A deposits were confirmed in serial sections by immunohistochemical and histochemical methods.

Results: **sAAa** complicated **RA** in **34 (21.12%)** of 161 patients; in **127 (78.88%)** of 161 patients amyloid A deposits were not found.

Amyloid A deposits were found in **29 (87.88%) kidneys** of 33 patients with **sAAa**; kidneys were negative for amyloid in **4 (12.12%)** of 33 cases (in 1 of 34 patients with **sAAa** tissue blocks of kidneys were not available).

Amyloid A deposits were found in **29 (87.88%) hearts** of 33 with **sAAa**; the heart was negative for amyloid in **4 (12.12%)** of 33 cases (the heart of one patient with **sAAa** was not available).

Renal amyloid A deposition led to death in **17 (50.0% of 34)** patients with **sAAa** due to massive amyloid A deposition in the kidneys, leading to renal insufficiency and uremia. Cardiac amyloid A deposition led to death in **3 (8.82% of 34)** patients with **sAAa** (and contributed to the lethal outcome in further 5). **Forteen (41.18% of 34)** patients with **sAAa** died of other causes such as peritonitis, lethal septic infection, etc.

sAAa was clinically diagnosed in **9 (26.47%)** and missed in **25 (73.52%)** of 34 patients, and only cases with massive renal amyloid A deposits were recognized. Cardiac **AAa** or its pathogenic role in mortality was not diagnosed.

Conclusion: **sAAa** is one of the main and the most insidious complications of **RA** affecting the kidneys and heart with high prevalence and severity. **sAAa** is related to the cardiovascular system, and **rAAa** or **cAAa** are associated with it. **sAAa**, **rAAa** and **cAAa** may developed in both sexes, and at any time in the course of the disease.

Systemic, renal and cardiac amyloid A deposition is a progressive and cumulative process, involving in its early stage only a few structures in some organs, and increasingly more in the later stages of the disease.

In **sAAa** the renal and cardiac amyloid A deposition starts after a latent stage. This latency may be caused by a not specified local protective mechanism, e.g. great excretion capacity of the kidneys, due to motility of the heart or oxygenisation etc.

Amyloid A deposition starts in the most frequently involved structures of the kidneys or heart with more massive deposits. The chronology of amyloid A deposition allows an indirect assessment of the stage of renal or cardiac amyloidosis, which may have a prognostic value in everyday surgical pathology.

Half of the patients with **sAAa** died of uremia caused by massive **rAAa** and only 9 of these were clinically recognized. Renal and cardiac amyloid A deposition should be considered a very serious, life-threatening complication of **RA**.

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FRI0027

PROGNOSTIC MARKERS FOR PRECLINICAL CARDIOVASCULAR DISEASE IN RHEUMATOID ARTHRITIS AND CORRELATION WITH DISEASE ACTIVITY

Annelies Blanken¹, Rabia Agca¹, C.J. van der Laken², Michael Nurmohamed^{1,2}.

¹Amsterdam Rheumatology and immunology Center location Reade, Amsterdam, Netherlands; ²Amsterdam Rheumatology and immunology Center location VUmc, Amsterdam, Netherlands

Background: Patients with rheumatoid arthritis (RA) have an elevated cardiovascular (CV) disease risk, explained both by an increased prevalence of traditional CV risk factors and the presence of chronic systemic inflammation that impairs vascular function, leads to thickening of the arterial wall and increased arterial stiffness.

Objectives: In this study we investigated the effect of anti-inflammatory treatment on prognostic markers for preclinical cardiovascular disease (arterial wall thickening and arterial stiffness) and the correlation of these markers with RA disease parameters.

Methods: Carotid ultrasound (using Artlab echotracking system) was used to determine carotid intima media thickness (IMT) and pulse wave analysis was done with SphygmoCor tonometry to calculate pulse wave velocity (PWV) and augmentation index (AIx). Paired t-test was used to compare PWV, AIx and IMT prior and after 6 months of therapy. Pearson correlation was calculated to investigate the correlation of PWV, AIx and IMT with (natural logarithm of) C-reactive protein (CRP), (natural logarithm of) erythrocyte sedimentation rate (ESR) and disease activity score-28 (DAS28). For correlations, data from both time points were pooled.

Results: In total 61 consecutive RA patients (50% early arthritis starting with csDMARD and 50% established RA starting with adalimumab) were asked to undergo arterial analysis just prior to start of therapy and after 6 months. PWV was performed in 45 patients at baseline and 39 at follow-up, IMT in 56 and 45 patients respectively and AIx in 51 and 44 patients respectively. Both signs of arterial stiffness (PWV and AIx) decreased after 6 months of therapy (mean difference 0.7 and 0.8 respectively; table 1), although this did not reach statistical significance. IMT remained stable during 6 months of therapy.

Table 1. Prognostic markers of atherosclerosis prior and after 6 months of anti-inflammatory therapy

	n	Baseline	6 months	Mean difference (95% CI)
PWV (m/s)	35	8.0	7.3	0.7 (-0.2;1.5)
AIx (%)	39	27.4	26.6	0.8 (-6.4;7.9)
IMT (mm)	43	0.68	0.68	-0.007 (-0.03;0.02)

PWV (n=84) showed a significant correlation with ESR (0.262, p<0.02) and DAS28 (0.269, p<0.02). Both AIx (n=95) and IMT (n=101) showed a significant correlation with CRP (-0.223, p<0.05 and 0.244, p<0.02, respectively). Other correlation coefficients were not statistically significant (data not shown, p>0.05).

Conclusion: Arterial stiffness as measured with PWV tended to decrease after 6 months of anti-inflammatory treatment. Arterial stiffness and arterial intima media thickness correlated with clinical disease parameters. Altogether, these changes might suggest that effective antirheumatic therapy has favorable cardiovascular effects. Whether or not this ultimately leads to a significant reduction of "hard" cardiovascular endpoints remains to be established in prospective studies.

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FRI0028

LOW SERUM IGF1 IS ASSOCIATED WITH AN INCREASED RISK AND HIGH PREVALENCE OF CARDIOVASCULAR EVENTS IN MIDDLE-AGED FEMALE PATIENTS WITH RA – A 5-YEAR FOLLOW-UP

Malin Erlandsson^{1,2}, Rachele Espino¹, Lovisa Lyngfelt¹, Sofia Töyrä Silfverswärd¹, Mitra Nadali^{1,2}, Karin Me Andersson¹, Rille Pullerits^{1,2,3}, Maria I Bokarewa^{1,2}.

¹University of Gothenburg, Dpt of Rheumatology and Inflammation Research, Gothenburg, Sweden; ²Sahlgrenska University Hospital, Rheumatology Unit, Gothenburg, Sweden; ³University of Gothenburg, Dpt of Clinical Immunology and Transfusion Medicine, Gothenburg, Sweden

Background: Recent meta-analysis reported that rheumatoid arthritis (RA) is associated with high frequency of hypertension and stroke (1). IGF1 is an important angioprotector and its deficiency predisposes to development of ischemic stroke (2).

Objectives: Since levels of active IGF1 are affected by systemic inflammation, we analyze if low IGF1 is associated with increased cardiovascular disease (CVD) in women with RA.

Methods: The CVD risk was estimated (eCVR) in 184 female RA patients (median age 53 years, range 21-71) using the Framingham

algorithm. A 5-year prospective follow-up for new CVD events, type II diabetes and medication for hypertension and hyperlipidemia was completed in all the patients. The event-free survival curves were built and the Mantel-Cox analysis was performed with respect to serum IGF1, where IGF1 levels below or equal to the median 139 ng/ml were considered low.

Results: Low IGF1 was clinically significant. These patients were recognized by high prevalence of hypertension (26% vs. 7.9%, $p=0.001$), overweight (19% vs 6.8%, $p=0.016$) and hypercholesterolemia (71% vs 48%, $p=0.0025$), which resulted in a higher eCVR in these RA patients (7.2% and 3.3%, $p<0.001$). When adjusted by age, low IGF1 group had higher serum IL6 (pg/ml: 2.1[0.2-3.0] vs 0.7[0.1-4.2], $p=0.038$) and ESR (mm/h: 12[7-15.5] vs 5.5[4-9], $p=0.02$), and higher prevalence of MTX monotherapy (56% vs. 39%, $p=0.024$). At prospective follow-up, 12 CVD events were registered. The median age at CVD event was 67 years and disease duration 14 years. Among the new CVD events were 4 ischemic strokes, 3 chronic atrial fibrillations and 2 incidental aorta aneurysms, which all could be viewed as directly related to hypertension. Low IGF1 showed high probability for new CVD events (OR 4.96, [95%CI:1.17-34.2], $p=0.029$). Additionally, low IGF1 group had a significant increase in medication for hypertension (+19.5% vs +4.8%, $p=0.00011$), but not type II diabetes and statins. In a prediction model, a combination of low IGF1 and RA duration>10 years indicated 80.5% specificity for development of new CV events.

Conclusion: We identified low normal levels of IGF1 to be associated with higher prevalence of CVD events in RA patients. Importantly, low IGF1 appeared to be an independent predictor of hypertension in middle-aged female patients.

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FRI0029 DEVELOPMENT OF AN ALGORITHM FOR THE CLASSIFICATION OF CARDIOVASCULAR COMORBIDITY IN RHEUMATOID ARTHRITIS: DATA FROM THE ONTARIO BEST PRACTICES RESEARCH INITIATIVE

Kangping Cui^{1,2}, Mohammad Movahedi³, Claire Bombardier^{2,4,5}, Bindee Kuriya^{3,6}.
¹Western University, London, Canada; ²University Health Network, Toronto, Canada; ³University Health Network, Toronto General Hospital Research Institute, Toronto, Canada; ⁴Institute for Health Policy, Management and Evaluation, Toronto, Canada; ⁵University of Toronto, Medicine, Toronto, Canada; ⁶Mount Sinai Hospital, Rheumatology, Toronto, Canada

Background: Cardiovascular disease (CVD) is increased in rheumatoid arthritis (RA). The ability to accurately identify CVD and its risk factors is important for primary and secondary prevention strategies. RA registries collect comorbidity data, but discordance between physician-reported and patient-reported comorbidities often exists.

Objectives: We aimed to develop an algorithm for the classification of CVD and CVD RF in a representative RA registry.

Methods: Data were collected from the Ontario Best-practices Research Initiative (OBRI), a clinical registry of RA patients followed in routine care in Ontario, Canada. Clinical information, including patient medication profile, was obtained at registry entry, through physician visits and patient telephone interviews. Cardiovascular disease (CVD) was defined as having ≥ 1 of myocardial infarction (MI), coronary artery disease (CAD), cerebral vascular accident (CVA, including transient ischemic attack and stroke), or peripheral arterial disease (PAD). CVD risk factors included hypertension (HTN), dyslipidemia (DLD), diabetes mellitus (DM), and current smoking.

Results: An algorithm for classifying CVD and CVD risk factors was developed including the 2033 subjects with baseline data. At cohort entry, the prevalence of CVD was 5.4% ($n=110$), HTN 670 (32.9%), DLD 401 (19.7%), DM 165 (8.1%), and current smoking 346 (17%). Seventeen (15.7%) subjects were not identified as having CVD by physician-report but were classified as having CVD upon medication review. Discrepancy between physician and patient-reported CVD RF were: 207 for HTN (31%), 291 for DLD (73%), and 22 for DM (13%). Chart review of 55 patients showed sensitivity of 100% for CVD, 78% for HTN, and 42% for DLD classification.

Conclusion: An algorithm for classification of CVD has been successfully developed in a representative RA registry. The discrepancy between physician and patient-reported CVD highlights the importance of utilizing information from multiple sources when classifying comorbidities.

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FRI0030 FEELINGS OF GUILT AND SHAME IN PATIENTS WITH RHEUMATOID ARTHRITIS

BOUSSAA HIBA, Alia Fazaa, Saoussen Miladi, Kmar Ouenniche, Leila Souabni, Selma Kassab, Selma Chekili, Leith Zakraoui, Kawther Ben Abdelghani, Ahmed Laatar. *Mongi Slim Hospital, Rheumatology, Tunis, Tunisia*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease which causes functional disability, pain, and joint destruction. The disease has a major impact on patient's independence, social activities and self-image.

Objectives: The aims of this study were to assess whether RA is associated with increased feelings of shame and guilt, and to examine possible correlates with socio demographic characteristics and disease activity.

Methods: To measure feelings of shame and guilt, in patients with RA (ACR/EULAR 2010), we used the Experience of Shame Scale (ESS) [1] and the Test of Self Conscious Affect- Version 3 (TOSCA-3S) [2].

The ESS is a 25-item questionnaire that assesses the frequency of characterological, behavioral and bodily shame experiences over the past year. Respondents rate each item on a scale ranging from 1 (not at all) to 4 (very much), with higher scores indicating greater shame.

The TOSCA-3S is presented with 11 brief hypothetical scenarios followed by 3 common reactions, which reflect shame, guilt and externalization of blame. Each possible response is rated on a five-point scale from 1(not likely) to 5 (very likely). For the purpose of this study, only the shame and guilt response items were analyzed. Total scores for Shame Self-Talk and Guilt Self-Talk were calculated and compared to the scoring interpretation. A $p<0.05$ was considered significant.

Results: A total of 40 patients with RA were included, 36 women and 4 men, with a mean age of 54.2 years old [25-75]. Nine patients (22%) were illiterate, 42.5% were professionally active and 82.5% were married. The mean disease duration was 12.8 years [3-33], 80% of patients were on prednisone at a daily posology of 7 mg [2.5-12.5], 82.5% were on csDMARDs and 27.5% on bDMARDs. The mean DAS 28 ESR and CRP were respectively 4.3 [1.6-6.9] and 3.6 [1-6.2].

The mean total score of the ESS was 45.3 [27-81] with subscale means of: 19 [12-37] for characterological shame, 19 [10-30] for behavioral shame and 7.4 [4-16] for bodily shame.

For the TOSCA-3S, the mean "shame self-talk Total" score was 33.8 [17-44], and the mean "guilt self-talk Total" score was 48 [37-55], which corresponds to "you often use" for men and "you use an average amount" for women, a shame and guilt self-talk.

A significant correlation was found between disease activity (DAS 28 ESR) and total score of ESS, shame self-talk total score and guilt shame self-talk score ($p=0.000$). A significant correlation was also found between these scores and gender, age, level of education, professional activity and marital status.

Conclusion: Our RA patients experienced general feelings of shame and guilt, which correlate with demographic items and disease activity.