Figure 1: Mean (SD) ABA Cmin values (top) and Mean Change From Baseline in SDAI (bottom) in Subjects in DE Arm C (ABA QW + MTX), D (ABA EOW + MTX followed by ABA placebo + MTX), and E (ABA QW + MTX placebo)

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FRI0039 LUNG ULTRASOUND UTILITY IN INTERSTITIAL LUNG DISEASE DETECTION IN RHEUMATOID ARTHRITIS

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Background:

Objectives: To analyze the diagnostic utility of lung ultrasound (US) to detect interstitial lung disease (ILD) in Rheumatoid arthritis (RA) patients comparing with high-resolution computed tomography (HRCT).

Methods: Study design: We performed a cross-sectional, observational study in patients with RA-ILD (cases) controlled with a group of RA patients without ILD (controls) paired by sex, age and time of disease evolution.

Protocol: Patients were selected between May and September 2019. Patients were interviewed by two rheumatologist for the protocolized collection of clinical data. The patients were assessed using HRCT, Pulmonary Function Test (PFT) and lung US. The rheumatology who performed the lung US were blinded to patients clinical data. Variables: (1) B-lines number; (2) evaluation of the lung-ultrasound score already described: L. Gargani, Gutiérrez comprehensivo, Gutiérrez reducido and Mohammadi; (3) pleural irregularities; (4) A pattern US lost; (5). Other variables included demographic, clinical-analytical, therapeutic and ILD-type description. Statistical analysis: descriptive, bivariate analysis. We applied Pearson's correlation coefficient between B-lines, PFT and clinical variable. Furthermore, to establish the cut-off point of the US B-lines number for detecting the presence of significant RA-ILD in relation to HRCT, we used the receiver operating characteristic (ROC) curve analysis. A logistic regression analysis was performed to identify the intercostal spaces (IV: B-lines number in each space) which were independently associated with ILD (DV: ILD in HRCT).

Results: 71 patients were included, 37 (52.1%) with ILD-RA and 34 (47.9%) RA controls. The main characteristics are shown in Table 1. RA-ILD presented more B-lines number than control without ILD (median IQR) 91.0 [31.0-149.0] vs 6.5 [1.5-30.5]; $p < 0.001$ and more pleural irregularities (PI) [PI-median(IQR) 41.0

(5.0-57.5) vs 2.5 (0.0-7.2); $p < 0.001$]. Furthermore, RA-ILD showed a negative correlation between B-lines and DLCO ($r = -0.337$, $p = 0.048$) and positive with DAS28 ($r = 0.347$, $p = 0.035$). Regarding US score, we found that the detection of 32.5 B-lines in 72 intercostal spaces, had a Sensitivity of 75.7%, Specificity=79.4%, PPV= 80% and NPV=75%, whilst in reduced score of 10 intercostal spaces, the detection of 5.5 B-lines had a sensitivity= 62.2%, Specificity= 91.3%, PPV=88.4%, NPV=69.5%. In multivariate analysis, the intercostal spaces which showed independent association with ILD were 3rd right anterior axillary space (OR [IC 95%] 19.0 [1.3-27.5]), 8th right posterior axillary space (OR [IC 95%] 0.04 [0.0-0.6]), 8th right subscapular space (OR [IC 95%] 16.5 [1.8-45.5]), 9th right paravertebral space (OR [IC 95%] 7.11 [1.0-37.1]) and 2nd left clavicular middle space (OR [IC 95%] 21.9 [1.26-378]).

Conclusion: Lung Ultrasound could be a useful tool for interstitial lung disease diagnosis associated with Rheumatoid Arthritis. A 10 space reduced score showed a similar total predictive capacity than 72-space score

References:

VARIABLE	RA-ILD n=37	RA n=34	P-VALUE
Epidemiological Characteristics			
Age in years, mean (±SD)	70.5 (9.1)	70.6 (7.5)	0.970
Sex, male, (%)	20 (54.1)	18 (52.9)	0.920
Body Mass Index, mean, (±SD)	27.5 (3.0)	29.2 (4.2)	0.106
Clinical-analytical characteristics			
Smoking			0.899
Smokers, n (%)	4 (11.8)	4 (10.8)	
RA evolution time, months, median, (p75-p25)	172.5 (100.4-234.4)	134.5 (106.5-211.9)	0.304
ILD evolution time, median, (p75-p25)	42.8 (21.3-101.3)	-	-
Rheumatoid Factor (RF)+ (>10), n (%)	35 (94.6)	27 (79.4)	0.055
RF (>60)	28 (77.8)	18 (52.9)	0.029
ACPA+ (>20), n (%)	34 (91.9)	26 (76.5)	0.073
ACPA (>340), n (%)	26 (72.2)	11 (32.4)	0.001
Erosive, n (%)	22 (59.5)	19 (55.9)	0.761
Clinical manifestation			
DAS28, mean (±SD)	3.1 (1.2)	2.7 (0.9)	0.151
Remission-LDA, n (%)	21 (56.8)	24 (72.7)	0.164
Mild-High activity actividad, n (%)	16 (43.2)	9 (27.3)	0.164
HAQ, mean (±DE)	1.1 (0.6)	0.7 (0.6)	0.021
Tratamiento			
sDMARDs, n (%)	32 (86.5)	34 (100)	0.026
bDMARDs, n (%)	11 (29.7)	11 (32.4)	0.811
Metotrexate, n (%)	19 (51.4)	28 (82.4)	0.060
Leflunomide, n (%)	4 (10.8)	4 (11.8)	0.899
Sulfasalazine, n (%)	5 (13.5)	2 (5.9)	0.281
Hidroxicloroquine, n (%)	4 (10.8)	2 (5.9)	0.456
Micofenolate, n (%)	4 (10.8)	0 (0.0)	0.048
Infliximab, n (%)	0 (0.0)	3 (8.8)	0.065
Etanercept, n (%)	3 (8.1)	4 (11.8)	0.606
Adalimumab, n (%)	0 (0.0)	1 (2.9)	0.293
Golimumab, n (%)	1 (2.7)	1 (2.9)	0.952
Certolizumab, n (%)	0 (0.0)	1 (2.9)	0.293
Tocilizumab, n (%)	2 (5.4)	0 (0.0)	0.169
Abatacept, n (%)	4 (10.8)	0 (0.0)	0.048
Rituximab, n (%)	1 (2.7)	0 (0.0)	0.334

Disclosure of Interests: None declared

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FRI0040 MULTI-VARIATE APPROACH INCLUDING SEROLOGY AND GENETICS FOR AN IMPROVED IDENTIFICATION OF PATIENTS AT RISK OF DEVELOPING RA

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Background: First-degree relatives of rheumatoid arthritis (RA) patients (FDR-RA) have a 3 - 5-fold increased prevalence of the disease [1]. RA development is triggered by an interaction between genetic and environmental factors. As the field is moving towards prevention in pre-clinical stages of RA, it is key to identify individuals with imminent RA, prior to onset of symptoms, which will presumably rely on both the measurement of autoantibodies and genetic risk markers.

Objectives: Assemble a pattern of serologic biomarkers in combination with genetics to improve the identification of individuals at high risk to develop RA.

Methods: The cohort included 827 serum samples from 601 individuals, followed within the Swiss multicenter cohort study SCREEN-RA of FDR [2]. FDR-RA were categorized into four groups according to the presence of symptoms and systemic autoimmunity associated with RA; 1: asymptomatic FDR-RA without anti-CCP or symptoms, 416 (69%); 2: FDR-RA with clinically suspect arthralgia (CSA) [3] or with signs of arthritis, without anti-CCP, 72 (12%); 3: FDR-RAs with no signs of arthritis, positive anti-CCP test, 55 (9%); 4: FDR with signs of arthritis or CSA, positive anti-CCP-test, 58 (10%).

Serum samples were analyzed for the presence of anti-CCP (IgG, IgA), RF (IgM, IgA) and anti-RA33 (IgM, IgA, IgG) using the EliA™ instrument platform (Phadia AB, Uppsala, Sweden).

Genetic measurements were performed using the AmpliSeq™ technology on the Ion GeneStudio™ instruments (Thermo Fisher Scientific, Carlsbad, USA), covered variants were analyzed using an algorithm focusing on the identification of RA patients.

Results: The overall prevalence of biomarkers, considering results above cutoff values, was 1% for anti-CCP IgG and IgA, 10% and 2% for RF IgM and RF IgA, respectively, and 6-15% for all three anti-RA33 isotypes. Several individuals had multiple positive serology tests (Fig 1): 3.6% (22) were positive for 2 tests and 1% (6) were positive for 3 or more tests. Among the 28 individuals positive for ≥ 2 tests, 17 (61%) were symptomatic.

Figure 1. Distribution of positive serology within the different groups. No positivity (none), positive for one (1), equal or more than 2 (2-5) of the serologic tests.

Nine of 604 FDR-RA subsequently developed classifiable RA and were positive for serologic biomarkers before date of RA diagnosis (Table 1). The RA converters had a mean age of 39 years (24-75 yrs) and an average follow-up time within the study of 3.6 years (1-7 yrs).

Table 1. Biomarker status of subsequent RA converters before date of diagnosis.

RA converters	CCP IgG	CCP IgA	RF IgM	RF IgA	RA33 total
1	+	+	+	+	+
2	+	-	+	+	-
3	-	-	+	-	+
4	-	-	+	-	-
5	-	-	+	-	-
6	-	-	-	-	+
7	-	-	-	-	+
8	-	-	-	-	-
9	-	-	-	-	-

Using an algorithm to analyze the RA-associated genetic SNPs, we could highlight 48 FDR-RA (8%) with an increased genetic risk to develop RA. 15 out of 48 individuals (31%) at high genetic risk reported CSA, and 12 out of 48 individuals (25%) displayed signs of systemic autoimmunity associated with RA.

Conclusion: When looking at FDR it could help to not only include anti-CCP autoantibody testing but also additional biomarkers like RF and anti-RA33. Furthermore, looking at the genetic risk factors could give additional information. The combination with the multi-variate profile could even improve the early diagnosis of these patients.

References:

- [1] Kuo et al. *Rheumatology* 2017; 56:928933
- [2] Finckh et al. *Ann Rheum Dis* 2011; 70: S3–282
- [3] van Steenberg HW, et al. *Ann Rheum Dis* 2017; 76:491–496

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FRI0041 ULTRASOUND-DETECTED SYNOVITIS AMONG INDIVIDUALS AT RISK OF RHEUMATOID ARTHRITIS INCREASES THE RISK OF DEVELOPING CLINICAL ARTHRITIS

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Background: During the transition to rheumatoid arthritis (RA) patients pass through several phases. In the preclinical phase, the presence of anti citrullinated protein antibodies (ACPA) can be detected [1]. A set of clinical characteristics for patients with arthralgia who are at risk of progression to RA was established (clinically suspected arthralgia; CSA) [2]. Ultrasound (US) is more sensitive diagnostic tool in detecting synovitis than clinical assessment and was recommended to use in diagnostics of RA.

Objectives: To test if ultrasound-detected synovitis among patients at risk of progression to RA increases the risk of developing clinical arthritis (CA) in the future.

Methods: ACPA+ individuals with arthralgia and/or those fulfilling CSA criteria were enrolled into the study and were assessed in 3 months interval (routine clinical investigation with laboratory tests, 68-joint count, US assessment). Tender and swollen joint counts were provided by an independent investigator. Sonographer was blinded to all clinical and laboratory data. CA was defined as clinically swollen and tender joint. All US assessments were provided by a single experienced investigator. Thirty joints US score was assessed bilaterally in wrist, MCP I-V, PIP II-V (dorsal and palmar approach), MTP II-V (dorsal approach), ankle (dorsal, medial and lateral approach). US synovitis was defined according the EULAR-OMERACT and scored separately in gray-scale (GS) 0-3 (zero to severe synovitis) and Power Doppler (PD) 0-3 (zero to high activity). Scores were calculated as sum scores. For the statistical analysis, we used GraphPad Prism 8.0.0 software (Wilcoxon-Mann-Whitney test), and relative risk ratio (RR).

Results: 93 patients were enrolled into the study (95% female). 58 patients were ACPA+ (all of them RF+), 35 were ACPA- (10 of them RF+). Of ACPA+ individuals, 100% fulfilled the CSA criteria, all seronegative individuals met the CSA criteria. At baseline, GS ≥ 1 was detected in 69 patients (74%), PD ≥ 1 was in 26 (28 %) patients. Single erosion was found by US in 1 patient (0.9%) at baseline. 14 patients (15%) developed CA within 30 months, 77% of them till month 10 from the baseline. No statistical difference in US synovitis score was found between ACPA+ vs. ACPA- and CSA+ vs. CSA- groups at baseline. RR to develop CA at the joint level in patients with GS ≥ 1 at baseline was 1.37 (95% CI 0.99-1.89; $p < 0.05$), with PD ≥ 1 the RR was 2.5 (95% CI 1.3-4.8; $p < 0.05$), in GS ≥ 2 RR was 3.8 (95% CI 2.6-5.6; $p < 0.0001$), in PD ≥ 2 RR was 5.3 (95% CI 2.4-11.7; $p < 0.0001$). US-detected synovitis preceded clinical finding of arthritis by 3 months (SD 1.2).

Conclusion: US-detected synovitis in patients at risk of RA further increases the risk of developing clinical arthritis in the future. US detected synovitis in joints appear about 3 months prior synovitis detected by routine clinical assessment.