Supplementary Material 1

Individual assessment of the studies included in the systematic review and meta-analysis.

Cohort studies on lung involvement in rheumatoid arthritis patients

In 1992 in a retrospective cohort study by **Solanki et al.**[24]**,** the authors investigated the association between BE and RA. They included 77 patients with bronchiectasis based on Walker's criteria[20], and 86 patients with interstitial lung disease (ILD) who were under follow up. ILD was diagnosed based on clinical and radiologic evidence with a restrictive pattern as well as reduced transfer of gasses. The patients were all assessed clinically and were controlled yearly. RA diagnosis was based on American Rheumatism Association (ARA) criteria. The prevalence of RA in the BE patients was 4/77 (5.2%), whereas 4/86 (4.7%) of the ILD patients had RA. The RA patients all had BE preceding their RA disease (mean 19 years prior). The authors state that there are no significant features in these forms of bronchiectasis that separate them from other types of bronchiectasis, and thus they conclude that BE should be remembered as an extra-articular manifestation of RA as much as ILD is.

In 1998 **Despaux et al.**[30] conducted an 18-month prospective study of 46 patients with ACR-criteria verified RA to detect the prevalence of BE using high-resolution computed tomography (HRCT). A total of 74% were women (mean age of 60 years). BE diagnosis was based on HRCT criteria described by Naidich et al.[22]. Radiologic BE was found in 19 patients (41.3%) with no significant difference in gender, age of RA onset, RA disease duration or disease severity based on Steinbrocker Functional Classification, nor any differences in rheumatoid factor (RF) seropositivity or use of corticosteroids or immunosuppressants in comparison to patients without BE. Those without BE were more likely to have impaired DLCO (diffusing capacity for carbon monoxide) when compared to those with BE. A limitation of this study is the small sample size to detect statistically significant differences for a lot of parameters, as the authors believe they had found clinically relevant differences in the lung function testing of RA patients with BE, but the study lacked statistical power to demonstrate it.

In the retrospective cohort study by **Duarte et al.** [27] in 2019, the aim was to characterize the different types of pulmonary diseases seen in RA patients. The study included 87 patients (75% women, mean age 63 years, mean follow-up time 6.7 years) with a mean RA duration of 14 years, with 14 being either current or former smokers. Lung involvement was based on HRCT

and histopathological data, where data was collected from patient records, including laboratory results of RF, anti-cyclic citrullinated peptide (anti-CCP), and pulmonary function test (PFT) results, as well as sputum cultures. A total of 31 of 87 patients had radiologic bronchiectasis. At the time of follow-up, 22 had been admitted to hospital due to respiratory infections, and the majority of these (64%) had bronchiectasis. Particularly female gender associated with higher risk of bronchiectasis (27 out of 31 BE patients were female ($p = 0.04$)). When compared with ILD (45/87), patients with isolated bronchiectasis had longer RA disease duration (OR = 1.05 95% CI: 1.01 – 1.09 ($p = 0.023$)).

Cross-sectional studies on the lung involvement in rheumatoid arthritis patients

In the 1997 study by **Allain et al.**[17], the authors aimed to evaluate the prevalence of symptomatic bronchiectasis in RA patients fulfilling the ACR criteria, using a retrospective cross-sectional study design. 453 patients (77% women, mean age 57.6 years) with a mean RA duration of 8.1 years were included. On chest X-ray (CXR) tram-track images were considered a sign of BE. In contrast to most other studies where radiology is used to diagnose bronchiectasis exclusively, Allain et al.[17] used symptom-based criteria (Walker et al.[20]) for diagnosis of BE. The patients filled out a questionnaire of symptoms relevant for BE, underwent CXR and a review of laboratory tests - If CXR was normal then a CT scan was performed. Thirteen (7 probable BE and 6 definite BE) patients (2.9%) had bronchiectasis based on above mentioned criteria, all of which were women. No laboratory findings were associated with BE. Of note, 12 of the 13 BE patients had onset of respiratory symptoms before joint symptoms (some even in childhood) supporting the theory that BE is important aetiologically in the development of RA in some patients.

Inspired by Despaux and co-workers[21], **Trevez et al.**[25] conducted a cross-sectional study of 100 RA patients and 88 healthy controls in 1997. The mean age of RA patients was 60.1 years and 56.8 in the control group. The BE diagnosis was based on bronchoscopy and /or computed tomography, with no diagnostic criteria presented. They identified radiologic BE in 6% of RA patients and none in the control group. In 5/6 the BE disease antedated joint disease. They concluded that bronchiectasis is likely to play a role in the development of RA, particularly as most had respiratory symptoms before RA.

In 2005**, Bilgici et al**.[44] aimed to assess clinical characteristics and prevalence of pulmonary involvement in RA patients. A total of 54 patients (85% women, mean age 53.6 years and mean duration of RA 8.4 years, 24% smokers) diagnosed with RA according to the 1987 ARA

criteria with no history of lung disease were included. BE definitions on HRCT based on Muller et al.[46] criteria. RA disease severity was determined using the Arthritis Impact Measurement Scale 2 short form (AIMS2-SF). On HRCT, 67.3% of patients had an abnormal scan, and radiologic BE was found in six patients. There was a significant correlation in RF values and some reduced PFT values: Forced expiratory volume in 1. second (FEV_1) and Peak expiratory flow (PEF) ($p<0.05$ and $p<0.01$, respectively). Patients with BE on HRCT had significantly lower FEV_1%pred and PEF%pred ($p<0.05$) when compared with patients with normal HRCT. Two of the six patients had clinical symptoms of BE. Abnormal HRCT findings were statistically significant in their association with patient global assessment of disease severity (OR 2.04, 95% CI: 1.14 – 3.66, $p<0.01$), as well as with old age and Larsen's score (scoring system for joint abnormalities on radiograph in RA patients). No correlation between disease duration and PFT values, however RF did associate with abnormal HRCT, but not specifically with radiologic BE.

While most studies have focused on how patients with long-lasting RA develop lung disease, **Metafratzi et al.**[23] have examined the lungs of individuals with early stages of RA using HRCT in a 2007 cross-sectional study. The cohort comprised 43 patients (88% women, mean age 56.5 years) with a mean RA disease duration of 10 months. BE definitions and scoring based on HRCT findings using Fleischner[47] and Naidich[22] criteria. The patients included were all non-smokers and asymptomatic in terms of respiratory disease. Disease Activity Score of 28 joints (DAS28 score) was used to measure RA disease activity. ACR criteria fulfilled for RA diagnosis. All patients had less than 1-year duration of RA and had not yet taken Disease-Modifying Anti-Rheumatic Drugs (DMARDs) or steroids. Radiologic bronchiectasis was found in 58.1% of patients, however the frequency was similar in the control group (44.4%). Severity of bronchiectasis, which was determined by the HRCT score, was higher compared to the control group, that did not have RA. The score difference was 2.9 vs. 1.3, $p<0.0001$ in the RA vs. control group, respectively. PFT, DAS28 and Larsen score did not show any significant correlation with HRCT findings or scores.

In a cross-sectional study by **Attar et al.**[26] in 2015, the authors aimed to assess the prevalence of bronchiectasis in patients with RA without respiratory symptoms and investigate possible risk factors associated with the presence of radiologic BE. A total of 100 patients (85% women, mean age 51 years), with a mean duration of RA of 6.2 years (12% active smokers) were included. RA diagnosis was based on the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification system. Clinical assessment and laboratory

findings were collected from all patients. The patients also underwent PFT and HRCT. Of the included patients, 35% of patients had radiologic bronchiectasis. Anti-CCP positivity was associated with higher risk of BE (OR 3.55 (p=0.052)), and the same association was found for age, disease duration and male gender.

Case-control studies on the lung involvement in rheumatoid arthritis patients

In the 1993 study by **McMahon et al.**[48], the authors claimed in their matched case-control design, that the development on BE in RA patients was not, in fact, an extra-articular manifestation of the RA disease. The study included 32 patients with BE and RA, 32 matched patients with RA but no BE and 31 patients with BE but no RA. BE definition was based on Walker's criteria[20]. They found that 30 out of 32 patients (93.8%) of the RA-BE group had BE preceding their RA disease. There were no differences between RA patients and RA-BE patients in terms of increased extra-articular activity and laboratory findings. They also found that there were no significant differences in circulating antibodies between RA-BE and RA groups. No differences in PFTs between RA and RA-BE groups except for reduced reversibility in the RA-BE group (p=0.036). The lack of increased activity of RA disease in RA-BE patients compared with RA is interpreted by the authors as a sign that BE do not result in a more severe course of RA, and because of the lack of laboratory findings to differentiate RA-BE from RA, it is less likely to be a systemic feature of RA. They did, however, concede that a fairly large number of patients in the RA-BE group had had surgical excision of their BE (seven patients), and the exact consequence of that is still debatable.

Case studies on the lung involvement in rheumatoid arthritis patients

Despaux et al.[21] studied the characteristics of RA patients with concurrent BE. In their 1996 study 100 RA cases and 80 BE cases were reviewed, of whom 14 cases had concomitant RA and BE. The 14 patients (71% women) included had a mean disease duration of 11.1 years. BE diagnostic criteria was either bronchography with increased bronchial diameter or computed tomography images with airway diameter larger than adjacent vessels. All met ARA criteria for RA disease. Exacerbations of bronchial and joint symptoms occurred simultaneously in 6 /14 (42.8%) of patients and for almost half of the patients the onset of symptoms of joint disease worsened respiratory symptoms. In 12 out of 14 cases, the BE antedated the RA. No correlation with duration of RA was found.