, Sanofi-Genzyme, Viatris Inc., Vertex Pharmaceuticals and Zambon, outside the submitted work. Prof. Crimi received honoraria for lectures from Fisher & Paykel Healthcare, outside the submitted work. All the other authors declare no conflict of interest.

[32] The prevalence of Allergic Bronchopulmonary Aspergillosis in Post-Tuberculosis sequelae patients presenting to a tertiary referral centre

animesh ray[1]; gagandeep singh[1]; immaculata xess[1]; naveet wig[1]

[1]*AIIMS, New Delhi, India*

Background/Aims:

Patients with past history of pulmonary tuberculosis are known to have a large number of complications including bronchiectasis and chronic pulmonary aspergillosis. However, outside of sporadic case reports, the occurrence of allergic bronchopulmonary aspergillosis (ABPA) has rarely been reported in these patients. This study aimed to study the prevalence of ABPA in patients with post-tubercular sequelae.

The primary objective of this study was to estimate the prevalence of ABPA in patients with post-tubercular sequelae presenting to a tertiary referral centre. The secondary objective was to compute the frequency of chronic pulmonary aspergillosis (CPA) in the same patient group as well as the response to treatment in the ABPA patients.

Methods:

This cohort study evaluated the prospectively collected data of 912 patients of post-tubercular sequelae patients presenting to a speciality clinic at a tertiary referral centre in the national capital region of New Delhi, India. All patients with radiological evidence of residual sequelae and with a documented history of pulmonary tuberculosis was included in the study. The diagnosis of ABPA and CPA was made as per ISHAM criteria and ESCMID/ERS criteria respectively. The presence of aspergillosis was confirmed by serological tests (IgG and IgE against *Aspergillus* by ImmunoCAP™ and LDBiolateral™ flow assay), *Aspergillus* PCR and fungal stains/culture.

Results:

In this study, a total of 912 patients were screened over a period of four years. Out of the patients screened, ABPA was seen in 14 (1.5%) patients, while CPA was seen in 112 (12.3%) patients. The mean age of the population was 40.2 ± 15 years and there were 602 males (66%). Cough (53%), breathlessness (46%) and hemoptysis (17%) were the most common complaints. On chest imaging (Figures 1 & 2), nodules (35%) and pleural

thickening (24%) were the most common radiological features. A total of five patients had unilateral/bilateral central bronchiectasis. The mean total IgE, IgG against *Aspergillus,* IgE against *Aspergillus, absolute eosinophil counts, KOH positivity and respiratory secretions culture positivity was 1722* ±212 *IU/ml, 45* ±6 IU/ml, *1.7* ±.2 kU/L , 830±150 cells/cmm,8% and 5% respectively. A total of 112 (12.3%) patients had a diagnosis of CPA. Eleven (78.6%) patients received treatment for a median duration of four months with oral itraconazole, while three(11.4%) patients received oral steroids for a median duration of six months. Twelve (85.7%) patients (10 patients: itraconazole group; 2 patients: steroid group) showed both clinical and serological response to treatment. None of them showed any features suggestive of reactivation of pulmonary tuberculosis.

Conclusion:

ABPA can occur in patients with post-tuberculosis sequeale and should be ruled out as a potential complication in these patients with suggestive clinical symptoms/radiological features. The findings of this study should be confirmed by future population-based multicentric studies.

Conflict of interest(s) (if any – not included in the 500 words):

[33] Efficacy of LD Bio Aspergillus ICT Lateral Flow Assay for Serodiagnosis of Chronic Pulmonary Aspergillosis

animesh ray[1]; gagandeep singh[1]; immanculata xess[1]; david dennings[2]

[1]*Aiims, New Delhi, India;* [2]*University of Manchester, Manchester, United Kingdom*

Background/Aims:

The diagnosis of CPA relies on the detection of the IgG Aspergillus antibody, which is not freely available, especially in resource-poor settings. Point-of-care tests like LDBio Aspergillus ICT lateral flow assay, evaluated in only a few studies, have shown promising results for the diagnosis of CPA. However, no study has compared the diagnostic performances of LDBio LFA in setting of tuberculosis endemic countries and have compared it with that of IgG Aspergillus.

This study aimed to evaluate the diagnostic performances of LDBio LFA in CPA and compare it with existing the diagnostic algorithm utilising ImmunoCAP IgG Aspergillus.

Methods:

Serial patients presenting with respiratory symptoms (cough, haemoptysis, fever, etc.) for >4 weeks were screened for eligibility. Relevant investigations, including direct microscopy and culture of respiratory secretions, IgG Aspergillus, chest imaging, etc., were done according to existing algorithm. Serums of all patients were tested by LDBio LFA and IgG Aspergillus (ImmunoCAP Asp IgG) and their diagnostic performances were compared.

Results:

A total of 174 patients were included in the study with ~66.7% patients having past history of tuberculosis. A diagnosis of CPA was made in 74 (42.5%) of patients. The estimated sensitivity and specificity of LDBio LFA was 67.6% (95% CI: 55.7–78%) and 81% (95% CI: 71.9–88.2%), respectively, which increased to 73.3% (95% CI: 60.3–83.9%) and 83.9% (95% CI: 71.7–92.4%), respectively, in patients with a past history of tuberculosis. The sensitivity and specificity of IgG Aspergillus was 82.4% (95% CI: 71.8–90.3%) and 82% (95% CI: 73.1–89%); 86.7% (95% CI: 75.4–94.1%) and 80.4% (95% CI: 67.6–89.8%), in the whole group and those with past history of tuberculosis, respectively. The diagnostic accuracies in various conditions are given in Figure 1.

Conclusion:

LDBio LFA is a point-of-care test with reasonable sensitivity and specificity. However, further tests may have to be done to rule-in or rule-out the diagnosis of CPA in the appropriate setting.

Conflict of interest(s) (if any – not included in the 500 words):

[35] Characteristics and risk of major adverse cardiovascular events after acute pulmonary exacerbations in bronchiectasis and bronchiectasis-COPD overlap syndrome

Freddy Frost[1,2]; Dennis Wat[2]; Gregory Lip[1,3]

[1]*Liverpool Centre for Cardiovascular Sciences, University of Liverpol, Liverpool, United Kingdom;* [2]*Adult Respiratory Medicine, Liverpool Heart & Chest Hospital, NHS Foundation Trust, Liverpool, United Kingdom;* [3]*Aalborg Thrombosis Research Unit, Aalborg University, Aalborg, Denmark*

Background/Aims:

Acute exacerbations of lung disease are known to be associated increased risk of acute cardiovascular events, however relatively little is known regarding the comparative risk in bronchiectasis overall, and when compared to those with bronchiectasis-COPD overlap syndrome (BCOS).

Methods:

A retrospective cohort study was conducted using anonymised electronic health records from 41 international healthcare organisations within the TriNetX Platform. Adults with bronchiectasis and five years of follow-up were included in the study. Major adverse cardiovascular events (MACE: Myocardial infarction, stroke, arrythmia or acute heart failure) were recorded. Clinical and characteristics were compared in univariate analyses. Propensity-matched logistic regression analyses compared risk of MACE between exacerbators and non-exacerbators. Propensity-matched logistic regression analyses also compared risk of 90-day MACE following exacerbations of bronchiectasis and BCOS respectively, as well as between macrolide users and non-users in each disease.

Results:

A cohort of 32,723 people with bronchiectasis were available for analysis. MACE was associated with older age (mean age 74.2 yrs vs. 68, p<0.001), male sex (45% vs. 35%, p<0.001) and classic cardiac risk factors such as obesity (37% vs. 26%, p<0.001), hypertension (88% vs. 61%, p<0.001) and diabetes (45% vs. 24%, p<0.001). In propensity-matched analyses with there was an increased risk of MACE after exacerbation compared to periods stability (Relative Risk [95% CI] 1.33 [1.2 to 1.5], p<0.001). Risk of 90-day MACE was significantly higher following an exacerbation of BCOS compared to bronchiectasis without COPD (RR 1.48 [1.4 to 1.6], p<0.001). Interestingly, all-cause mortality was reduced in BCOS exacerbators compared to bronchiectasis without COPD (RR 0.46 [0.4 to 0.6], p<0.001). Chronic macrolide use was associated with reduced risk of 90-day MACE in exacerbating BCOS (RR 0.81 [0.76 to 0.86], p<0.001) and also

exacerbations of bronchiectasis without COPD (RR 0.69 [0.55 to 0.89], p<0.001).
Conclusion:

This study confirms an increased risk of cardiovascular events in people living with bronchiectasis, particularly after an acute exacerbation. Risk was particularly high in BCOS, where optimisation of modifiable risk factors may be particularly important. Despite increased MACE, all-cause mortality was lower in BCOS exacerbations compared to bronchiectasis suggesting more work is needed to understand comparative outcomes following exacerbations of bronchiectasis and BCOS. Despite some concerns regarding cardiovascular safety, long-term macrolide use at the time of exacerbation was associated with reduced risk of MACE after an exacerbation, perhaps suggesting macrolides' benefical immunomodulatory/anti-inflammatory properties have net-beneficial effect in cardiovascular outcomes of bronchiectasis exacerbations.

Conflict of interest(s) (if any – not included in the 500 words):

No competing interests

[36] Phenotypical Characteristics of Nontuberculous Mycobacterial Infection in Patients with Bronchiectasis

Shimon Izhakian[1]; Frajman Assaf[1]; Mekiten Ori[1]; Hadar Ori[1]; Heching Moshe[1]; Kramer Mordechai R.[1]

[1]*Pulminary Institute, Rabin Medical Center, Petah Tikva, Israel*

Background/Aims:

Patients with bronchiectasis have a greater prevalence of nontuberculous mycobacteria (NTM) pulmonary infection, however the clinical markers for NTM infection in this cohort are heterogeneous and reported findings vary in part based on geography location. The aim of this study was to describe the phenotype of bronchiectasis patients with NTM infection in Israel.

Methods:

We conducted a retrospective single-center observational study of adult bronchiectasis patients who underwent bronchoscopy between January 2007 and August 2020. Demographic, [clinical], laboratory, pulmonary function test and radiological data were collected and were analyzed according to presence (NTM group) and absence (non-NTM group) of a positive NTM culture.

Results:

Compared to patients from the non-NTM group (n=677), those in NTM group (n=94) were older (p=0.008), with a greater proportion of women (p=0.04), having gastroesophageal reflux disease (GERD, p=0.05) and using muco-active medications (p=0.01). They have lower body mass index (BMI, p<0.001), serum albumin (p=0.02), blood counts of lymphocytes (p=0.02) and eosinophils (p=0.04). The forced expiratory volume in one second (FEV1, p=0.01), forced vital capacity (FVC, p=0.04), FEV1/FVC ratio (0.04) and diffusing lung capacity for carbon monoxide (DLCO, p=0.02) were also lower in this group. The proportion of patients with radiological location of bronchiectasis in both lungs (p<0.001), upper lobes (p<0.001) as well as the mean number of involved lobes (p<0.001), were higher in the NTM group. Patients in the NTM group had more exacerbations in the year prior to the bronchoscopy (p=0.02). On multivariate analysis, older age (odds ratio [OR 1.05], 95% confidence interval [CI] 1.02-1.07, p=0.001), lower BMI (OR 1.16, 95% CI 1.16-1.07, p<0.001) and increased number of involved lobes (OR 1.26, 95% CI 1.01-1.44, p=0.04) were associated with NTM infection.

Conclusion:

Patients with NTM infection are older and more likely to be women, and have more severe clinical, laboratory, pulmonary function and radiological characteristics than those without NTM. This phenotype can be used by clinicians for screening of patients with suspected NTM disease.

Conflict of interest(s)None

[37] Primary ciliary dyskinesia: genotype characterization and lung function in a group of Italian patients

L. Petrarca[1]; V. Guida[2]; G. Cimino[3]; F. Piceci-Sparascio[2]; R. Nenna[4]; A. De Luca[2]; M.G. Conti[4]; A. Frassanito[3]; M. Goldoni[2]; E. Mancino[1]; G. Di Mattia[4]; L. Matera[4]; C. Cappelli[3]; DP La Regina[4]; F. Midulla[4]

[1]*Department of Translational and Precision Medicine, Sapienza University, Rome, Italy;* [2]*Medical Genetics Division, Fondazione IRCCS Casa Sollievo della Sofferenza, San Giovanni, Italy;* [3]*Policlinico Umberto I, Rome, Italy;* [4]*Department of Maternal Infantile and Urological Sciences, Sapienza University, Rome, Italy*

Backgorund/Aims: Primary ciliary dyskinesia (PCD) is a rare and genetically heterogeneous disease, characterized by abnormalities in structure and/or motility of motile cilia. Genetic could be important to define prognosis.

Our aim was to report detailed knowledge about the clinical manifestations, ciliary phenotypes, genetic spectrum as well as phenotype/genotype correlation in PCD in a group of Italian patients.

Methods: We enrolled 30 patients (median age 31.3 range 2.25-53.14 years) with PCD. For each patient, a clinical evaluation, consultation of clinical charts and genetic tests (NGS, CGH-Array) were performed to characterize the phenotypes and genotypes and their correlation.

Results: All patients showed common clinical features, that included situs inversus viscerum in 18 (60.0%) of patients, chronic rhinitis in 25 (83,3%), rhinosinusitis in 21 (70%), neonatal respiratory distress in 26.1% (6/23), deafness in 14/19 patients. 25/29 patients have bronchiectasis at CT scan. The mean percentage of the predicted values of forced expiratory volume in 1 second (FEV1%) were 79.3 (range 25-105), and 5/27 (18.5%) patients presented a restrictive spirometry pattern, three (11.1%) had an obstructive spirometry pattern, 7/27 (25.9%) had a mixed obstructive/restrictive pattern. NGS analysis identified a bi-allelic mutation in 21/26 patients, involving ten genes: *DNAH5* (n=6), *DNAH11* (n=1), *CCDC39* (n=2)*, CCDC40* (n=5), *CCDC114* (n=1), *CCNO (N=1)*, *HYDIN* (n=1), *SPAG1* (n=1), *RSPH4A* (n=2), *CCDC103* (n=1).

In one patient with a known pathogenic variant in *DNAH5*, CGH-array analysis found a microduplication of 5p15.2, involving *DNAH5* gene. Dividing cases into three groups according to the genetic defect (*"DNAH5",* "*CCDC39/40*" and "*others*"), we found that patients with *CCDC39/40* defect had a lower FEV1% and more frequently a ventilatory impairment in spirometry although this did not reach statistical significance.

Conclusions: We confirm the high heterogeneity of genetic in our PCD patients' group. CCDC39/40 defects seem to have a worst prognosis with respect to the other genetic defects.

- I (the presenting author) accept full responsibility for the content, submission and presentation of the scientific work, and retain full copyright of the scientific work and presentation.
- I have no Conflict of Interest do declare.
- The study has been approved by the Ethical Committee of Policlinico Umberto I hospital of Rome (Prot. number 0580/2022)

[38] Amikacine Liposome Inhalation Suspension (ALIS) in refractory Mycobacterium Avium Complex (MAC) pulmonary disease

Federica Viola Piedepalumbo[1]; Federica Bellino[1]; Chiara Premuda[1]; Maurizio Ferrarese[2]; Luigi Ruffo Codecasa[2]; Francesco Blasi[1]

[1]*Department of Pathophysiology and Transplantation, University of Milan; Internal Medicine Department, Respiratory Unit and Cystic Fibrosis Adult Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy;* [2]*TB Reference Center, Villa Marelli Institute, Niguarda Hospital, Milan, Italy*

Nontuberculous mycobacteria (NTM) are environmental organisms that can cause lung disease (LD). The most common mycobacterium responsible for LD in Europe is Mycobacterium Avium Complex (MAC), which includes M.intracellulare.

The management of MAC-LD can be challenging and treatment outcomes are often disappointing.

Despite therapy with a multidrug regimen based on guidelines, failure to achieve culture conversion is common.

Treatment failure, according to the NTM-NET consensus, is defined as either the persistence of positive sputum cultures for mycobacterium or the reappearance of mycobacterium after 12 months of antimycobacterial therapy while the patient is still being treated. Treatment refractory patients are defined as those who have no negative sputum culture for mycobacterium after six months of antimycobacterial therapy.

A treatment strategy for refractory MAC-LD involves adding Amikacin liposome inhalation suspension (ALIS) to the standard therapy. According to the CONVERT study, the addition of ALIS provides a higher culture conversion rate compared to the standard treatment. Patients treated with ALIS also continue to have negative cultures during the 12 months of post-conversion therapy.

We discuss a case of a patient who was treated with ALIS in our reference center.

She was a 66-year-old woman, with a history of breast cancer treated with left radical mastectomy and chemotherapy. She had a previous diagnosis of MAC-LD with positive bronchoalveolar lavage (BAL) for M. intracellulare treated with a combination of clarithromycin, rifampicin and ethambutol for six months, then discontinued for ethambutol-induced optic neuropathy.

The patient presented to us with recurring episodes of hemoptysis, nonproductive cough, anorexia and fatigue. The spirometry showed a moderate airway obstruction with ppFEV1 62%. Chest CT demonstrated disease progression with bronchiectasis and pseudonodular thickening in every lobe. She repeated a BAL, which revealed M. intracellulare. Initial

treatment included clarithromycin, rifampicin, clofazimine and levofloxacin for 24 months, after which she did not achieve culture conversion. The symptoms persisted and there were no radiological changes. Moreover, M. intracellulare showed newly developed clarithromycin resistance.

Because of treatment failure, we considered adding ALIS to oral therapy on a daily regimen. Shortly after initiation of treatment, she experienced dysphonia and haemoptoe that led to discontinuation of treatment. She restarted ALIS on a triweekly regimen, which was better tolerated. At 12 months of ALIS plus oral therapy, there was the first evidence of negative sputum culture. This was associated to clinical and functional improvements, with a raise in ppFEV1 up to 80%. CT scan at 12 months showed the reduction of the diffuse thickenings. At the end of the 24-months treatment sputum culture confirmed negative.

Our results are consistent with what is reported in literature. ALIS appeared to be the determinant factor responsible for culture conversion, but results regarding sputum culture after the discontinuation of the treatment are still ongoing.

In our experience ALIS was relatively safe, showing only minor adverse events which decreased importantly after optimization of the dosage.

As of today, guidelines recommend the use of ALIS only for refractory LD, but, even in this situation, access to the drug is difficult for both patients and physicians. Further evidence are needed to determine whether its use could be extended to patients without refractory LD.