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 alpha 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)	1.39 (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)	1.20 (0.38-3.03)	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)

REFERENCE:

[1] Mantel A, et al, 2015. PMID 26138387

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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 $2.21\text{FT}+7.28$ in males and $1.45\text{FT}+14.46$ in females by a simple linear regression model. This means that $\text{FT}>8.0$ mm in males and $\text{FT}>10.7$ 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. $\text{FT}>8.0$ in males and $\text{FT}>10.7$ 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.

REFERENCE:

[1] Kawai H., Kera T., Obuchi S., et al. Morphological and qualitative characteristics of the quadriceps muscle of community-dwelling older adults based on ultrasound imaging: classification using latent class analysis. Aging Clin Exp Res. 2018; 30:283-29.

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FRI0073

SWELLING OR TENDERNESS, WHICH ONE CORRESPONDS BETTER WITH ULTRASOUND-DETECTED SYNOVITIS?

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Background: Ultrasound (US) is a sensitive method for detecting joint inflammation in patients with rheumatoid arthritis (RA). The relationship between tender or swollen joints and ultrasound-detected synovitis has not been well explored in patients with RA.

Objectives: The purpose of the present study was to compare the correlation between ultrasound-detected synovitis and joint tenderness or swelling at the wrists and hands in RA patients.

Methods: Twenty-two joints, including bilateral wrists, proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints, were respectively evaluated by physical examination (PE) and ultrasound scan in 258 RA patients. All patients had at least 1 tender or swollen joint out of 22 joints. Synovitis was detected by using semi-quantitative scoring systems (0-3) for grey scale(GS) and power Doppler(PD). Positive synovitis was defined as $GS \geq 2$ and/or $PD \geq 1$. All correlations among US variables and clinical variables were assessed using Spearman's rank correlation test. Cohen's kappa (κ) between clinical and sonographic findings was calculated.

Results: Their median age was 51.2 years, median disease duration was 57 months, with 83.33% females. The mean (SD) Disease Activity Score based on 28 joints (DAS28)-ESR and DS28-CRP were 4.47 ± 1.62 and 3.99 ± 1.51 , respectively. In a total of 5676 joints assessed, 968 swollen joints (17.05%) and 1296 tender joints (22.83%) were found, while on ultrasonography GS synovial hyperplasia was present in 801 (14.11%) joints, positive PD in 476 (8.38%) joints. There were more tender joints without swelling ($n=574$) than those swollen joints without tenderness ($n=246$). In all joints, higher κ coefficient was observed in joint swelling ($\kappa=0.367$, $p<0.01$) with ultrasound-detected synovitis compared with tenderness ($\kappa=0.281$, $p<0.01$). Similarly, swollen joint counts of 22 joints showed higher Spearman's correlation coefficient with either total GS scores ($r=0.499$, $p<0.01$) or total PD scores of 22 joints ($r=0.430$, $p<0.01$) than tender joint counts of 22 joints ($r=0.354/0.308$, $p<0.01$). GS and PD synovitis were more frequently detected in swollen joints without tenderness compared with tender joints without swelling. This discrepancy tend to be more significant in MCP2, MCP3, and MCP4 joints ($p<0.05$).

Conclusion: In RA patients with at least 1 tender or swollen joint of wrists and hands, a higher frequency of joint tenderness was observed than swelling. However, swelling had better agreement with ultrasound detected synovitis compared with tenderness. Joint swelling is more associated with ultrasound-detected synovitis than tenderness. Without swelling, joint tenderness tends to be less associated with ultrasound-detected synovitis.

REFERENCE:

- [1] Tan YK, Moorakonda RB, Allen JC Jr, Chew LC, Thumboo J. Back to the basics: Understanding joint swelling and tenderness at the wrist in rheumatoid arthritis through the use of ultrasonography. *Int J Rheum Dis*. 2018 Oct 21.

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Rheumatoid arthritis – biological DMARDs

FRI0074

UPDATE FOR THE CLINICAL PRACTICE: INTEGRATED, EVIDENCE-BASED APPROACH FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS

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Background: The management of rheumatoid arthritis has evolved in the last few years with greater emphasis on a treat-to-target strategy rather than specific drug regimens. Technologies such as ultrasound have been increasingly used for diagnosis and monitoring of synovitis where it is unclear from clinical examination. These aspects of management were investigated by the Guideline Committee, and recommendations have been updated using new evidence [1, 2].

Objectives: To develop an updated evidence-based, interdisciplinary recommendations for the management of rheumatoid arthritis (RA).

Methods: The task force comprised rheumatologists, epidemiologists, health economists, and patients. A systematic literature analysis was conducted using the Cochrane Database of Systematic Reviews and MEDLINE. Data regarding the drugs prices and product information were collected to evaluate drug cost and safety. Evidence and recommendations were graded, and an algorithm for treatment and final statements were discussed in a consensus meeting (Nominal Group Technique). Recommendations were developed using a Delphi method by a multidisciplinary panel including patients.

Results: Consensus was reached on recommendations, including a standardized treatment strategy according to the RA severity, activity and prognostic factors in the individual patient. In this updated interdisciplinary guideline for RA the treat to target strategy was considered the cornerstone in these recommendations (figure 1). RA patients should reach clinical, ultrasonographic and functional remission. Treatment decisions should incorporate the disease activity status, structural damage progression (radiologic/sonographic), comorbidities, quality of life and patient motivation. Psychiatrist, psychologist and occupational therapist should be included in interdisciplinary treatment team for RA.

Conclusion: The treatment strategy included a total of twenty-one evidence based interdisciplinary recommendations for management of RA (figure 1), and is accompanied by a more in-depth discussion of key management principles. These recommendations provide a step-wise approach to treatment, to enable practitioners to develop and support the most effective method of achieving and maintaining remission in RA patients. These recommendations are not to remove the physician's autonomy, and physicians must select the most appropriate therapeutic option, taking into consideration the patient's preferences.