FRI0071

ANTI-CITRULLINATED PROTEIN ANTIBODY SPECIFICITIES, RHEUMATOID FACTOR ISOTYPES AND RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENTS

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Background: The association and role of antibodies to citrullinated proteins (ACPA) on the risk of cardiovascular (CV) co-morbidity in patients with rheumatoid arthritis (RA) is incompletely understood. We have previously reported an association between high levels of CCP2 and risk of acute coronary syndrome (ACS) in RA¹.

Objectives: To further investigate any association between specific ACPA or rheumatoid factor (RF) isotypes, and CV events (ACS, stroke, CV death, and major adverse CV event (MACE)).

Methods: 2533 patients with RA from the Swedish EIRA study were tested for ACPA specificities on a custom-made microarray chip. All antibodies (Ab) detected with a prevalence $\geq 10\%$ were included in the analysis. "Ab load" was defined as the number of specificities expressed in an individual, and categorized into four groups. ACPA was also measured by a commercial anti-CCP2 assay and anti-CCP2 levels divided into <25 , $25 - < 75$, $75 - < 1500$ and >1500 arbitrary units/mL, where <25 defines negativity. IgA, IgG and IgM RF positivity was assessed using ELISA immunoassay. For each RF isotype, cutoff level was determined as above the 98th percentile among controls.

The data was linked to the National Patient Register and the Cause of Death register, and events of ACS (ICD10=I20.0, I21, or cause of death listed as "I21"), stroke (ICD10=I60-I64), CV death (cause of death listed as "I"), or MACE (any of the above) identified.

We used Cox proportional hazard model, adjusted for sex, age and calendar period of RA diagnosis, to assess associations between ACPA/RF status and each CV outcome.

Results: Median age at diagnosis was 52 years, and median follow-up was 12 years. The incidences per 1000 person-years were 4.3 for ACS, 4.0 for stroke, 2.4 for CV deaths, and 9.4 for MACE.

66% were anti-CCP2 positive. This was associated with ACS, stroke and MACE. There was a trend with increasing CV risk with increasing anti-CCP2 levels (Table).

For RF, the pattern was markedly different across isotypes; IgM RF associated with ACS, stroke and MACE whereas IgA RF associated to CV death (Table).

18 different ACPA specificities (Fil 307-324 (CPP-1), Vim 60-75, Vim 2-17, Fib β 36-52, Fib α 580-600, Eno 5-21 (CEP-1), Fib α 621-635, Fib α 36-50, Fib β 60-74, Ptm13, Ptm36, Pept Z1, Pept Z2, Pept 1, Pept 5, Bla26) had a frequency $>10\%$ and included in the analyses. Median Ab load was 6 (IQR:2). There was a significant p-value for trend between Ab load and CV risk for stroke and MACE. Fib β 36-52 was the only Ab associated with all 4 outcomes, and, together with CPP3 and ptm13, the only ACPAs associated to ACS. No association to ACS remained when all Abs were jointly included in the model. For stroke, 13 of the 18 Abs associated with risk, but only Fib β 60-74 remained (HR 1.91 (95% CI 1.07-3.42)) in the full model. For CV death and MACE, 14 Abs were associated, but no associations remained in the full model.

Conclusion: In patients with RA, RF and ACPA are linked to CV risk. For RF, CV risks differ with isotype. For ACPAs, very high levels, and the number of individual ACPAs, are linked to CV risk, suggesting that Ab load may be more important than individual ACPAs.

CCP2	Frequency	ACS ^a	Stroke ^a	CV Death ^a	MACE ^a
HR (95% CI)	0.60	1.45 (1.00-2.10)	2.79 (1.17-2.56)	2.43 (0.89-2.30)	2.41 (1.10-1.82)
ACPA level					
Low	0.07	1.48 (0.69-3.16)	1.30 (0.51-2.86)	0.91 (0.38-2.03)	1.20 (0.69-2.07)
High	0.44	1.41 (0.95-2.10)	1.70 (1.12-2.57)	1.21 (0.72-2.04)	1.16 (1.04-1.78)
Anti-CCP2					
Extreme	0.14	1.60 (0.95-2.69)	2.01 (1.19-3.41)	2.17 (1.18-3.98)	1.60 (1.13-2.28)
Specificities expressed					
Low	0.27	1.45 (0.85-2.47)	1.45 (0.80-2.63)	0.90 (0.44-1.83)	1.26 (0.88-1.82)
Medium	0.27	1.61 (0.95-2.71)	2.05 (1.18-3.59)	1.47 (0.78-2.77)	1.51 (1.06-2.14)
High	0.26	1.55 (0.90-2.66)	2.57 (1.44-4.65)	1.58 (0.83-3.03)	1.72 (1.20-2.46)
Rheumatoid factor					
IgA RF	0.58	0.92 (0.59-1.43)	0.78 (0.50-1.22)	1.95 (1.04-3.65)	0.96 (0.71-1.30)
IgG RF	0.68	0.95 (0.62-1.45)	1.02 (0.66-1.57)	0.93 (0.54-1.60)	0.92 (0.69-1.23)
IgM RF	0.57	2.47 (0.94-2.30)	1.70 (1.08-2.67)	0.84 (0.45-1.58)	1.44 (1.06-1.95)

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Disclosure of Interests: Helga Westerlind: None declared, Johan Rönnelid: None declared, Monika Hansson: None declared, Lars Alfredsson: None declared, Linda Mathsson Employee of: employed by Thermo Fisher Scientific, Guy Serre: None declared, Martin Cornillet: None declared, Rikard Holmdahl: None declared, Per-Johan Jakobsson: None declared, Karl Skriver: None declared, Lars Klareskog Grant/research support from: Yes, but not for the presented study., Saedis Saevardottir Employee of: Part-time employee at deCODE Genetics/Amgen Inc, working on genetic research unrelated to this project., Johan Askling Grant/research support from: Karolinska Institutet (JA) has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATRIS national safety monitoring programme for rheumatology biologicals: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB., Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer.

DOI: 10.1136/annrheumdis-2019-eular.1930

FRI0072

PREDICTING SARCOPENIA AND OBESITY BY MEASURING THIGH MUSCLE AND FAT THICKNESS BY ULTRASOUND IN PATIENTS WITH RHEUMATOID ARTHRITIS: FROM THE CHIKARA STUDY

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Background: Rheumatoid arthritis (RA) patients often have sarcopenia. The thickness of the quadriceps muscle, easily measurable by ultrasound (US), is known to be related to skeletal muscle mass, and its decreased thickness may suggest sarcopenia.

Objectives: To investigate the utility of US for predicting sarcopenia by examining the anterior thigh in RA patients.

Methods: Ninety-four patients (66 female) enrolled in the prospective CHIKARA study (UMIN000023744) underwent US muscle (MT) and fat thickness (FT) examinations of the anterior thigh. Muscle and body fat mass were also examined by a body composition analyzer (MC-780A; TANITA, Tokyo, Japan). Whether MT and FT can predict sarcopenia and obesity was also examined. Sarcopenia was diagnosed based on the Asian Working Group on Sarcopenia definition, and obesity was diagnosed by% body fat (%BF).

Results: MT was significantly lower in RA patients with sarcopenia than in those without (24.8 ± 3.5 mm vs. 29.6 ± 3.8 mm, $p=0.01$). MT was related to sarcopenia (males $r=0.56$, $p=0.02$; females $r=0.32$, $p=0.01$). The MT cut-off value for sarcopenia was 24.7 mm in males and 19.7 mm in females on receiver operating curve (ROC) analysis. FT was correlated with%BF (males $r=0.66$, $p<0.01$; females $r=0.62$, $p<0.001$).%BF was estimated by $2.21FT+7.28$ in males and $1.45FT+14.46$ in females by a simple linear regression model. This means that $FT>8.0$ mm in males and $FT>10.7$ mm in females indicate obesity (Table 1). When assessing the accuracy of these cut-off values, the kappa values were 0.541 and 0.469, respectively

Table 1. Relationship between%BF and FT. $FT>8.0$ in males and $FT>10.7$ in females indicate obesity.

FT: the fat thickness (FT) at anterior thigh measured by ultrasound,%BF:% body fat measured by body composition analyzer.

Conclusion: Sarcopenia and obesity can be predicted by US examination of the anterior thigh in RA patients.

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