Lung involvement in Rheumatic Diseases

**POS0061** THE RISK OF LUNG CANCER IN RHEUMATOID ARTHRITIS AND IN RELATION TO AUTOANTIBODY POSITIVITY AND SMOKING

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**Background:** Lung cancer is a common malignancy in rheumatoid arthritis (RA)2, 5. Since smoking is a risk factor for both (seropositive) RA and lung cancer, it remains unclear whether RA, in itself, increases lung cancer risk.

**Objectives:** The aim of this study was to examine whether and to what extent the increased risk of lung cancer in RA may (or may not) be attributable to smoking, and to examine this association, both in terms of absolute and relative risks, specifically in relation to RA serostatus.

**Methods:** We performed a population-based cohort study of RA patients and individually matched general population reference individuals identified in Swedish registers and from the EIRA early RA study, prospectively followed for lung cancer occurrence 1995 through 2018. We calculated incidence rates and performed Cox regression to estimate hazard ratios (HR) including 95% confidence intervals (CI) of lung cancer, taking smoking and sero-status into account.

**Results:** Overall, we included 44,101 RA patients (590 incident lung cancers, 56 per 100,000), and 216,495 matched general population individuals (1,691 incident lung cancers, 33 per 100,000), corresponding to a crude HR (95% CI) of 1.76 (1.60-1.93). In subset analyses this increased risk remained after adjustment for smoking (HR=1.77, 95% CI 1.06-2.97). Compared to general population subjects who were never smokers, RA patients who were ever smokers had almost 7 times higher risk of lung cancer.

Positive autoantibody status was associated with an at least doubled risk of lung cancer in ACPA positive patients (vs. ACPA negative patients) and double seropositive (vs. double seronegative) patients after adjusting for comorbidities and smoking (Table 1).

Table 1. Number of events, person-years of follow-up, number of events per 100,000 person-years, and relative risk of lung cancer according to autoantibody status (RA).  

| Autoantibody Status | No of events/100 000 person years | Crude Hazard ratio (95% CI) | Model A Hazard ratio* (95% CI) | Model B Hazard ratio** (95% CI) | Model C Hazard ratio* (95% CI) | Model D with smoking as risk factor | Pack-years of follow-up |
|---------------------|---------------------------------|-----------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|----------------------------
| RF (N=2060)         | 30                              | 2.78 (1.66-6.69)             | 3.01 (1.25-7.26)              | 2.82 (1.17-6.82)              | 2.44 (1.01-5.89)              | 2.16 (0.88-5.28)              | 6 (136)                    |
| (49,440; 60.7)      | (49,440; 12.1)                  |                             |                               |                               |                               |                               |                           |
| ACPE (N=2060)       | 30                              | 3.13 (1.30-7.51)             | 3.43 (1.42-8.25)              | 3.22 (1.33-7.77)              | 2.88 (1.16-9.55)              | 3.29 (1.26-8.58)              | 6 (136)                    |
| (49,440; 60.7)      | (49,440; 12.1)                  |                             |                               |                               |                               |                               |                           |
| RF and/or ACPE (N=2060) | 34                          | 6.38 (1.53-26.56)            | 7.62 (1.83-31.83)             | 7.20 (1.72-30.11)             | 6.29 (1.51-26.30)             | 5.76 (1.37-24.21)             | 6 (136)                    |
| (49,440; 68.8)      | (49,440; 4.0)                   |                             |                               |                               |                               |                               |                           |
| RF and/or ACPE (positive vs. double negative) (N=1608) | 26                          | 6.67 (1.58-28.08)            | 7.98 (1.87-33.50)             | 7.08 (1.67-29.98)             | 6.21 (1.47-26.33)             | 5.86 (1.37-25.01)             | 6 (136)                    |
| (38,592; 674)       | (38,592; 5.2)                   |                             |                               |                               |                               |                               |                           |

**Conclusion:** Despite a high morbitality-rate, there are no definite strategy for subclinical interstitial lung disease (ILD) screening in patients with rheumatoid arthritis (RA).

**Background:** Despite a high morbitality-rate, there are no definite strategy for subclinical ILD screening in patients with rheumatoid arthritis (RA).

**Objectives:** Our objectives were: 1) to identify risk factors for subclinical RA-ILD in a prospective discovery cohort (ESPOIR) 2) to develop a risk score for subclinical RA-ILD and 3) to validate the risk score in an independent replication cohort (TRANSLATE). 2).

**Methods:** Patients without pulmonary symptoms from 2 prospective RA cohorts who underwent chest HRCT scans were included. All patients were genotyped for MUC5B rs35709580. A risk score based on independent risk factors was developed using multiple logistic regression in the discovery cohort. The risk score was validated in the replication cohort.

**Results:** Discovery and replication cohorts included 163 and 89 patients, respectively. Subclinical ILD was detected in 19.0% and 16.9% of the patients, respectively. In the discovery cohort, independent risk factors for subclinical RA-ILD were older age at RA onset (for each year, OR=1.10; 95%CI [1.04-1.16]) and increased mean DAS28-ESR (for each unit, OR=2.03; 95%CI [1.24-3.42]). We developed a risk score for subclinical RA-ILD with AUC=0.82; 95% CI [0.70-0.94] (sensitivity (Se)=71.0%) and specificity (Sp)=79.6%). The risk score was validated in the replication cohort with AUC=0.78; 95% CI [0.65-0.92] (Se=86.7%, Sp=62.2%).

**Conclusion:** Our risk score could help identifying patients at high-risk for subclinical RA-ILD before the onset of pulmonary symptoms.

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PROGRESSIVE INTERSTITIAL LUNG DISEASE IS FREQUENT ALSO IN LATE DISEASE STAGES IN SYSTEMIC SCLEROSIS PATIENTS FROM EUSTAR

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Background: Short disease duration is a predictor for progressive systemic sclerosis-associated interstitial lung disease (SSc-ILD), but studies assessing ILD progression in late disease stages are lacking. To individually tailor management of ILD in SSc patients in clinical practice it is, however, of high importance to understand disease behaviour also in patients with late disease.

Objectives: Analyse ILD progression in SSc-ILD patients from the EUSTAR cohort segregated by subgroups of disease duration.

Methods: We segregated SSc-ILD patients into four categories of disease duration (<3 years, >3-<7 years, >7-<15 years and >15 years after onset of Raynaud’s phenomenon). We assessed progressive ILD, defined as forced vital capacity (FVC) decline >10% or FVC decline ≥10% and FVC decline ≥5–10% and diffusing capacity of the lungs for carbon monoxide (DLCO) decline ≥15% (composite decline) over the first and second 12+/-3 months period after first registration in the EUSTAR database, there were no significant difference in FVC decline ≥10% or composite FVC and DLCO decline within the four subgroups. For example, patients with disease duration >7-<15 years and >15 years frequently showed disease progression of FVC >10%, 41/347 (11.8%) and 32/228 (14%) compared to 38/244 (15.6%) and 33/273 (15.6%) for disease duration ≤3 years and >3-<7 years (P=0.529), respectively (Figure 1).

Results: In total, 2258 SSc-ILD patients were included, with 469 (20.8%) having a disease duration <3 years, 550 (24.4%) between >3-<7 years, 752 (33.3%) between >7-<15 years and 488 (21.6%) of >15 years (Table 1). Baseline characteristics and treatment patterns differed between the four subgroups, with more younger patients with diffuse cutaneous SSc, anti-topoisomerase I antibody and higher Rodnan skin score having ≤3 years disease duration. Lung function with FVC and DLCO were similar between the four groups (Table 1). Notably, in the first and second 12+/-3 months periods after first registration in the EUSTAR database, there were no significant difference in FVC decline >10% or composite FVC and DLCO decline within the four subgroups. For example, patients with disease duration >7-<15 years and >15 years frequently showed disease progression of FVC >10%, 41/347 (11.8%) and 32/228 (14%) compared to 38/244 (15.6%) and 33/273 (15.6%) for disease duration ≤3 years and >3-<7 years (P=0.529), respectively (Figure 1).

Conclusion: It was long believed that ILD burned out in late disease stages. In our analysis of ILD progression by four disease duration categories, we showed that ILD frequently progressed also in late disease stages. This has important implications for clinical practise, as SSc patients need to be regularly monitored for ILD progression independent of disease duration.

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Table 1. Demographics and baseline clinical characteristics of EUSTAR patients


| p-value | Age, years (SD) | 65 (11.5) | 0.001 | Male, n (%) | 112 (14.9) | 38 (78) | 0.001 | DLCO, % pred, mean (SD) | 87 (22.8) | 0.770 | NHYA class 3-4, n (%) | 125 (175) | 22.6 (70) | 0.030 |

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Figures:

Figure 1. FVC decline >10% and composite FVC and DLCO decline in the first and second 12+/-3 months within the four subgroups segregated by disease duration.