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Registries, Lungs, Comorbidities

Impact of inflammation on interstitial lung disease in patients with rheumatoid arthritis - an analysis of the German biologics register RABBIT

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Background:

Ten percent of patients with prevalent rheumatoid arthritis (RA) develop an interstitial lung disease (ILD), which is associated with higher mortality *(1).* A previous study identified high/moderate disease activity, but not CRP, as a risk factor for RA-ILD *(2).*

Objectives:

To analyse whether systemic inflammation (CRP and ESR) and/or disease activity measured with a composite score (DAS28-ESR) are associated with the occurrence of ILD in patients with RA.

Methods:

Data from RA patients observed in the biologics register RABBIT until 10/2020 were included. Patients with incident ILD were selected as cases and matched 1:5 to controls using a modified risk-set sampling (controls had no ILD during the entire observation time). Matching criteria were age, sex, RA duration, date of enrolment and observation time. Odds ratios (OR) and 95% confidence intervals (CI) were computed by conditional logistic regression and adjusted for factors identified by a directed acyclic graph (DAG), namely smoking, rheumatoid factor (RF), chronic obstructive pulmonary disease, number of biologics until index date (date of ILD-diagnosis in cases, date after the respective observation time in controls) and mean glucocorticoid dosage (12 months prior index date). For the regression, CRP and ESR were log-transformed due to their skewed distribution, and missing values were addressed by multiple imputations (n=10).

Results:

Out of 19,148 RA patients enrolled since 2001, 133 patients with incident ILD were identified. Half of the ILDs were diagnosed by computed tomography (n=67), 8% by x-ray (n=10) and in 42% the method was unknown (n=56).

At baseline, cases and controls had a mean age of 61 years, 68% were female, and mean RA disease duration was 9 years. Differences were observed in smoking status (59% ever smokers in cases vs. 48% in controls), RF positivity (84% vs. 72%) and the sum of comorbidities (means 3.1 vs. 2.3).

During the 12 months prior to the index date, mean values of CRP and especially of ESR were significantly higher in cases compared to controls. This difference was not observed for DAS28 (upper figures). Furthermore, more cases than controls were in a high inflammatory status, but not in at least moderate disease activity (lower figures). The adjusted regression analyses confirmed these results: CRP and ESR were significantly associated with incident ILD both at the time of diagnosis and in the 12 previous months, and results were even more pronounced with elevated CRP and ESR, which was not the case for DAS28 (table).

Conclusion:

In contrast to other data, our analyses found that markers of systemic inflammation, but not the DAS28 composite score, are associated with the occurrence of incident ILD in patients with RA and can be predictors for the development of RA-ILD. Therefore, in a treat-to-target approach, rheumatologists should pay particular attention to controlling systemic inflammation.

References:

(1) PMID: 20851924

(2) PMID: 30951251

Upper figures: Unimputed and untransformed CRP, ESR and DAS28 12 months prior to the index date as means with 95% CI, computed by mixed models with matching strata as random effects. The left y-axis refers to CRP and ESR, the right to DAS28.

Lower figures: Percentages of patients with CRP≥5, ESR>21 and DAS28>3.2 12 months prior to the index date.

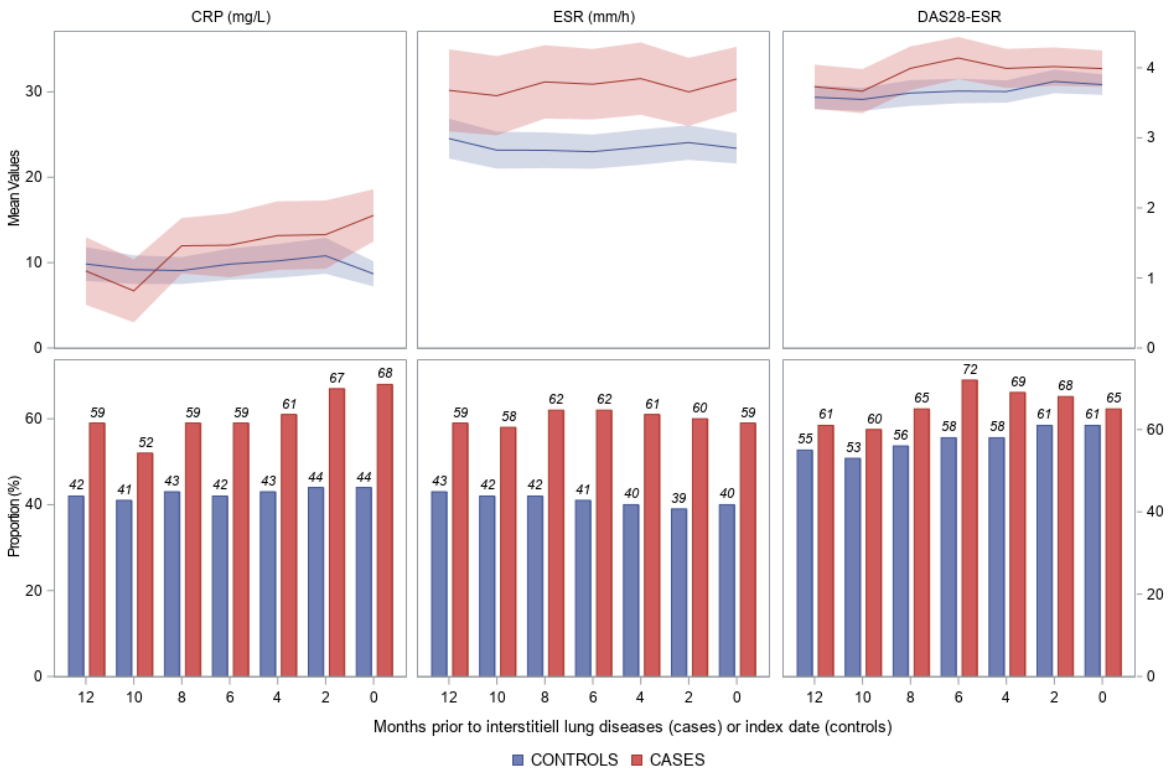

Table: Results of the conditional logistic regression for the risk of ILD.

	Crude OR (95% CI)	**Adjusted OR (95% CI)**
At index date		
Log CRP	1.55 (1.25 – 1.92)	1.55 (1.24 – 1.94)
CRP≥5 vs. CRP<5	2.43 (1.55 – 3.81)	2.41 (1.49 – 3.88)
Log ESR	1.56 (1.22 – 2.00)	1.56 (1.21 – 2.01)
ESR >21 vs. ESR ≤21	2.12 (1.40 – 3.19)	2.12 (1.37 – 3.29)
DAS28	1.17 (1.01 – 1.35)	1.16 (0.99 – 1.35)
DAS28 >3.2 vs. DAS28 ≤3.2	1.31 (0.86 – 1.99)	1.32 (0.85 – 2.06)
Within 12 months prior to index date		
Log CRP	1.41 (1.14 – 1.75)	1.38 (1.09 – 1.74)
CRP≥5 vs. CRP<5	2.60 (1.59 – 4.27)	2.60 (1.54 – 4.41)
Log ESR	1.65 (1.26 – 2.16)	1.60 (1.21 – 2.12)
ESR >21 vs. ESR ≤21	2.43 (1.53 – 3.86)	2.35 (1.45 – 3.81)
DAS28	1.16 (0.99 – 1.36)	1.13 (0.95 – 1.34)
DAS28 >3.2 vs. DAS28 ≤3.2	1.37 (0.82 – 2.30)	1.37 (0.79 – 2.35)

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