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## Rheumatoid arthritis - clinical aspects: 134. Predictors of joint damage in South Africans with rheumatoid arthritis

Ickinger, C ; Musenge, E ; Tikly, M

**Abstract:** Background: Rheumatoid arthritis (RA) causes progressive joint damage and functional disability. Studies on factors affecting joint damage as clinical outcome are lacking in Africa. The aim of the present study was to identify predictors of joint damage in adult South Africans with established RA. Methods: A cross-sectional study of 100 black patients with RA of >5 years were assessed for joint damage using a validated clinical method, the RA articular damage (RAAD) score. Potential predictors of joint damage that were documented included socio-demographics, smoking, body mass index (BMI), disease duration, delay in disease modifying antirheumatic drug (DMARD) initiation, global disease activity as measured by the disease activity score (DAS28), erythrocyte sedimentation rate (ESR), C reactive protein (CRP), and autoantibody status. The predictive value of variables was assessed by univariate and stepwise multivariate regression analyses. A p value <0.05 was considered significant. Results: The mean (SD) age was 56 (9.8) years, disease duration 17.5 (8.5) years, educational level 7.5 (3.5) years and DMARD lag was 9 (8.8) years. Female to male ratio was 10:1. The mean (SD) DAS28 was 4.9 (1.5) and total RAAD score was 28.3 (12.8). The mean (SD) BMI was 27.2 kg/m<sup>2</sup> (6.2) and 93% of patients were rheumatoid factor (RF) positive. More than 90% of patients received between 2 to 3 DMARDs. Significant univariate predictors of a poor RAAD score were increasing age (p = 0.001), lower education level (p = 0.019), longer disease duration (p < 0.001), longer DMARD lag (p = 0.014), lower BMI (p = 0.025), high RF titre (p < 0.001) and high ESR (p = 0.008). The multivariate regression analysis showed that the only independent significant predictors of a higher mean RAAD score were older age at disease onset (p = 0.04), disease duration (p < 0.001) and RF titre (p < 0.001). There was also a negative association between BMI and the mean total RAAD score (p = 0.049). Conclusions: Patients with longstanding established RA have more severe irreversible joint damage as measured by the clinical RAAD score, contrary to other studies in Africa. This is largely reflected by a delay in the initiation of early effective treatment. Independent of disease duration, older age at disease onset and a higher RF titre are strongly associated with more joint damage. The inverse association between BMI and articular damage in RA has been observed in several studies using radiographic damage scores. The mechanisms underlying this paradoxical association are still widely unknown but adipokines have recently been suggested to play a role. Disclosure statement: C.I. has received a research grant from the Connective Tissue Diseases Research Fund, University of the Witwatersrand. All other authors have declared no conflicts of interest

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Depression Questionnaire was administered at baseline and follow up (when 322 men and 320 women were seen).

**Results:** The mean age of males and females was 64.3 years and 65.6 years respectively. Circulating 25(OH)D concentrations were higher in those attending clinic in summer/autumn compared to those attending in winter/spring ( $p < 0.001$ ). 12.1% men and 17.2% women were vitamin D deficient (concentration  $< 25$  nmol/l) and 45.7% men and 47.0% women had concentrations between 40 and 75 nmol/l. We found no relationship between pain at baseline and circulating 25(OH)D concentration in either sex. Similarly there was no relationship between depression score and vitamin D status. However, women who had the highest circulating 25(OH)D concentrations ( $> 75$  nmol/l) had the highest risk of incident bodily pain (OR 6.31 CI 1.15, 34.7,  $p = 0.034$ ) after adjustment for age, body mass index, season of baseline 25(OH)D and of 4-year assessment, social class, cigarette and alcohol consumption, physical activity, number of co-morbidities, cod-liver oil intake, physician diagnosed osteoarthritis and fracture since aged 45. No such relationships were observed in men.

**Conclusions:** We report an unexpected finding of a positive association between development of bodily pain and vitamin D concentration measured 4 years prior. Although confounding by indication remains a possibility, our results remained after adjustment for age, body mass index, season of measurement, social class, cigarette and alcohol consumption, physical activity, number of co-morbidities, cod-liver oil intake, OA, and osteoporotic fracture; further studies are now indicated to reproduce this finding.

**Disclosure statement:** The authors have declared no conflicts of interest.

### 133. ARTHRITIS HURTS: A STUDY OF HOW ARTHRITIS PAIN AFFECTS PEOPLE LIVING WITH ARTHRITIS IN THEIR EVERYDAY LIFE

Kate Llewelyn<sup>1</sup>, Federico Moscogiuri<sup>2</sup> and Annie Gilbert<sup>3</sup>  
<sup>1</sup>Information, Arthritis Care, London, United Kingdom; <sup>2</sup>Policy and campaigning, Arthritis Care, London, United Kingdom; <sup>3</sup>Arthritis Care, London, United Kingdom

**Background:** Whilst we know pain affects the majority of people living with arthritis in the UK, a user-led arthritis charity wanted to know more about how this pain affects them in their everyday life in order to raise public awareness and take the necessary steps to improve the provision of services in this area. Arthritis is the biggest cause of physical disability in the UK affecting up to 10 million people, including 12,000 children, and accounting for 30% of GP visits. It carries a huge economic as well as human and social cost, estimated at £7 billion annually in terms of lost labour in 2007. It is the most common cause of chronic pain in the UK, with pain being the most common symptom of living with arthritis. An average of 85% of contacts to the charity's helpline are about pain. Around 5,150 people per year received information about pain management via the helpline.

**Methods:** An email was sent directly to 14,776 of the charity's supporters living with arthritis inviting them to take part in the survey. This online survey was also promoted from 24 March to 5 April 2010 to supporters via the charity's website home page, social networking outlets and via its on line discussion forum. A total of 2,263 surveys were analysed.

**Results:** Out of the 2,263 responses collected, 78.7% were female and 89.3% of the participants were white British. 59.7% were aged between 45 and 64 years and 82% were of working age. The results of this survey showed that a majority of respondents are putting up with severe levels of pain on a regular basis. 56.7% stated they would wait until it was 'often unbearable and frequently stops me doing daily activities'. 77% of participants stated their arthritis pain prevents them from sleeping through the night. 57% stated their every day arthritis pain caused them difficulties coping at work. We asked people whether pain caused them difficulty carrying out certain activities. When pain is everyday pain, 50% of people had difficulty getting out of bed, 41% had difficulty making a cup of tea, 58% had difficulty sleeping, 42% having a hug, 49% having sex.

When pain is at its most severe, 62% of people had difficulty getting out of bed, 65% of people had difficulty making a cup of tea, 58% had difficulty sleeping, 65% had difficulty having a hug, 63% having sex.

**Conclusions:** These figures indicate that people have to endure significant limitations in everyday life due to unmanaged pain. Greater awareness of arthritis and the importance of seeking proper medical attention would lead to earlier interventions and therefore mitigate this situation.

**Acknowledgments:** This work has been supported by an educational grant from MSD, by way of the secondment of A K Gilbert, researcher and employee of MSD.

**Disclosure statement:** A.G. has received research support from MSD and is the employer of Annie Gilbert. All other authors have declared no conflicts of interest.

## Rheumatoid arthritis - clinical aspects

### 134. PREDICTORS OF JOINT DAMAGE IN SOUTH AFRICANS WITH RHEUMATOID ARTHRITIS

Claudia Ickinger<sup>1</sup>, Eustasius Musenge<sup>2</sup> and Mohammed Tikly<sup>1</sup>  
<sup>1</sup>Division of Rheumatology, Chris Hani Baragwanath Hospital and University of the Witwatersrand, Johannesburg, South Africa;  
<sup>2</sup>Epidemiology Centre, School of Public Health, University of the Witwatersrand, Johannesburg, South Africa

**Background:** Rheumatoid arthritis (RA) causes progressive joint damage and functional disability. Studies on factors affecting joint damage as clinical outcome are lacking in Africa. The aim of the present study was to identify predictors of joint damage in adult South Africans with established RA.

**Methods:** A cross-sectional study of 100 black patients with RA of  $> 5$  years were assessed for joint damage using a validated clinical method, the RA articular damage (RAAD) score. Potential predictors of joint damage that were documented included socio-demographics, smoking, body mass index (BMI), disease duration, delay in disease modifying antirheumatic drug (DMARD) initiation, global disease activity as measured by the disease activity score (DAS28), erythrocyte sedimentation rate (ESR), C reactive protein (CRP), and autoantibody status. The predictive value of variables was assessed by univariate and stepwise multivariate regression analyses. A  $p$  value  $< 0.05$  was considered significant.

**Results:** The mean (SD) age was 56 (9.8) years, disease duration 17.5 (8.5) years, educational level 7.5 (3.5) years and DMARD lag was 9 (8.8) years. Female to male ratio was 10:1. The mean (SD) DAS28 was 4.9 (1.5) and total RAAD score was 28.3 (12.8). The mean (SD) BMI was 27.2 kg/m<sup>2</sup> (6.2) and 93% of patients were rheumatoid factor (RF) positive. More than 90% of patients received between 2 to 3 DMARDs. Significant univariate predictors of a poor RAAD score were increasing age ( $p = 0.001$ ), lower education level ( $p = 0.019$ ), longer disease duration ( $p < 0.001$ ), longer DMARD lag ( $p = 0.014$ ), lower BMI ( $p = 0.025$ ), high RF titre ( $p < 0.001$ ) and high ESR ( $p = 0.008$ ). The multivariate regression analysis showed that the only independent significant predictors of a higher mean RAAD score were older age at disease onset ( $p = 0.04$ ), disease duration ( $p < 0.001$ ) and RF titre ( $p < 0.001$ ). There was also a negative association between BMI and the mean total RAAD score ( $p = 0.049$ ).

**Conclusions:** Patients with longstanding established RA have more severe irreversible joint damage as measured by the clinical RAAD score, contrary to other studies in Africa. This is largely reflected by a delay in the initiation of early effective treatment. Independent of disease duration, older age at disease onset and a higher RF titre are strongly associated with more joint damage. The inverse association between BMI and articular damage in RA has been observed in several studies using radiographic damage scores. The mechanisms underlying this paradoxical association are still widely unknown but adipokines have recently been suggested to play a role.

**Disclosure statement:** C.I. has received a research grant from the Connective Tissue Diseases Research Fund, University of the Witwatersrand. All other authors have declared no conflicts of interest.

### 135. WHAT ARE THE PREDICTORS FOR OSTEOPOROSIS AT DIFFERENT SITES IN RHEUMATOID ARTHRITIS?

Jonathan Barnes<sup>1</sup>, C. Donnison<sup>1</sup>, M. Scott<sup>1</sup>, Peter Bartholomew<sup>1</sup>, Martin Rynne<sup>1</sup>, Jennifer Hamilton<sup>1</sup>, V. Saravanan<sup>1</sup>, Carol Heycock<sup>1</sup> and Clive Kelly<sup>1</sup>  
<sup>1</sup>Rheumatology, QEHS Gateshead, Gateshead, United Kingdom

**Background:** Osteoporosis is common in patients with rheumatoid arthritis (RA) and is associated with an increased fracture risk. Indeed, RA is recognised as a specific risk factor in the FRAX score calculation. Previous work by our group has shown a high prevalence of osteoporosis in cortical bone using peripheral bone mineral density (BMD) scanning. This was related to disease duration and steroid use. We wished to assess the prevalence of axial osteoporosis in our current rheumatoid population, and to perform multivariate analysis to

calculate which risk factors were predictors for osteoporosis at hip and spine.

**Methods:** We measured BMD at hip and spine using a Hologic Discovery C scanner in 196 patients with RA who were over 50 or who had at least a 10 year history of the disease. We recorded the patients' age, gender, disease duration, disease activity score in 28 joints (DAS28), ESR, presence of erosions, RF and CCP levels, together with all treatment including steroid dose and duration. We calculated the overall prevalence of osteoporosis and performed a multivariate analysis, assuming a linear model for continuous variables, to assess the factors predictive of reduced BMD in individuals.

**Results:** Osteoporosis (T score < -2.5) was present at either hip or spine in 61 RA patients (31%). Multivariate analysis showed that the predictors for decreased BMD at the spine were female gender and CCP positivity, while decreased BMD at the hip was associated with female gender, age and ESR. In addition, use of bisphosphonates was associated with lower BMD at both sites, as would be expected. We also noted a higher than expected number of patients with degenerative spinal disease which reduced the amount of reliable data available at this site.

**Conclusions:** Osteoporosis at hip and/or spine is common in patients with RA over 10 years duration. Bisphosphonate therapy appears to be appropriately targeted. However, there appear to be site specific risk factor profiles for osteoporosis in RA. Disease duration has been previously associated with peripheral bone loss; our present work suggests that disease severity is important in predicting spinal BMD whilst disease activity influences bone density at the hip. Females are at greater risk of osteoporosis at both these sites. Degenerative spinal disease may be more common in RA and this needs to be considered when assessing bone density at this site.

**Disclosure statement:** The authors have declared no conflicts of interest.

### 136. BAFF BINDING RECEPTORS RELATED TO RELAPSE AFTER RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

Inmaculada de la Torre<sup>1,2</sup>, Rita A. Moura<sup>3</sup>, Maria Leandro<sup>1</sup>, Jonathan Edwards<sup>1</sup> and Geraldine Cambridge<sup>1</sup>  
<sup>1</sup>Rheumatology, University College London, London, United Kingdom; <sup>2</sup>Rheumatology, Gregorio Maranon Hospital, Madrid, Spain; <sup>3</sup>Rheumatology Research Unit, Instituto de Medicina Molecular, Lisbon, Portugal

**Background:** Coordinated expression of BAFF binding receptors (BBRs) (BAFF-R, TACI, BCMA) control differentiation of B cells into immunoglobulin (Ig) secreting cells. We have reported that i) BAFF levels rise after B cell depletion with rituximab (RTX) in patients with RA, remaining raised even after B cell return ii) BAFF-R expression in naïve B cells (NB) and memory B cells (MB) is reduced after RTX and related to clinical relapse independently of serum BAFF levels or time to relapse after B cell return iii) Class-switch recombination (CSR) and autoantibody production is also related to clinical relapse after RTX. When B cells differentiate into Ig secreting cells, BAFF-R is lost and BCMA up-regulated. TACI is induced upon B cell activation, being present on most MB. Although expressed on <20% activated (CD86+) NB, TACI is more related to CSR and plasma cell differentiation. BBR expression was therefore investigated in relation to clinical relapse in RA patients after RTX.

**Methods:** Phenotypic analysis of BAFF-R, TACI and BCMA expression on PBMC were performed using combinations of CD19, CD27, CD38 and IgD (% and mean fluorescence intensity-MFI) in normal controls (NC) (n=5) and patients pre (n=10) and after RTX, classified as concordant ie relapsing at B cell return (C-R, n=16), or discordant (relapsing > 3 months after repopulation; D-R, n=10) or non-relapsing after B cell return (D-NR, n=11).

**Results:** Mean % of NB cell BAFF-R+ was significantly lower only in patients relapsing (C-R: 65.3%, D-R: 89.7%) when compared to NC (p=0.027, p=0.026). Percentage and MFI of MB cell BAFF-R+ was significantly lower in all patients when compared to both NC and pre-RTX (%: p<0.05; MFI: p<0.005). In patients relapsing, % NB cell TACI+ tended to be higher in C-R than D-R (23.4% vs 9.9%). All patients pre and after RTX had significantly lower % of TACI+ MB cells when compared to NC (p<0.05). However % of MB cell TACI+ was significantly higher in D-NR when compare to D-R (p=0.001). BAFF-R and BCMA did not always had an inverse correlation in plasma cell populations after RTX. Finally, C-R patients had higher % of plasma cells than D-R and D-NR (16.5% vs 2.06% and 1.85; p=0.03 and p=0.06).

**Conclusions:** Rises in autoantibody levels have been related to clinical relapse after RTX. Modulation of BBR expression permissive to plasma cell formation in C-R patients, associated with an earlier down

regulation of BAFF-R and up regulation of TACI on (presumably activated autoreactive) NB cells may explain clinical relapse closer to B cell return. Normal BAFF-R expression on NB cells in D-NR patients may reduce the chance of becoming Ig-producing cells, thereby lowering the chance of the autoreactive NB population differentiating into autoantibody producing cells. The consequences of disturbed BBR expression on B cell selection and the advancement or inhibition of progression to autoantibody production may help explain timing of relapse after RTX.

**Disclosure statement:** The authors have declared no conflicts of interest.

### 137. DYSREGULATED TOTAL SERUM IMMUNOGLOBULIN LEVELS IN PATIENTS WITH RA: RELATIONSHIPS WITH CLINICAL RESPONSE TO RITUXIMAB

Inmaculada de la Torre<sup>1,2</sup>, Maria Leandro<sup>1</sup>, Johnathan Edwards<sup>1</sup> and Geraldine Cambridge<sup>1</sup>  
<sup>1</sup>Rheumatology, University College London, London, United Kingdom; <sup>2</sup>Rheumatology, Gregorio Maranon Hospital, Madrid, Spain

**Background:** In patients with RA treated with BCDT, IgA levels do not decrease to the same extent or in as many patients as IgM or IgG levels. Preliminary analysis of serum Ig levels in 131 patients in the UCL cohort of patients with RA showed that IgA levels were actually raised in 30 RA patients before treatment and did not always normalize following BCDT. IgG and IgM levels were raised in 29 and 16 patients respectively, normalizing in most after the first cycle of BCDT. In this prospective study we investigated whether levels of Ig isotypes at baseline were associated with clinical pattern of response.

**Methods:** 131 patients with RA treated with RTX were studied. Baseline serum Ig levels, CRP, DAS28, CD19+ve B cell count at baseline, 1, 3 and 5 months after first cycle of rituximab, were collected prospectively. Groups were defined related to baseline total Ig levels: Normal IgA (0.7-4.0 g/L), High IgA (>4.0 g/L), Normal IgG (7.0-16.0 g/L), High IgG (>16.0 g/L), Normal IgM (0.4-2.3 g/L), High IgM (>2.3 g/L). Adequate depletion and B cell repopulation were defined as having <5 or ≥5 CD19+ cells/μl respectively. Mann Whitney U and Wilcoxon tests were performed for independent and paired parameters.

**Results:** All patients were adequately depleted at 1 month. Baseline CRP levels were significantly higher in the High IgA and IgG groups compared with those with normal baseline Igs (p=0.0002; p=0.03 respectively). Minimum CRP levels reached in all groups were significantly lower compared to pre-RTX levels (p<0.0001) but patients starting with High IgA had a significantly higher minimum CRP (p=0.002) and also remained with higher minimum DAS28 when compared to those starting with Normal IgA (p=0.05). After 5 months, patients in the High IgA group had significantly more CD19+ cells (p=0.003) than those with normal baseline IgA and the proportion of patients repopulating at 5 months was also significantly greater in the High IgA group (\*\*p=0.004, Fisher's exact test) (Table 1). Baseline levels of IgM were not correlated with any parameters evaluated.

**Conclusions:** Baseline levels of Ig may be predictive of the pattern of clinical response to rituximab. Patients with initially higher total serum IgA and IgG had significantly higher levels of baseline CRP and those in the High baseline IgA group had higher minimum DAS28 scores after rituximab than those with Normal baseline IgA. In addition, a larger proportion of patients with higher baseline IgA were more likely to have detectable B cells at 3 and 5 months and also had significantly higher numbers of repopulating B cells at five months post rituximab despite successful depletion.

**Disclosure statement:** The authors have declared no conflicts of interest.

TABLE 1.

Baseline Ig Group	Number and % patients with CD19+ cells > 5/μl 3 months after RTX	Number and % patients with CD19+ cells > 5/μl 5 months after RTX
High IgA	9/26 (34.6)	15/23 (65.2)**
Normal IgA	6/44 (13.6)	13/49 (26.5)**
High IgG	4/20 (20.0)	10/17 (58.8)
Normal IgG	8/40 (20.0)	15/44 (34.1)

\*\*P=0.004, Fisher's exact test

### 138. ASSESSMENT OF SYNOVITIS IN RHEUMATOID ARTHRITIS AND THE EFFECT OF ULTRASOUND JOINT COUNTS ON DAS28 VALUES

Louise E. Daniels<sup>1</sup>, Nicola J. Gullick<sup>1,2</sup>, Jonathan D. Rees<sup>1,3</sup> and Bruce W. Kirkham<sup>1,2</sup>

<sup>1</sup>RA Centre, Rheumatology, Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom; <sup>2</sup>NIHR Comprehensive Biomedical Research Centre, Guy's & St Thomas' Hospitals & King's College London, London, United Kingdom; <sup>3</sup>Rheumatology, DMRC Headley Court, Surrey, United Kingdom

**Background:** The DAS28 is a composite measure of disease activity in patients with Rheumatoid Arthritis (RA). Patients with a moderate DAS 28 (3.2-5.1) have ongoing loss of function and continued joint damage. Current UK treatment guidelines require DAS 28 >5.1 to qualify for anti-TNF therapy. Ultrasound (US) assessment of joint swelling is more sensitive than clinical examination, and clinical joint counts may have moderate interobserver variability. We conducted a study to investigate patients for subclinical synovitis and evaluate effects on DAS28 scores and potential treatment options.

**Methods:** 20 patients with RA had 28 joint counts performed by a consultant and a trainee rheumatologist. 10 MCP and PIP joints (total 400 joints) were scanned in two planes with grey scale and power Doppler US by an independent assessor. Agreement between clinical examinations and US was assessed by intraclass correlation coefficients (ICC) and percentage absolute agreement. DAS28 scores were calculated using both standard joint counts, then substituting the US swollen joint count or Doppler count for clinical swollen (SJC) or tender joint counts (TJC).

**Results:** ICC for SJC and TJC were 0.50 and 0.90, with high agreement of DAS28 scores (ICC 0.93) between the two observers. Exact agreement was seen in 187/240 joints (68%) for swelling and 201/240 joints (84%) for tenderness. US detected more synovitis and joint effusion (349/380 joints, 92%) than clinical swelling (87/380 joints, 23%) ( $p < 0.001$ ). It also detected more vascularity on PD (224/380 joints, 59%), compared to clinical tenderness (94/380 joints, 24%) ( $p = 0.0012$ ). There were no significant correlations between clinical and US scores. The mean DAS 28 based on clinical scores was 4.1 (SD 1.3). This increased to 4.9 (SD 1.3) ( $p < 0.001$ ) when US swelling was substituted for SJC. The mean DAS 28 increased further and significantly to 5.7 (SD 0.8) ( $p < 0.001$ ) when US vascularity was also substituted for TJC.

**Conclusions:** The consultant detected significantly more swelling than the trainee, but this had little effect on the DAS 28, due to a low weighting of swelling in the score. US detected significantly more synovitis and substitution of US derived counts had a significant effect on the DAS28. Four additional patients (29%) had a DAS28 >5.1 based on US swelling assessments, and an additional 9 patients had a DAS28 >5.1 if the Doppler count was additionally substituted for the clinical tender joint count. We suggest that a large number of RA patients with moderate DAS 28 scores have significant ongoing disease activity. This supports the recent BSR guidance that biologic therapies should be available to patients with moderate disease activity.

**Disclosure statement:** B.K. has served on advisory boards for Abbott, Bristol-Myers Squibb, Centocor, Pfizer, Roche and UCB, and has received research grants from Abbott, Centocor and Pfizer. All other authors have declared no conflicts of interest.

TABLE 1. Effects of US joint counts on DAS28 scores

DAS28	<2.6	2.7-3.1	3.2-5.1	>5.1
DAS1 (TJC, SJC)	2	3	10	4
DAS2 (US synovitis count, TJC)	1	0	10	8
DAS3 (US synovitis + PD counts)	0	0	6	13

### 139. A COMPARISON OF 3D AND 2D ULTRASOUND IN THE DETECTION OF SYNOVITIS, EROSIONS AND POWER DOPPLER ACTIVITY IN RHEUMATOID ARTHRITIS

Louise E. Daniels<sup>1</sup>, Nicola J. Gullick<sup>1</sup>, Bruce W. Kirkham<sup>1</sup> and Jonathan Rees<sup>1,2</sup>

<sup>1</sup>Department of Rheumatology, Guy's and St Thomas' Hospitals, London, United Kingdom; <sup>2</sup>DMRC Headley Court, Surrey, United Kingdom

**Background:** Rheumatoid Arthritis (RA) is a common chronic, symmetrical inflammatory polyarthritis characterised by joint swelling resulting in damage and reduced physical function. Two-dimensional (2D) Ultrasound (US) is a highly sensitive and specific tool which has greatly assisted the diagnosis and determination of clinical activity and

structural damage in RA. 3D US is an emerging imaging modality that has yet to be studied systematically in relation to arthritis of small joints in RA. We wanted to determine the utility of 3-D US in comparison to 2-D US in established RA patients in terms of assessment of synovitis and structural damage.

**Methods:** 20 patients with a diagnosis of RA were recruited. All 10 MCP and 10 PIP joints were scanned with a 2D and 3D probe. This gave a total of 400 joints in the 20 patients. Images were scored using standard semi-quantitative systems for three criteria; synovitis and joint effusion, power Doppler (PD) and erosions.

**Results:** Erosions were detected in 70% of joints with 3D US compared to 47% with 2D US ( $p = 0.009$ ). Furthermore 3D US demonstrated greater severity of erosions than was demonstrated in 2D US. 3D US detected synovitis and joint effusions in 96% of joints compared with 91% with 2D US ( $p = 0.046$ ). It was not possible to accurately detect synovial vascularity using 3D PDUS due to movement artefact from the 3D probe.

**Conclusions:** 3D US is more sensitive than 2D US for the detection of synovitis, joint effusions and erosions than 2D US. 3D US may have a role in confirming disease activity and structural damage in RA over and above that of 2D US. Further work is required to optimise the PD feature of 3D US.

**Disclosure statement:** B.K. has served on advisory boards for and received research support from Bristol-Myers Squibb, Pfizer, Abbott, Centocor, Roche and UCB. All other authors have declared no conflicts of interest.

### 140. CARDIOVASCULAR DISEASE IN RHEUMATOID ARTHRITIS IS PREDOMINANTLY DRIVEN BY TRADITIONAL CARDIOVASCULAR RISK FACTORS

Ian C. Scott<sup>1</sup>, Deborah Johnson<sup>2</sup>, David L. Scott<sup>3</sup> and Gabrielle Kingsley<sup>2</sup>

<sup>1</sup>Rheumatology, Guy's and St Thomas' NHS Trust, London, United Kingdom; <sup>2</sup>Rheumatology, University Hospital of Lewisham, London, United Kingdom; <sup>3</sup>Rheumatology, King's College Hospital, London, United Kingdom

**Background:** The excessive cardiovascular (CV) risk in rheumatoid arthritis (RA) is well known. It reflects both the effects of traditional CV risk factors and systemic inflammation in RA. Currently rheumatologists mainly focus on reducing systemic inflammation in RA, which is known to reduce atherosclerosis. Although reducing conventional risks like hypertension may be equally important they are not always assessed by rheumatologists. We therefore evaluated the overall management of CV risk factors in RA patients and examined the relative contribution of conventional risk factors to CV morbidity.

**Methods:** We cross-sectionally studied 305 RA patients attending specialist clinics in South East London. We assessed RA characteristics, screening/treatment of CV risk factors (hypertension, hyperlipidaemia, diabetes, obesity, smoking) and RA/CV treatments. Atherosclerosis was defined as a previous CV event. Factors associated with atherosclerosis were evaluated using binary logistic regression.

**Results:** The patients comprised 81% females of median age 60 years and median disease duration 8 years. Disease activity was moderate (mean DAS28 3.45). 28 (9%) had a previous CV event. CV risk factors were common: hypertension (57%), hyperlipidaemia (30%), diabetes (11%), ex/current smokers (52%) and obesity (31%). Screening for risk factors was inadequate: only one third of patients without known diabetes or hyperlipidaemia had ever had fasting glucose or lipid levels performed. CV risk factors were undertreated: 52% of patients on anti-hypertensives had ongoing hypertension. Hyperlipidaemia and hypertension were significantly associated with atherosclerosis (Table 1). Indirect markers of long-term inflammation - disease duration and erosions - were associated with atherosclerosis to a lesser extent. Hypertension (OR 4.3, 95%CI 1.1-16.8) and disease duration (OR 1.1, 95%CI 1.0-1.1) retained their significance in a multivariate model that did not include hyperlipidaemia (as statin use in CV events may be independent of lipid status).

**Conclusions:** Although chronic inflammation contributes to atherosclerosis in RA, hyperlipidaemia and hypertension are dominant factors. Despite this association CV risk factors were insufficiently screened for and under treated in this population. We recommend rheumatologists should take responsibility for CV risk factor assessment. Once identified they can be treated in primary care.

**Disclosure statement:** The authors have declared no conflicts of interest.

TABLE 1. The significant associations between clinical characteristics and atherosclerosis

Characteristic	Univariate Analysis P-value	Multivariate Analysis P-value	Univariate Logistic Regression-Odds Ratio (95% CI)
Age	0.002	0.682	1.05 (1.02, 1.09)
Erosions	0.056	1.000	2.53 (0.98, 6.52)
Disease Duration	0.000	0.002	1.09 (1.05, 1.13)
Non-Steroidal Anti-Inflammatory Drugs	0.032	0.209	0.20 (0.47, 0.87)
Leflunomide	0.015	0.117	3.49 (1.27, 9.59)
Hypertension	0.004	0.038	4.85 (1.63, 14.4)
Hyperlipidaemia	0.000	–	19.1 (6.39, 57.0)
Ex-Smoker	0.017	0.242	2.98 (1.21, 7.32)

#### 141. PERSISTING REMISSION IS ESSENTIAL TO ACHIEVE LOW HAQ SCORES IN RHEUMATOID ARTHRITIS

Margaret H. Ma<sup>1,2</sup>, Andrew P. Cope<sup>2</sup>, David L. Scott<sup>1</sup> and Bruce W. Kirkham<sup>2</sup>

<sup>1</sup>Rheumatology, King's College Hospital, London, United Kingdom;

<sup>2</sup>Rheumatology, Guy's and St Thomas' Hospital, London, United Kingdom

**Background:** Remission has become the treatment target in RA. Goal directed therapy (GDT) targeting remission has the propensity to reduce disability and minimise radiographic progression. However, the relative benefits of sustained over intermittent remission are uncertain. There is also limited data about those patients most likely to achieve sustained remission. We addressed both these questions using real life data collected in a clinical practice setting.

**Methods:** We examined the frequency, predictors and impact of remission in prospectively collected routine practice data. The dataset comprised of demographics descriptors, disability (HAQ), disease activity (DAS28), C-reactive protein (CRP) and Rheumatoid Factor. DAS28 < 2.6 was used as the definition of remission. Sustained remission is defined as persistent remission over 4 consecutive visits. One-way ANOVA analysis and Spearman's correlation were used to assess the relationship of HAQ and disease activity and logistic regression analysis was used to evaluate the predictors of sustained remission.

**Results:** We studied 316 RA patients followed over 4 consecutive visits. 249 (79%) were female and their mean age was 56 years (SD 14). 174 patients (55%) were rheumatoid factor positive, 32 patients (10%) had nodules and 133 patients (42%) had erosions on plain film x-rays. 45% of patients achieved remission at some point during the follow-up period. 57 (18%) of patients were in remission at 1 time point (point remission), 54 (17%) were in remission over 2-3 time points (intermittent remission) and 31 (10%) of patients were in sustained remission. Average HAQ and average DAS across the 4 visits were highly correlated (Spearman's R=0.54) with no evidence of a floor effect. Patients in remission achieved lower HAQ scores than patients with active disease and this effect was greater with increasing length of remission. Patients in sustained remission achieved the lowest HAQ scores (Table 1). This effect was persistent over time. Multivariate logistic regression showed initial tender joint counts (OR 0.51, 95% CI 0.29 - 0.93) and ESR (OR 0.81, 95% CI 0.70 - 0.93) were the key predictors of sustained remission.

**Conclusions:** Despite using GDT approach, only 10% of patients achieved sustained remission. This was predicted by initial tender joint count and ESR. Low HAQ scores are associated with remission, but sustained remission is vital to minimise HAQ. As sustained remission should be the ultimate treatment goal, the ideal treatment regime still needs to be determined.

**Disclosure statement:** The authors have declared no conflicts of interest.

TABLE 1. Relationship between remission and HAQ over the consecutive visits.

	Mean HAQ (s.d.)			
	Visit 1	Visit 2	Visit 3	Visit 4
Persistent Active disease	1.52 (0.70)*	1.52 (0.67)*	1.57 (0.06)*	1.52 (0.07)*
Point remission	1.07 (0.18)*	1.10 (0.10)*	1.17 (0.11)*	1.16 (0.10)*
Intermittent remission	0.85 (0.11)*	0.69 (0.10)*	0.74 (0.10)*	0.73 (0.10)*
Sustained remission	0.46 (0.09)*	0.42 (0.10)*	0.45 (0.14)*	0.45 (0.10)*

\*ANOVA: p < 0.001 between different disease activity groups.

#### 142. DO WE NEED SAME-DAY ESR FOR DAS-28 MEASUREMENT?

Sven Brode<sup>1</sup>, Muhammad K. Nisar<sup>2</sup> and Andrew J. Östör<sup>2</sup>

<sup>1</sup>School of Clinical Medicine, University of Cambridge, Cambridge, United Kingdom; <sup>2</sup>Rheumatology Clinical Research Unit, Addenbrooke's Hospital, Cambridge, United Kingdom

**Background:** The Disease Activity Score (DAS-28) is the most widely used composite index of disease activity in Rheumatoid Arthritis (RA). The components include the number of swollen and tender joints, erythrocyte sedimentation rate (ESR) and visual analogue scale (VAS). Serial measurements of the DAS-28 are strong predictors of physical disability and radiological progression, and can sensitively discriminate between high and low disease activity. National Institute of Health and Clinical Excellence recommends the use of DAS-28 to initiate and monitor biologic therapy for RA. In clinical practice, rheumatologists have been reluctant to calculate the DAS-28 without a same-day ESR leading to unnecessary delay in adjusting targeted therapy. The aim of this prospective study was to assess whether ESR blood samples taken prior to the clinic appointment were adequate to accurately assess disease activity using DAS-28.

**Methods:** Patients with RA (N=130) attending rheumatology outpatient clinics at Addenbrooke's Hospital were selected and assessed at baseline. Seventy three participants, mean age 61.8 years (range 20-85yr) and disease duration of 12.0 years (range 0.1-40yr) completed the study. The tender and swollen joints were counted and the global disease activity was assessed using a VAS. Blood samples were collected for the ESR on the day of the appointment. ESR results up to six months prior were obtained and used for comparison.

**Results:** Comparing the same-day ESR versus pre-recorded ESR (range 6-190 days, mean interval=47 days) showed a statistically significant reduction in the same day ESR (K=0.88 mm, CI95% 0.79-1.07 mm, student t test, p<0.01). However, this small difference in ESR did not significantly alter the DAS-28 score which remained strongly linearly correlated. Changes in the ESR were not significantly associated with the other clinical parameters used in the DAS-28 score (p=0.157). In addition, any differences between ESR pairs were not correlated with the overall DAS-28 score. Time-dependent comparison over a six month period showed a difference in DAS-28 of less than +/- 0.6 using even up to three months old ESR results.

**Conclusions:** Our results indicate that in clinical practice changes in DAS-28 due to an "out-of-date" ESR are minimal. The difference in ESR values over a period of up to three months have no clinically significant contribution to variations in DAS-28, especially in the absence of any preceding changes in RA management. A decision to adjust treatment may therefore be confidently made using latest ESR for calculating DAS-28 even if ESR sample was not acquired during clinic appointment.

**Disclosure statement:** The authors have declared no conflicts of interest.

#### 143. ACHIEVING REMISSION DURING GOAL DIRECTED THERAPY IMPROVES FUNCTIONAL OUTCOME OF RA IN ROUTINE PRACTICE

Nicola J. Gullick<sup>1,2</sup>, Stephen P. Oakley<sup>1,3</sup>, Jonathan D. Rees<sup>1,4</sup>, Tim Jones<sup>1,4</sup>, Alan Mistlin<sup>1,4</sup>, Gabriel S. Panayi<sup>1,2</sup> and Bruce W. Kirkham<sup>1,2</sup>

<sup>1</sup>RA Centre, Rheumatology, Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom; <sup>2</sup>NIHR comprehensive Biomedical Research Centre, Guy's & St Thomas' Hospitals & King's College London, London, United Kingdom; <sup>3</sup>Rheumatology, Royal Newcastle Centre, Newcastle, NSW, Australia; <sup>4</sup>Rheumatology, DMRC Headley Court, Surrey, United Kingdom

**Background:** Recent EULAR guidelines recommend that RA patients should be treated to a target of remission, but there is little data from routine practice to suggest that this benefits patients. The RA Centre at Guy's & St Thomas' has used this strategy aiming for DAS28 remission for all patients with RA since 2005.

**Methods:** We performed a longitudinal cohort study involving all patients attending the RA Centre. DAS28 and HAQ are collected at each visit. Baseline and follow up at years 1, 2 and 3 have been included in this analysis. All eligible patients were included in the analysis. Comparisons were made between yearly timepoints. P values less than 0.05 were considered statistically significant.

**Results:** 3 year follow up data were available for 281 patients, with baseline visits occurring between 2005 and 2007. A variety of therapies were used, with increasing numbers of patients receiving biologic therapies during the follow up period, and reduced systemic

steroids. Increasing numbers of patients achieved remission or low disease activity during follow up with statistically significant improvements in DAS28 at all time points vs. baseline (Table 1). For the whole group, there was no significant change in HAQ. Of the 228 patients with active disease (DAS28  $\geq$  2.6) at baseline, 119 achieved remission at least once during follow up. These patients had a small but significant improvement in HAQ from baseline to year 3 (median 1.25 vs. 1.0  $p = 0.001$ ). Patients in remission at baseline generally remained in remission and had stable lower HAQ values over three years.

**Conclusions:** Routine use of the DAS28 to guide changes in therapy improves disease activity and maintains functional capacity in an unselected group of patients with established RA. In addition, patients who achieve remission for even short periods had improved function. This data supports the use of a goal directed strategy with a target of DAS28 remission for patients with established RA in routine practice. Achieving low DAS28 states is a relevant goal to prevent functional decline. We suggest that increasing loss of function is another significant adverse outcome of patients with even moderate disease activity, and supports the use of more aggressive therapy in this group.

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TABLE 1. Follow-up clinical data

	Baseline	Year 1	Year 2	Year 3
DAS28, median (IQR)	4.0 (1.3)	3.3 (2) $\$$	3.2 (2.1) $\phi$	3.1 (2.2) $\phi$
Activity				
Remission n (%)	64 (22.8)	82 (29.2) $\phi$	89 (31.7) $\$$	90 (32) $\phi$
LDAS n (%)	35 (12.5)	51 (18.1)	50 (17.8)	55 (19.6)
low MDAS n (%)	47 (16.7)	56 (19.9)	40 (21.7)	43 (18.5)
high MDAS n (%)	77 (27.4)	50 (17.8)	47 (16.7)	46 (16.4)
HDAS n (%)	58 (20.6)	47 (16.7)	40 (13.9)	43 (15.3)
Patient global score, mean (s.d.)	41.8 (27.4)	39.4 (27.3)	36.1 (25.8)	36.8 (25.4)
Pain VAS, mean (s.d.)	40.6 (27.9)	38.5 (27.4)	36.3 (24.6)	38.6 (26.3)
ESR, mean (s.d.)	25.6 (21.8)	24.2 (19.6)	22.0 (18.6) $*$	19.6 (16.7) $\phi$
HAQ, median (IQR)	1.35 (0.9)	1.32 (0.9)	1.27 (0.8)	1.25 (0.9)

\*  $p < 0.05$ ,  $\$ p < 0.01$   $\phi p < 0.001$

#### 144. INFliximab INFUSION THERAPY IN INFLAMMATORY ARTHRITIS: ASSESSMENT OF THE ACCELERATED INFUSION PROTOCOL IN COMPARISON TO THE STANDARD INFUSION APPROACH

Yasser El Miedany<sup>1</sup> and Deborah Palmer<sup>1</sup>

<sup>1</sup>Rheumatology, Darent Valley Hospital, Dartford, United Kingdom

**Background:** Objectives: To assess the safety and prevalence of infusion reactions in patients suffering from inflammatory arthritis receiving infliximab via an accelerated infusion protocol in comparison to the standard infliximab infusions (over 2-hour period). Also to identify factors that may increase risk of an infusion reaction.

**Methods:** This was a retrospective study examining patients with inflammatory arthritis receiving infliximab via the accelerated infusion protocol (first four infusions over 2 h, with 2 h of monitoring, the next five infusions over 1 h, and subsequent infusions over 30-60 min) in comparison to the standard infliximab infusions administered over minimum of 2 hours and patients are monitored for a further 2 hours. Patients' notes and prescription sheets were reviewed. Number of patients who had to stop infliximab infusions due to allergic reactions was recorded. Also the consumption of hydrocortisone and anti-histamine injections was recorded. Disease characteristics including rheumatoid factor and ANA were recorded in both groups and compared.

**Results:** 112 patients received the accelerated protocol in comparison to 139 patients treated using the standard infusion protocol. There was a significant increase in infusion related reactions in the accelerated infusions group 43/112 received anti-allergic therapy, in comparison to 29/139 in the second group ( $p < 0.01$ ). In the accelerated infusion group 9/112 patients had to stop their infliximab infusions permanently due to allergic reactions that could not be treated medically, in comparison to none in the second group ( $p < 0.001$ ). The prevalence of allergic reactions among the first group who received the accelerated infusion protocol was, 16/43 had mild reaction, 24/43 had moderate reactions and 3/43 had delayed hypersensitivity. In contrast, in the standard infusion patients group 18/29 had mild reactions whereas 11/29 had moderate reactions. No body in the standard infusion group developed delayed hypersensitivity reactions ( $p < 0.01$ ) No differences in disease characteristics or serology were associated with the

development of an infusion reaction. There was no significant difference in adverse effects between patients receiving one or several infusions.

**Conclusions:** There was a significant increase in the prevalence of allergic reactions and use of anti-allergic injection therapy in the patients who received the fast infliximab infusions. The prevalence of allergic reactions among the standard infusion group agrees with the data published earlier about the safety of infliximab infusion therapy. Infusion allergic reaction varied in symptoms and duration, however, it was not related to the number of infusions the patient might have. This leaves every patient prone to allergic reactions at any time. Speeding the infusion therapy was the main factor that may increase risk of an infusion reaction.

**Disclosure statement:** The authors have declared no conflicts of interest.

#### 145. RENAL INVOLVEMENT IN RHEUMATOID ARTHRITIS AND JUVENILE IDIOPATHIC ARTHRITIS

Ramanathan Porkodi<sup>1</sup> and Panchapakesa Rajendran<sup>1</sup>

<sup>1</sup>Rheumatology, Madras Medical College, Chennai, India

**Background:** Haematuria and proteinuria in RA, JIA can occur independent of drugs or urological disorders. This can be due to a primary lesion associated with RA or due to amyloidosis. This study was conducted to assess the renal involvement in RA and JIA.

**Methods:** During the period 1997-2010, patients with RA and JIA who had symptoms of renal involvement, such as oliguria, haematuria, leg oedema were included in the study.

Details of drug therapy were noted. Urine analysis, 24 hours urinary protein, urea, creatinine, RF, ANA, C3, C4 levels, USG abdomen were done. Renal biopsy for light microscope and immunofluorescence studies was done by a nephrologist.

**Results:** 12 patients with RA, 4 patients with JIA had renal involvement. The rheumatoid group consisted of 11 females and 1 male; while all the JIA patients were males. 3 JIA patients had systemic onset, one had polyarticular RF negative onset. Mean age at the time of inclusion in the study was 39.33 years (range 22-58 years) for RA and 19.75 years (range 17-25 years) for JIA patients. Mean duration of arthritis before the onset of renal involvement was 6.52 years (3 months-15 years) in RA and 11.25 years (7-15 years) in JIA.

Renal biopsy in RA patients showed membranous nephropathy in 5 (41.66%) diffuse mesangial proliferation in 4 (33.33%), IgA nephropathy in 2 (16.66%), crescentic glomerulo nephritis in 1 (8.33%). In JIA 1 patient had membranous nephropathy (25%), 3 had amyloidosis (75 %).

In RA: Membranous Nephropathy in 5 females. One had been on d.pencillamine, stopped 3 years before renal involvement. All had nephrotic proteinuria, no haematuria, 2 had hypertension. Diffuse mesangial proliferation in 3 females, 1 male. 2 patients had been on d.pencillamine, stopped 2 and 3 years respectively before renal involvement. One had hypertension, 3 had nephrotic proteinuria, 1 non-nephrotic proteinuria, 3 had microscopic haematuria. IgA nephropathy in 2 females. One was on parenteral gold, stopped 3 years before renal involvement. Both had non-nephrotic proteinuria, one had macro haematuria, one micro haematuria. Crescentic glomerulo nephritis in one female patient who presented with oliguria, macro haematuria, no nephrotic proteinuria, elevated urea and creatinine.

In JIA Amyloidosis: 3 systemic onset JIA had nephrotic proteinuria. Membranous Nephropathy: One JIA patient with polyarticular RF negative onset had nephrotic proteinuria.

**Conclusions:** Membranous nephropathy was the commonest lesion in RA followed by diffuse mesangial proliferation and IgA nephropathy. Crescentic glomerulo nephritis occurred in one patient. In JIA amyloidosis was the most common lesion while one patient had membranous nephropathy. These lesions seemed to be independent of drug therapy and should be due to chronic inflammation of the rheumatoid disease itself.

**Disclosure statement:** The authors have declared no conflicts of interest.

#### 146. THE SWINDON RA FOOT AND ANKLE QUESTIONNAIRE: IS A PICTURE WORTH A THOUSAND WORDS?

Rosemary Waller<sup>1</sup>, Lyn Williamson<sup>1</sup>, David Collins<sup>1</sup>, Elizabeth Price<sup>1</sup> and Maria J. Juarez<sup>1</sup>

<sup>1</sup>Rheumatology, Great Western Hospital, Swindon, United Kingdom

**Background:** Despite increased awareness of the high prevalence and significance of foot and ankle problems in Rheumatoid Arthritis (RA), feet remain a neglected area and provision of care a 'Cinderella'

service in many NHS Trusts. Reasons may include the perception that feet are difficult to assess and foot and ankle is not included in the standard DAS28 score. Currently available tools screening for foot problems are either not freely available, not specific for RA or are lengthy to complete.

**Methods:** We designed a short, simply worded questionnaire to screen for foot and ankle problems in rheumatology outpatients. Key features are 10 short questions on 1 side of A4 covering the domains of symptoms, function, disability and previous intervention. The unique feature of the questionnaire is the inclusion of pictures of dorsal, plantar and lateral views of both feet. The questionnaire was piloted and modified after an anonymous survey of 448 patients at our institution in December 2009. All RA patients on our database were sent the questionnaire and invited to attend clinic for a detailed foot and ankle assessment. Each question was answered yes or no: yes score 1; no score 0; maximum score 10. Patients assessed in clinic were scored out of 10 using the same parameters as the questionnaire. The picture was reviewed at the end of the consultation and scored as 'accurate', 'not accurate' or 'not completed'. Any intervention (including injection, orthotics or surgical review) arranged as a result of the clinic was documented.

**Results:** 597 questionnaires were sent, 301 returned and 137 patients were seen in clinic; 69% female; median age 62; mean RA duration 14 years (range 1 - 40 years). There was good correlation between the postal questionnaire score, the score assigned at clinic ( $r=0.63$ ) and the Manchester foot score (MFS) ( $r=0.65$ ). Neither score correlated with other disease outcome measures used to assess RA, including DAS28, Health Assessment Questionnaire, Overall Status in Rheumatoid Arthritis & Hospital Anxiety & Depression scores.

96 (75%) patients completed the picture. Those who did had higher scores and 73% corresponded well to clinical findings. 124 (91%) patients had at least one foot or ankle problem: MTP synovitis (17%); peroneal and tibialis posterior tendonopathies (22%); hallux valgus (38%) and callosities (18%) were the most common. 45% of patients received an intervention as a result of their clinic review. Those requiring intervention had a trend towards a higher score.

**Conclusions:** The Swindon RA Foot and Ankle Questionnaire was quick to complete, did not add to consultation length and correlated well with the MFS. Lack of association with other standard RA outcome measures suggests that relying on measures such as DAS28 alone may miss clinically important foot pathology. The picture was a useful complement to the questionnaire. This simple screening tool used regularly in clinic could aid early identification and treatment of RA foot and ankle problems.

**Disclosure statement:** The authors have declared no conflicts of interest.

#### 147. TOWARD UNIFYING FUNCTIONAL DISABILITY MEASUREMENT: INTERCONVERSION OF HAQ AND THE COMBINED INFLAMMATORY ARTHRITIS QUESTIONNAIRE FOR FUNCTIONAL DISABILITY SCALES

Yasser El Miedany<sup>1,2</sup>, Maha El Gaafary<sup>3</sup>, Sally Youssef<sup>1,2</sup> and Deborah Palmer<sup>1</sup>

<sup>1</sup>Rheumatology, Darent Valley Hospital, Dartford, United Kingdom;

<sup>2</sup>Rheumatology and Rehabilitation, Ain Shams University, Cairo, Egypt; <sup>3</sup>Community, Environmental and Occupational Medicine, Ain Shams University, Cairo, Egypt

**Background:** The combined inflammatory arthritis questionnaire for functional disability (CIAQ-Fn) and quality of life was recently published [1] and included as part of the multidimensional PROM questionnaire [2]. In comparison to the standard HAQ, the new questionnaire for functional disability includes 10-items scale that is easier than the HAQ to use and score. However, HAQ remains the standard and most common questionnaire to be used in standard practice. Objective: To compare: 1. the ability of the HAQ and CIAQ-Fn disability questionnaires to perform in standard clinical practical setting, 2. the Change in HAQ and CIAQ-Fn disability scores over time and 3. the possibility of interconversion of HAQ and CIAQ-Fn disability scales.

**Methods:** 562 RA patients who received DMARD(s) therapy for their inflammatory arthritis over 6-months period were included in this work. The HAQ and CIAQ-Fn questionnaires were completed simultaneously by every patient whilst waiting for their assessment in the rheumatology clinic once at baseline before starting their DMARDs therapy and the other time was after 6-months of treatment. The comprehensibility of both questionnaires was assessed using VAS (0-100). The ability of the HAQ and CIAQ-Fn to perform in a standard clinical practice setting over a 6-month period was compared. Linear regression for prediction of HAQ from CIAQ-Fn disability has been carried out too.

**Results:** At the start of therapy, the scales were so closely allied and have mean scores that differed by only 0.02 units (HAQ score was (1.50) and the CIAQ-Fn score was (1.52). There was no significant difference on assessment of the comprehensibility of both questionnaires ( $p > 0.05$ ). Effect sizes were calculated for the before-after difference for the HAQ and CIAQ-Fn. The effect size for the CIAQ-Fn was 23.9 (95% confidence interval [95% CI] 19.4-28.4). The effect size for the HAQ was 24.8 (95% CI 20.5-29.1). These differences were not significant ( $P < 0.216$ ). Linear regression described the relationship between variables by the regression intercept and coefficient. For the current study, the intercept was ranging between 0.05 and 0.17 and the regression coefficient was 0.98 with a standard error of 0.01. Based on the linear regression for prediction:  $Y$  (CIAQ) =  $0.172 + 0.912$  (X) HAQ.

**Conclusions:** Assessment of HAQ and CIAQ-Fn disability in the standard clinical practice revealed that both questionnaires are applicable and that it is relatively easy to substitute one scale for the other. The large sample size of this work as well as the strong relationship between the HAQ and the CIAQ-Fn provide assurance of the accuracy and reliability of the process of score inter-conversion from the HAQ to the CIAQ-Fn and from the CIAQ-Fn to the HAQ.

**Disclosure statement:** The authors have declared no conflicts of interest.

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#### 148. A CONTROLLED PILOT ASSESSMENT OF THE UTILITY OF VISUAL FEEDBACK IN THE TREATMENT OF EARLY RHEUMATOID ARTHRITIS

Yasser El Miedany<sup>1,2</sup>, Maha El Gaafary<sup>3</sup> and Deborah Palmer<sup>1</sup>

<sup>1</sup>Rheumatology, Darent Valley Hospital, Dartford, United Kingdom;

<sup>2</sup>Rheumatology and Rehabilitation, Ain Shams University, Cairo, Egypt; <sup>3</sup>Community, Environmental and Occupational Medicine, Ain Shams University, Cairo, Egypt

**Background:** Visual feedback has contributed in the management of neuromuscular and psychiatric disorders, however, it has not yet been applied in rheumatology. Visual feedback is a relatively new tool that enables the patients to visualize and monitor a real-time change of their disease activity parameters as well as the patient's reported outcome measures. Integrating electronic data recording in the standard rheumatology clinical practice made visual feedback possible. Objective: To evaluate the feasibility of using the visual feedback in patients with early inflammatory arthritis (EA) and how ubiquitous computing technology can improve the patients' compliance and adherence to therapy.

**Methods:** This was a double-blind randomized controlled study, which included 111 patients diagnosed to have EA according to the new ACR/EULAR criteria. All patients received DMARDs therapy and were monitored over the period of 1-year. By the 6th month of treatment, the patients were randomly allocated to an active group (55 patients) to who the visual feedback (visualization of the charts showing the disease progression) was added to their management protocol, and a control group (56 patients) who continued their routine management. The patients were monitored for another 6-months period. All the patient's disease activity parameters, patient reported outcome measures (PROMs), medications and co-morbidity scores were recorded using the EROMIA software [1]. Primary outcome was the patients' adherence to their medications; change in disease activity score (DAS-28) and PROMs. Secondary outcome was the outcome of a questionnaire completed by every patient in both the active group and control group (using VAS) by the end of 1-year of management, to rate the patient's perspective regarding their condition and treatment.

**Results:** The visual feedback provided a significant reduction of disease activity parameters as well as improvement of the patients' adherence to anti-rheumatic therapy ( $p < 0.01$ ). Also stopping the DMARDs therapy because of intolerance was significantly less in the active group. The improvement of disease activity parameters was associated with improvement in functional disability and quality of life scores. Mean changes in disease parameters showed no significant differences at 3 and 6 months of therapy but differences were



statistically significant at 12 months follow up ( $p < 0.01$ ). Medication compliance was significantly correlated with changes in all measured disease parameters

**Conclusions:** By recording and monitoring disease activity electronically and introducing visual feedback therapy into clinical practice, a new experience can be created. Visual feedback enabled the patients to see how they are doing regarding their disease activity and helped to optimize their adherence to their treatment. Visual feedback had a positive and significant impact on the disease activity control.

**Disclosure statement:** The authors have declared no conflicts of interest.

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#### 149. SIX-YEAR OUTCOME OF EARLY ARTHRITIS CLINIC: IMPLEMENTATION OF THE MATRIX MODEL FOR THE PREDICTION OF RAPID RADIOGRAPHIC PROGRESSION AND COMMENCING BIOLOGIC THERAPY

Yasser El Miedany<sup>1</sup>, Maha El Gaafary<sup>2</sup> and Deborah Palmer<sup>1</sup>  
<sup>1</sup>Rheumatology, Darent Valley Hospital, Dartford, United Kingdom;  
<sup>2</sup>Community, Environmental and Occupational Medicine, Ain Shams University, Cairo, Egypt

**Background:** The current paradigm for early arthritis suggests that the inflammatory process is at its peak in the first few years, leading to erosive joint damage and functional disability. Identifying patients with RA at high risk of rapid radiographic progression (RRP) is critical for making appropriate treatment decisions. The latest NICE guidelines (2009) supported the recent trend of early diagnosis and management of the condition. An early arthritis clinic has been set up at Darent Valley Hospital, Dartford, for the past 6 years. Aim: To assess the feasibility of implementing the visual matrix model, which would predict the 1-year risk of rapid radiographic progression, for individual patients diagnosed and managed in the early arthritis clinic. Also to assess the ability of the matrix model to identify patients who might need combination of DMARDs /commencing biologic therapy.

**Methods:** This was a case-control retrospective study. The matrix model was applied to 102 patients who were diagnosed to have RA according to the new ACR/EULAR criteria and treated according to NICE guidelines (2009) (Mean time to start biologic therapy was 6.4+0.52 months). The control group included 105 patients diagnosed to have early inflammatory arthritis in the period of 2005-2008 (Mean time to start biologic therapy was 14.3+1.8 months). The matrix model was applied at 0 time (before starting DMARDs therapy), 3, 6 and 12 months after starting treatment. Biologic therapy was commenced in group 1 by 6-months time of DMARDs therapy, whereas the patients in group 2 continued on DMARDs therapy for the whole of first year. Modified Sharp/van der Heijde score (SHS) was assessed for all patients by the end of the first year of treatment. Coordinates were illustrated to identify the best discriminating point that shows the highest sensitivity and the lowest 1-specificity (false positives) values.

**Results:** There was no significant difference on comparing the baseline characteristics in both groups included in this work. By the end of 1-year of therapy, there was significant difference ( $p < 0.001$ ) between the matrix score in both groups assessed (being significantly lower in group 1) supporting the favorable effect of the biologic over DMARDs therapy. Also, the matrix score correlated significantly with the SHS score. AUC and coordinate points showed that the sensitivity as well as specificity of the matrix score were highest at baseline, as well as at 6-months of therapy followed by at 3 months of therapy.

**Conclusions:** The matrix models predicted the risk of RRP at 1-year using initiated treatment and easily accessible clinical and laboratory variables. The matrix model can be implemented in the early arthritis clinic to identify those patients at risk who should receive the combination of DMARDs therapy by 3-months or should start biologic therapy by 6-months of starting DMARDs therapy.

**Disclosure statement:** The authors have declared no conflicts of interest.

#### 150. IN THE AGE OF BIOLOGIC THERAPY: WHICH ANTI-TNF AGENT IS SAFE TO USE IN PATIENTS WITH LATENT TUBERCULOSIS

Yasser El Miedany<sup>1</sup> and Deborah Palmer<sup>1</sup>  
<sup>1</sup>Rheumatology, Darent Valley Hospital, Dartford, United Kingdom

**Background:** The failure to screen for tuberculosis before the initiation of biologic therapy may result in adverse outcomes for both the patient and the overall health of the community. Similarly, reactivation of latent tuberculosis (patients infected with *M. tuberculosis* but does not have active tuberculosis disease) is a high risk in inflammatory arthritis patients treated with anti-TNF therapy, as this may lead to activation of the infection. Antigen-specific  $\gamma$ -IFN release assays such as T-SPOT have been evaluated in various populations and are reported to perform better than tuberculin skin testing in the diagnosis of TB infection (high specificity (93-99%).

**Aim:** to assess the safety of the different anti-TNF agents in patients with latent tuberculosis and the impact of anti-tuberculous therapy on the disease activity.

**Methods:** Upon referral for biologic therapy, all patients were assessed in the pre-biologic therapy assessment clinic. Assessment of tuberculosis infection risk includes history of specific symptoms (productive cough of stained sputum or TB travel risk factors for individual or close relatives), BCG scar, chest X-ray and T-spot test. 21 patients with latent TB were identified and treated with antituberculous agent under care of the chest clinic for 3 months following which anti-TNF therapy was started. Patient choice approach was implemented, after explaining all pros and cons of different anti-TNF agents available. Patients were monitored 3 monthly for symptoms of active TB disease, disease activity and compliance to their medications. Chest x-ray was taken every 3 months. Primary outcome was the chest status at the end of the year and whether there has been flare up of the TB infection. Secondary outcome was the disease activity score at the end of the year.

**Results:** 8 patients received enbrel, 7 patients received humira whereas 6 patients received infliximab infusions. There was no significant difference on comparing, age, sex or disease activity parameters between the 3 groups ( $p > 0.05$ ). Prior to therapy, chest x-ray did not show any active lung lesion in all patients presented with reactive T-spot test. At one year of anti-TNF therapy there was no activation of TB infection in any patient in the 3 groups. There was no significant difference between the 3 patients groups in terms of disease activity parameters ( $p > 0.05$ ).

**Conclusions:** It is relatively safe to use any of the anti-TNF agents, enbrel, humira, or infliximab in patients with latent TB. Having a reactive T-spot test/ latent tuberculosis is not a contraindication to anti-TNF therapy. Using anti-tuberculous therapy for 3 months after which the patient can start his anti-TNF therapy with 3 monthly X-ray chest seems a safe protocol for this group of patient.

**Disclosure statement:** The authors have declared no conflicts of interest.

#### 151. SYSTEMATIC REVIEW AND META-ANALYSES OF NON-PHARMACOLOGICAL INTERVENTIONS FOR FATIGUE IN RHEUMATOID ARTHRITIS

Fiona Cramp<sup>1</sup>, Sarah Hewlett<sup>1,2</sup>, Celia Almeida<sup>1,2</sup>, John Kirwan<sup>2</sup>, Ernest Choy<sup>3</sup>, Trudie Chalder<sup>4</sup>, Jon Pollock<sup>1</sup> and Robin Christensen<sup>5</sup>  
<sup>1</sup>Department of Allied Health Professions, University of the West of England, Bristol, United Kingdom; <sup>2</sup>Academic Rheumatology Unit, University of Bristol, Bristol Royal Infirmary, Bristol, United Kingdom; <sup>3</sup>Section of Rheumatology, Cardiff University, Cardiff, United Kingdom; <sup>4</sup>Department of Psychological Medicine, Institute of Psychiatry, King's College London, London, United Kingdom; <sup>5</sup>The Parker Institute: Musculoskeletal Statistics Unit (MSU), Copenhagen University Hospital at Frederiksberg, Copenhagen, Denmark

**Background:** Fatigue is a common and distressing symptom for patients with rheumatoid arthritis (RA) with no accepted evidence based management guidelines. Non-pharmacological interventions, such as physical activity and psychosocial interventions have been shown to help people with a range of other long term conditions manage subjective fatigue. The objective of this review was to evaluate the effectiveness and safety of non-pharmacological interventions for the management of fatigue in people with RA.

**Methods:** The following electronic databases were searched: Cochrane Central Register of Controlled Trials; Cochrane Database of Systematic Reviews; Current Controlled Trials Register; The National Research Register Archive; The UKCRN Portfolio Database; MEDLINE; EMBASE; AMED; CINAHL; PsycINFO; Social Science Citation Index; Web of Science; Dissertation Abstracts International. In addition reference lists of articles identified for inclusion were checked for additional studies and key authors were contacted. Randomised controlled trials were included if they evaluated a non-pharmacological intervention in people with RA, with self-reported fatigue as an outcome measure. Two reviewers selected relevant trials, assessed methodological quality and extracted data. The Standardized Mean Difference (SMD) was applied as the effect

measure applicable across different outcome measures. Data were pooled using meta-analysis with a random-effects model with inconsistency evaluated based on the I-squared value.

**Results:** Of 54 studies initially identified, 19 met the inclusion criteria with a total of 2240 participants with RA. Included studies investigated physical activity interventions ( $k=5$ ), psychosocial interventions ( $k=10$ ), herbal medicine ( $k=1$ ), omega-3 fatty acid supplementation ( $k=1$ ), Mediterranean diet ( $k=1$ ) and the provision of Health Tracker information ( $k=1$ ). The risk of bias in the included studies varied from high (53%) to low (37%). No adverse effects were reported in any of the studies. Only three studies reported adverse events but there was no clear difference in incidence or severity between the intervention and control groups. At the end of the intervention period a non-significant trend in favour of physical activity was demonstrated for pre-post test mean change in self-reported fatigue (SMD -0.17, 95% CIs -0.53 to 0.18; I-sq=56%). A non-significant trend in favour of psychosocial interventions was also demonstrated (SMD -0.14, 95% CIs -0.30 to 0.02, I-sq = 19%). The remaining four studies investigated diverse non-pharmacological interventions and were therefore not appropriate for combining within a meta-analysis.

**Conclusions:** This systematic review shows that there is currently insufficient evidence of the effectiveness of non-pharmacological interventions in the management of self-reported fatigue in RA patients. Psychosocial interventions and physical activity show some promise but require further investigation.

**Disclosure statement:** S.H. has received research grants from GlaxoSmithKline and Arthritis Research UK. All other authors have declared no conflicts of interest.

#### 152. FACTORS ASSOCIATED WITH EXCESS ATHEROSCLEROTIC PLAQUE IN EARLY INFLAMMATORY POLYARTHRITIS: RESULTS FROM THE NORFOLK ARTHRITIS REGISTER

Hoda Mirjafari<sup>1</sup>, Suzanne Verstappen<sup>1</sup>, Diane Bunn<sup>2</sup>, Helena Edlin<sup>3</sup>, Valentine Charlton-Menys<sup>4</sup>, Philip Pemberton<sup>5</sup>, Tarnya Marshall<sup>2</sup>, Paddy Wilson<sup>2</sup>, Mark Lunt<sup>1</sup>, Deborah Symmons<sup>1</sup> and Ian N. Bruce<sup>1</sup>  
<sup>1</sup>Arthritis Research UK Epidemiology Unit, University of Manchester, Manchester, United Kingdom; <sup>2</sup>Rheumatology Department, Norfolk and Norwich University Hospitals, Norwich, United Kingdom; <sup>3</sup>Department for Vascular Studies, Manchester Royal Infirmary, Manchester, United Kingdom; <sup>4</sup>Cardiovascular Research Group, The University of Manchester, Manchester, United Kingdom; <sup>5</sup>Biochemistry Laboratory, Manchester Royal Infirmary, Manchester, United Kingdom

**Background:** Patients with inflammatory polyarthritis (IP) have excess cardiovascular (CVD) mortality due to accelerated atherosclerosis. Identifying individuals with subclinical atheromatous plaque and markers associated with it may allow for targeted CVD risk management early in disease. We aimed to compare the prevalence of carotid atherosclerosis in early IP and controls and to identify risk factors associated with this in early IP.

**Methods:** Consecutive patients with early IP ( $\geq 2$  joints swollen for  $\geq 4$  weeks) aged 18-65 years, who were within 24 months of symptom onset were recruited as part of a primary-care based inception cohort between 2004-2008. Patients were age and gender frequency matched with controls. At baseline, subjects had classic risk factors assessed, underwent joint examination, had blood taken to assess serological status, the acute phase response as well as paroxonase 1 (PON1) apolipoprotein (Apo) A1 and B, markers of endothelial activation (E-selectin, vascular cell adhesion molecule (VCAM)) and adipocytokines (leptin and adiponectin). All subjects had a B mode Doppler ultrasound examination of the carotid arteries for the presence of plaque. In univariate logistic analyses we identified factors that were associated with plaque after age and gender adjustment. An additive stepwise multivariable regression model was developed to investigate independent associations with plaque.

**Results:** Of the 329 patients and 67 controls studied 96 (29%) and 26 (33%) were male respectively. In patients the median (IQR) age and symptom duration at study entry were 51 (42-58) years and 6.6 (4.2-11.2) months. 14 (4%) patients had prior CVD. Patients were more likely to smoke (75 [23%] vs 3 [4%]  $p < 0.05$ ), be on antihypertensives (42 [13%] vs. 2 [2%]  $p < 0.05$ ) and have previous steroid exposure (62 [19%] vs. 2 [3%]  $p < 0.05$ ). Carotid plaque was more prevalent in patients than controls on baseline scans (151[46%] vs 16 [24%] OR [95% CI] 2.9 [1.6, 5.2]). In univariate analysis; age, smoking, BP, total cholesterol, LDL, triglyceride, hs-CRP, adiponectin and Apo B were significantly associated with plaque in patients. In an additive stepwise multivariable regression model age, BP, Apo B, and adiponectin remained independent predictors of plaque (Table 1).

**Conclusions:** Carotid plaque is more prevalent in IP patients from early in the disease course and is driven principally by traditional risk factors.

**Disclosure statement:** The authors have declared no conflicts of interest.

TABLE 1. Cardiovascular, IP and novel risk factors associated with plaque in IP subjects at baseline.

Variable	IP Subjects Odds Ratio (95% CI)
Age when seen (per year)	1.10 (1.06, 1.14)
Apo B (per g/L)	211.47 (8.73, 5123.04)
Adiponectin (per mg/L)	1.17 (1.04, 1.31)
Systolic BP (per mmHg)	1.02 (1.00, 1.04)

Logistic regression producing ORs used for binary outcomes. ORs are considered significant if the 95% CIs do not include 1. Adjustments were made for age and gender.

#### 153. THE RECOGNITION AND ASSESSMENT OF CARDIOVASCULAR RISK IN PEOPLE WITH RHEUMATOID ARTHRITIS IN PRIMARY CARE: A QUESTIONNAIRE-BASED STUDY OF GENERAL PRACTITIONERS

Carolyn Bell<sup>1</sup> and Ian F. Rowe<sup>1</sup>

<sup>1</sup>Rheumatology, Worcestershire Acute NHS Trust, Worcester, United Kingdom

**Background:** Rheumatoid arthritis (RA) is a chronic, inflammatory disease affecting approximately 1% of the adult population. Patients with RA are recognised as having increased cardiovascular morbidity and mortality. Within the UK the majority of cardiovascular risk assessment and management occurs within primary care. This study aimed to determine how well recognised the association between RA and excess cardiovascular risk is within primary care and the current assessment strategies being employed by general practitioners (GPs).

**Methods:** Questionnaires were sent to all 376 GPs in the Worcestershire Primary Care Trust.

**Results:** Of the 207 GPs responding to the questionnaire 32% identified RA as an independent risk factor for cardiovascular (CV) disease. 15% and 34% respectively assessed their RA patients for primary and secondary prevention of their CV risks. Of those who made an assessment 18.4% of GPs adjusted the calculated risk derived from standard charts. The frequency of assessment was statistically significantly greater ( $p < 0.0001$ ) among those GPs who had received a form of education about the association between CV disease and RA. However of the GPs identifying this susceptibility only 40% performed any form of primary prevention risk assessment. 5.3% of GPs felt that CV risk management should occur in secondary care with 84% and 85% respectively reporting that a review article or presentation about cardiovascular risk in RA would be useful to their daily practice.

**Conclusions:** At present the excess risk of CV disease conferred by RA is under-recognised and under-assessed in primary care. Currently educational resources on this topic targeted at GPs are lacking and may in part account for our findings. However, even when GPs did identify the risk of CV disease in RA or had received education about it, this did not consistently change their clinical management. Further work to promote knowledge and management strategies for CV disease in RA is therefore needed to improve the care of patients with this condition.

**Disclosure statement:** C.B. has received sponsorship to attend a conference from Roche. All other authors have declared no conflicts of interest.

#### 154. SUSTAINED CLINICAL REMISSION IN RA: PREVALENCE AND PROGNOSTIC FACTORS IN AN INCEPTION COHORT OF PATIENTS TREATED WITH CONVENTIONAL DMARD THERAPY

Keeranur Jayakumar<sup>1</sup>, Sam J. Norton<sup>2</sup>, Josh Dixey<sup>1</sup>, Peter Williams<sup>1</sup> and Adam Young<sup>1</sup>

<sup>1</sup>Rheumatology, ERAS, St Albans, United Kingdom; <sup>2</sup>Centre for Lifespan & Chronic Illness Research, University of Hertfordshire, Hatfield, United Kingdom

**Background:** Clinical remission is now a realistic goal in managing rheumatoid arthritis (RA) since the introduction of biologics. However, data on sustained clinical remission in conventionally treated RA is limited. This study examines prevalence/predictive factors of sustained clinical remission in patients treated with standard DMARD

therapy prior to the biologic era in an inception cohort over the first 5 years.

**Methods:** Consecutive newly diagnosed RA patients (<2yrs from symptom onset and DMARD naïve) were recruited at presentation from 9 centres across England into an inception cohort (1986-1998) (n=1460), and followed annually employing standard clinical, laboratory and radiological assessments. Disease activity was assessed using the original 3-variable DAS that uses swollen/tender joint counts, and acute phase response (ESR/CRP). Point remission (DAS at one point) was defined by DAS < 1.6 according to EULAR response criteria (DAS28<2.6). For this study, sustained clinical remission was defined by DAS<1.6 at all 3, 4 and 5yr follow ups, non remission if DAS>=1.6 at all 3 follow ups, and partial remission for other combinations. Outcomes included structural damage (Larsen scores of hand/foot X-rays) and functional ability (HAQ). Odds ratios (OR) with 95% confidence intervals (95%CI) were calculated to examine the strength of predictive factors for clinical remission. 704 patients had minimum 5yrs follow-up with DAS recorded at baseline, 3rd, 4th and 5th yr follow-ups, and were included in the analysis. Monotherapy was used in 43%, sequential monotherapy 30%, combination therapy 18%, the remainder 9% steroidal/non-steroidal drugs only.

**Results:** Point remission based on DAS at 3, 4 and 5yrs was 25%, 26% and 22% respectively, but only 11% (n=78) had sustained DAS remission. Baseline predictors for sustained DAS remission using univariate analysis were men (OR 2.6, 95%CI 1.6-4.2), 6 or less months of symptoms prior to study entry (OR 1.6, 95%CI 1.0-2.7), <10 tender joints (OR 3.0, 95%CI 1.7-5.0), <13 swollen joints (OR 1.9, 95%CI 1.1-3.0), DAS < 4.1 (OR 2.7, 95%CI 1.6-4.6) and HAQ <1.0 (OR 2.1, 95%CI 1.3-3.6). Only men, symptom duration and tender joints remained independent predictors of sustained DAS remission in multivariate analysis. Patients with sustained DAS remission by 5yrs had better outcomes over time as assessed by less DMARD therapies, radiographic progression and functional impairment. Mean HAQ decreased from 0.17-0.13 (p<0.001) in sustained DAS remission, compared to an increase from 0.92-1.1 (p<0.001) in the non-remission group.

**Conclusions:** In RA patients managed with conventional DMARDs, point remission rates were around 25%. 11% had sustained DAS remission by 5yrs with a positive impact on structural/functional outcomes. These results provide a benchmark for modern pharmacological approach to RA. Remission maintenance, not only induction should be the main therapeutic target.

**Disclosure statement:** The authors have declared no conflicts of interest.

#### 155. THE SAFETY AND ACCEPTABILITY OF ULTRASOUND-GUIDED BIOPSY IN EARLY ARTHRITIS PATIENTS

Hariney Kurunadalingam<sup>1</sup>, Iram Parwaiz<sup>1</sup>, Kanta Kumar<sup>1</sup>, Kath Howlett<sup>1</sup>, Becki Hands<sup>2</sup>, Karim Raza<sup>1</sup>, Costantino Pitzalis<sup>2</sup>, Chris Buckley<sup>1</sup>, Stephen Kelly<sup>2</sup> and Andrew Filer<sup>1</sup>  
<sup>1</sup>Rheumatology Research Group, University of Birmingham, Birmingham, United Kingdom; <sup>2</sup>Rheumatology Department, Barts and the Royal London, London, United Kingdom

**Background:** Current research strategies addressing prediction of outcome in early arthritis such as PEAC (the Pathobiology of Early Arthritis Cohort) and the Birmingham Very Early Arthritis Clinic rely upon the procurement of tissue from patients at the earliest stages of disease, necessitating safe, minimally invasive techniques which are acceptable to newly presenting arthritis patients. We assessed the safety and acceptability of ultrasound guided biopsy, a less invasive alternative to formal arthroscopy, used by centres in Birmingham and London.

**Methods:** Patients with treatment naïve early synovitis of at least one joint, up to one year symptom duration, and at least one joint amenable to synovial biopsy gave written informed consent to be recruited from hospitals in London and Birmingham, representing the first cohort of patients in the UK upon whom these procedures were performed. The patients were assessed pre, intra and 2 weeks post biopsy on a standard proforma. Patient reported information on joint status and patient acceptability was recorded by likert scales, visual analogue scales (VAS) and free text entry in a confidential proforma.

**Results:** 123 participants were included (mean age 53 (19-83) years, M:F 53:70). Adverse events were compared with data for conventional arthroscopy. During biopsy arthralgia occurred in 24%, while minor complications of presyncope and syncope occurred below 3%, with no DVT, joint infection, thrombophlebitis or neurovascular damage. The only significant complication was a wound infection, used as a critical event to inform further practice in the collaborative network. A single, mild haemarthrosis occurred, giving a similar rate to major

haemarthrosis seen with conventional arthroscopy (0.8% vs 0.9%). Patient acceptability of biopsy procedures was excellent. The majority (81%) of biopsies involved either minimal or no discomfort. Biopsies of small joints involved significantly less discomfort than large joints (p<0.0001), but provided less tissue for analysis. Two weeks post procedure, most patients (98% Birmingham, 91% London) felt the biopsied joint was "the same" or "better". Significantly more patients in Birmingham felt the joint was improved (p<0.05), due to a higher number of very early patients with resolving arthritis. Corresponding improvements in VAS scores for pain, swelling and stiffness were seen. Crucially, most patients (81% in Birmingham and 72% in London) would be likely to consent to a repeat procedure.

**Conclusions:** Acknowledging a single early wound infection, the side effect profile of US guided biopsy matches or improves upon conventional arthroscopy with an excellent acceptability profile. Patients are happy to undergo repeat procedures (12 repeat biopsies in the Birmingham cohort to date). This novel technique has the potential to replace arthroscopy as a research and clinical trial procedure.

**Disclosure statement:** The authors have declared no conflicts of interest.

TABLE 1.

Joint	PIP	MCP	Wrist	Elbow	Knee	Ankle	MTP
n	1	20	12	6	74	8	2

#### 156. SUPPRESSION OF BONE TURNOVER BY B-CELL DEPLETION IN PATIENTS WITH RHEUMATOID ARTHRITIS

Gill Wheeler<sup>1</sup>, Vanessa E. Hogan<sup>2</sup>, YK Onno Teng<sup>3</sup>, Janneke Tekstra<sup>4</sup>, Stephen P. Tuck<sup>5</sup>, Floris P. Lafeber<sup>4</sup>, Tom W. Huizinga<sup>3</sup>, Johannes W. Bijlsma<sup>4</sup>, Roger M. Francis<sup>2</sup>, Harish K. Datta<sup>2</sup> and Jaap van Laar<sup>2,5</sup>  
<sup>1</sup>Biochemistry, The James Cook University Hospital, Middlesbrough, United Kingdom; <sup>2</sup>Musculoskeletal Research Group, Newcastle University, Newcastle upon Tyne, United Kingdom; <sup>3</sup>Rheumatology, Leiden University Medical Centre, Leiden, Netherlands; <sup>4</sup>Rheumatology and Clinical Immunology, University Medical Centre Utrecht, Utrecht, Netherlands; <sup>5</sup>Rheumatology, The James Cook University Hospital, Middlesbrough, United Kingdom

**Background:** Recent investigations have provided abundant evidence for an intricate interaction between the immune and skeletal systems. Rheumatoid arthritis (RA) is the most prevalent inflammatory joint disease, in which B cells play an important role. The skeletal complications of RA consist of focal erosion of marginal and subchondral bone, juxta-articular osteoporosis and generalised bone loss with reduced bone mass. The role of B-cells in bone turnover is controversial and RA subjects treated with rituximab therapy provide an ideal model for determining the role of B cells in inflammatory bone resorption. This study was undertaken to investigate changes in biochemical markers of bone turnover before and after B cell depletion therapy in RA patients.

**Methods:** Serum from 46 patients with refractory RA, collected pre- and post-rituximab, was analysed for biomarkers of bone turnover (procollagen type 1 amino-terminal propeptide [PINP], osteocalcin, beta-isomerised carboxy terminal telopeptide of type I collagen [bCTX], osteoprotegerin [OPG]).

**Results:** A significant decrease in bone resorption was observed 6 months after rituximab (median change bCTX -50 ng/L, 95%CI -8,-136, p<0.001), mirrored by a significant reduction in disease activity. There was a significant increase in PINP (median change 5.0 µg/L, 95%CI -1.0, 11.2, p=0.02), a marker of bone formation, but no significant change in osteocalcin or OPG levels. The percentage change from baseline of bCTX in a subgroup of patients (not on prednisolone or a bisphosphonate) was significantly correlated with the percentage reduction in DAS28 score (rs=0.570, p=0.014).

**Conclusions:** B-cell depletion with rituximab in RA results in a significant suppression in bone resorption accompanied by an increase in bone formation. This may be a direct effect on osteoblasts and osteoclasts respectively, and be at least partially explained by the decreased inflammation and disease activity.

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### 157. DOES TESTING FOR CIRCULATING AUTOANTIBODIES AGAINST DISEASE-RELEVANT CITRULLINATED ANTIGENS ADD VALUE TO THE CCP2 ASSAY IN DIAGNOSING RA AMONG EARLY UNDIFFERENTIATED ARTHRITIS PATIENTS?

Arthur G. Pratt<sup>1</sup>, Peter J. Charles<sup>2</sup>, Muslima Choudhury<sup>2</sup>, Gill Wilson<sup>1</sup>, Patrick J. Venables<sup>2</sup> and John Isaacs<sup>1</sup>

<sup>1</sup>Institute of Cellular Medicine, Musculoskeletal Research Group, Newcastle University, Newcastle-upon-Tyne, United Kingdom;

<sup>2</sup>The Kennedy Institute of Rheumatology, Imperial College, London, United Kingdom

**Background:** The antigen substrates employed in the widely-used CCP2 assay do not correspond to in vivo-generated citrullinated proteins so far implicated in the pathogenesis of RA. We assessed the diagnostic utility of circulating autoantibodies to a panel of such peptides amongst UA patients, and whether permutations thereof might improve upon the diagnostic utility of CCP2 testing alone.

**Methods:** UA patients presenting to the Newcastle Early Arthritis Clinic who were naïve to immunomodulatory treatment were recruited. In addition to routine testing using the CCP2 assay, baseline sera were tested for reactivity to citrullinated forms of fibrinogen (cFbg), vimentin (cVim), cyclic alpha enolase peptides 1 and 11 (CEP-1 and CEP-11), linear filaggrin (Fil-LC), and a panel of 6 citrullinated pro-filaggrin-derived peptides. Corresponding native forms of the same peptides were used as negative controls where possible, and testing for IgA and IgM rheumatoid factor (RF) was also undertaken, with assay cut-offs being determined based on healthy control populations. Clinicians were blinded to all but the CCP2 results, and follow-up was for >1 year (median 28 months) Individuals for whom definitive outcome diagnosis was not reached within the study period were excluded from analysis. The 1987 ACR classification criteria were used for the diagnosis of RA.

**Results:** Assays were carried out for 75 newly presenting UA patients, of whom 29 (39%) developed RA. The specificity, sensitivity, positive and negative predictive values (PPV and NPV) of CCP2 with respect to an RA outcome in this cohort (95% confidence intervals) were 0.98 (0.87-1.0), 0.48 (0.30-0.67), 0.93 (0.66-1.0) and 0.75 (0.62-0.85) respectively. No single assay evaluated displayed superior NPV over CCP2 without compromising the PPV afforded by that test. Neither did combinations of assays, considered in permutations with or without CCP2, add value to CCP2-testing alone in predicting RA. Hierarchical clustering of all assay profiles revealed cFbg reactivity to correlate most closely with CCP2 test positivity amongst these sera (PPV and NPV 0.80 [0.51-0.95] and 0.70 [0.56-0.81]) respectively. In general, IgM RF positivity had a NPV equivalent to that of the CCP2 test, but an inferior PPV (0.65 [0.44-0.82]), and, after the CCP test, the best assay with regards PPV for RA was found to be CEP-1 (0.83 [0.36-0.99]).

**Conclusions:** The CCP2 test remains an invaluable diagnostic tool in the assessment of UA because of its impressive PPV, but the identification of biomarkers for the diagnosis of autoantibody negative RA must remain a priority.

**Disclosure statement:** The authors have declared no conflicts of interest.

### 158. DELAYS IN ASSESSMENT OF PATIENTS WITH NEW ONSET RHEUMATOID ARTHRITIS: VARIATIONS ACROSS EUROPE

Karim Raza<sup>1</sup>, Kanta Kumar<sup>1</sup>, Rebecca Stack<sup>1</sup>, Brygida Kwiatkowska<sup>2</sup>, Solbritt Rantapaa-Dahlqvist<sup>3</sup>, Tore Saxne<sup>4</sup>, Prodromos Sidiropoulos<sup>5</sup>, Eleni Kteniadaki<sup>5</sup>, Chariklia Misirlaki<sup>5</sup>, Herman Mann<sup>6</sup>, Jiri Vencovsky<sup>6</sup>, Adrian Ciurea<sup>7</sup>, Giorgio Tamborini<sup>7</sup>, Diego Kyburz<sup>7</sup>, Hans Bastian<sup>8</sup>, Gerd R. Burmester<sup>8</sup>, Jacqueline Detert<sup>8</sup> and Christopher D. Buckley<sup>1</sup>

<sup>1</sup>Immunity and Infection, University of Birmingham, Birmingham, United Kingdom; <sup>2</sup>Rheumatology, Institute of Rheumatology, Warsaw, Poland; <sup>3</sup>Department of Rheumatology, University Hospital, Umea, Sweden; <sup>4</sup>Department of Clinical Sciences, Section of Rheumatology, Lund University, Lund, Sweden; <sup>5</sup>University of Crete, University of Crete, Crete, Greece; <sup>6</sup>Institute of Rheumatology, Charles University, Prague, Czech Republic; <sup>7</sup>Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; <sup>8</sup>Department of Rheumatology and Clinical Immunology, Charité, Berlin, Germany

**Background:** The first 3 to 4 months after symptom onset represent an important therapeutic window in RA. Delays in assessment by rheumatologists, and consequently in DMARD initiation, reflect a composite of 4 time intervals: [1] Onset of symptoms to request to see health care professional (HCP); [2] Request to see HCP to assessment by HCP; [3] Initial assessment by HCP to referral to rheumatologist; [4] Referral to rheumatologist to assessment by rheumatologist. In previous work from the UK, the median delay from symptom onset to rheumatology assessment was over 20 weeks. We sought to quantify delays in assessment of RA patients across Europe and to identify the principal reasons for delay in different countries.

**Methods:** Data (the 4 levels of delay listed above, age, gender and the initial HCP of contact) were collected from consecutively presenting RA patients fulfilling 1987 ACR criteria at initial assessment in Birmingham, Umeå, Lund, Berlin, Warsaw, Prague, Zurich and Crete.

**Results:** Details of patients are shown (Table 1). The median delay from onset of inflammatory joint symptoms to assessment by a rheumatologist ranged from 20 to 38 weeks. The relative contributions of each level of delay to the total delay varied between units. In Birmingham and Crete, the greatest contribution was delay on the part of the patient in consulting a HCP. In Umeå, Lund, Prague and Zurich, delay on the part of the patient in consulting a HCP, and delay on the part of the HCP in referring to a rheumatologist were equivalent contributors to overall delay. In Berlin and Warsaw, delay on the part of the patient in seeking medical advice was relatively short, with other components accounting for the majority of the overall delay.

**Conclusions:** Across Europe, delays in the assessment of RA patients by rheumatologists are too long. Tackling this should represent an important priority for strategies to improve RA outcomes. This study highlights the levels of delay that need to be targeted in individual countries.

TABLE 1.

	Birmingham	Umea	Lund	Berlin	Warsaw	Prague	Zurich	Crete
Number of patients	50	50	48	50	50	50	49	42
Age, median (IQR), years	55 (44-69)	55 (42-67)	58 (45-68)	44 (35-59)	55 (47-62)	56 (40-60)	53 (36-62)	53 (43-62)
Gender: female, number (%)	33 (66)	36 (72)	35 (73)	35 (70)	41 (82)	35 (70)	37 (76)	36 (86)
Initial health care professional (HCP) of contact								
GP	49	47	46	26	36	35	46	2
Rheumatologist	0	0	0	2	7	4	0	12
Internist	0	0	0	2	3	1	1	9
Company health service	0	3	0	0	0	0	0	0
Orthopaedic surgeon	0	0	0	13	2	9	1	19
Emergency department	1	0	0	5	0	0	0	0
Neurologist	0	0	0	0	1	0	0	0
Not recorded / other	0	0	2	2	1	1	1	0
Delay 1: Patient delay in seeking appointment with initial HCP, median (IQR), weeks	12 (3-64)	8 (2-17)	8 (4-8)	2 (1-8)	4 (1-8)	8 (2-12)	8 (4-13)	22 (8-72)
Delay 2: Delay in assessment by initial HCP once decision to seek advice made, median (IQR), weeks	1 (<1-1)	1 (<1-2)	2 (1-2)	2 (1-4)	2 (1-8)	<1 (<1-2)	1 (1-2)	12 (6-63)
Delay 3: Initial HCP delay in referral to Rheumatologist, median (IQR), weeks	2 (1-5)	8 (2-20)	8 (4-12)	10 (3-23)	12 (2-48)	10 (3-52)	8 (4-15)	3 (0-4)
Delay 4: Rheumatologist delay in seeing patient once referral made, median (IQR), weeks	4 (2-6)	4 (2-5)	3 (2-4)	11 (4-14)	4 (1-8)	4 (2-8)	2 (1-3)	4 (0-8)
Total delay from symptom onset to assessment by Rheumatologist, median (IQR), weeks	21 (13-63)	25 (14-53)	22 (15-32)	27 (19-43)	35 (14-74)	25 (12-77)	20 (13-36)	38 (16-192)
P value across levels of delay 1-4 <sup>a</sup>	<0.0001	<0.0001	<0.0001	<0.0001	0.0028	<0.0001	<0.0001	<0.0001

<sup>a</sup>Kruskal Wallis test comparing across levels of delay 1-4.

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**159. DAS28 USING CRP IS SIGNIFICANTLY LOWER THAN DAS28 ESR IN RA PATIENTS**

Claire Sheehy<sup>1</sup>, Alexa Shipman<sup>1</sup>, Irina Stech<sup>1</sup> and Chetan Mukhtyar<sup>1</sup>  
<sup>1</sup>Rheumatology, Norfolk and Norwich University Hospital, Norwich, United Kingdom

**Background:** The disease assessment score 28 joint count (DAS28) is a validated tool to assess disease activity in rheumatoid arthritis (RA) and is widely used in clinical trials. The original DAS28 has four components: tender joint count, swollen joint count, visual analogue score (VAS) of the patient's global health and erythrocyte sedimentation rate (ESR). Versions of DAS28 which substitute C-reactive protein (CRP) instead of the ESR have been developed because CRP is not affected by age, gender and globulin levels. A three variable DAS28 without the VAS is also available. A DAS28  $\leq 2.6$  has been proposed as remission and  $\geq 5.1$  as high disease activity. It is recognised that the DAS28 CRP values tend to be lower than the DAS28 ESR values but the quantum of difference is unknown. We aimed to quantify the difference and find the equivalent values for 'remission' and 'high disease activity' in the versions using the CRP.

**Methods:** Consecutive outpatient letters from general rheumatology and biologics clinic were reviewed. Data collected included swollen joint count, tender joint, global health assessment, ESR and CRP. If any of these variables was not described, or the inflammatory markers had not been measured, then the letter was disregarded. Four versions of the DAS28 score were then calculated i.e. the DAS28 ESR 4 variables (4V), DAS28 CRP 4V, DAS28 ESR 3 variables (3V) and DAS28 CRP 3V. Statistical analysis was performed using SPSS 17.0; descriptive statistics, paired t-tests, and Spearman's rank correlation tests were applied as appropriate. Receiver operating characteristic (ROC) curves were then constructed to find corresponding values of DAS28 CRP 3V, DAS28 CRP 4V and DAS28 ESR3V, for DAS28 ESR 4V values of 2.6 and 5.1.

**Results:** 366 patients with RA were analysed. The mean DAS28 ESR 4V of 3.59 differed significantly from the mean DAS28 CRP 4V of 3.00 ( $p < 0.001$ ), DAS28 CRP 3V of 3.15 ( $p < 0.001$ ), and DAS28 ESR 3V of 3.80 ( $p < 0.001$ ). All 4 versions of the DAS28 were shown to be significantly correlated (using Spearman's correlation) with each other,  $p < 0.001$  for all comparisons. Values corresponding to DAS28 ESR 4V values of 2.6 and 5.1 are as in Table 1.

**Conclusions:** There is a strong correlation between all 4 versions of the DAS28, but the versions using CRP have statistically significant and clinically meaningful lower values. This should be borne in mind at a time that we are being encouraged to treat all of our patients DAS targets, as the inflammatory marker used will have significant impact on the ultimate DAS score.

**Disclosure statement:** The authors have declared no conflicts of interest.

TABLE 1.

DAS28 ESR 4V	DAS28 CRP 4V			DAS28 CRP 3V			DAS28 ESR 3V		
	Value	Sens	Spec	Value	Sens	Spec	Value	Sens	Spec
5.1	4.135	95.8%	95.6%	4.445	94.4%	94.9%	5.09	97.2%	95.6%
2.6	1.89	88.1%	87.0%	2.150	88.1%	87.8%	2.98	97.0%	99.2%

Sens: sensitivity; Spec: specificity

TABLE 1. Baseline characteristics and incidence of infections

	DMARD	All anti-TNF	ETN	INF	ADA
Subjects, n	3666	11864	4136	3472	4256
Mean age (s.d.), years	60 (12)	56 (12)	56 (12)	56 (12)	57 (12)
Female gender, n (%)	2648 (72)	9038 (76)	3190 (77)	2624 (76)	3224 (76)
Disease Duration, median (IQR), years	6 (1-15)	11 (6-19)	12 (6-19)	12 (6-19)	10 (5-18)
Baseline steroid use, n (%)	834 (23)	5243 (44)	1977 (48)	1609 (46)	1657 (39)
DAS28, mean (s.d.)	5.1 (1.3)	6.6 (1.0)	6.6 (1.0)	6.6 (1.0)	6.5 (1.0)
Exposure, pyrs	12592	53715	23026	13476	17211
All rare / opportunistic infections: n	5	53	18	21	14
Incidence rate / 10000 pyrs (95% confidence interval)	4.0 (1.3, 9.3)	10.0 (7.4, 12.9)	7.8 (4.6, 12.4)	15.6 (9.6, 23.8)	8.1 (4.4, 13.6)
Bacterial endocarditis: n	1	13	6	3	4
Invasive fungal infection: n	1	4	1	3	0
Legionellosis: n	0	6	0	2	4
Listeriosis: n	1	8	2	4	2
Multidermatomal shingles: n	0	8	3	3	2
Pneumocystis pneumonia: n	1	7	2	3	2
Invasive salmonellosis: n	1	7	4	3	0

**160. PRECLINICAL ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS: FROM ENDOTHELIAL DYSFUNCTION TO ATHEROSCLEROSIS**

Fabiola Atzeni<sup>1</sup>, Simona Sitia<sup>2</sup>, Livio Tomasoni<sup>2</sup>, Luigi Gianturco<sup>2</sup>, Cristian Ricci<sup>3</sup>, Piercarlo Sarzi-Puttini<sup>1</sup>, Vito De Gennaro Colonna<sup>4</sup> and Maurizio Turiel<sup>2</sup>

<sup>1</sup>L.Sacco University Hospital, Rheumatology Unit, Milan, Italy; <sup>2</sup>Dep. of Health Technologies, University of Milan, Cardiology Unit, IRCCS Galeazzi Orthopedic Institute, Milan, Italy; <sup>3</sup>University of Milan and Clinical Epidemiology and Biometry Unit, IRCCS Policlinico San Donato, Milan, Institute of Medical Statistic and Biometry "G.A.M." Faculty of Medicine, Milan, Italy; <sup>4</sup>Pharmacology Department, University of Milan, Milan, Italy

**Background:** Rheumatoid arthritis (RA) is characterized by an increase in cardiovascular (CV) mortality compared to the general population. Endothelial dysfunction begins early after the onset of the disease and plays a pathogenetic role in the development of accelerated atherosclerosis. An impaired coronary flow reserve (CFR $<2.5$ ) has been proved to detect an early impairment of coronary microcirculation before the onset of clinical evidence of CV disease. Our objective was to evaluate the relationship between CFR, common carotid intima-media thickness (IMT) and asymmetric dimethylarginine (ADMA) in RA patients.

**Methods:** 120 adult patients with RA who fulfilled the ACR classification criteria [M 20 (16.6%), F 100 (83.4%)], mean age 61 $\pm$ 13 years) without clinical evidence of CV disease underwent standard echocardiography and dipyridamole stress echo was performed to evaluate CFR in the left descending coronary artery. Carotid ultrasound was performed to evaluate common carotid IMT and a blood sample was collected to measure plasma ADMA levels.

**Results:** 72/120 patients (60%) had CFR $<2.5$  of which 14/120 (12%) had CFR $<2$ . All patients had normal wall motion at rest and during stress. Common carotid IMT was in normal range (0.73 $\pm$ 0.13mm) while plasma ADMA levels were increased (0.72 $\pm$ 0.10). Linear regression analysis showed a significant negative correlation between CFR and common carotid IMT ( $P < 0.001$ ), plasma ADMA levels ( $P < 0.001$ ) and patient's age ( $P = 0.019$ ). Moreover, CFR resulted negatively related with rheumatoid factor levels ( $P = 0.0009$ ) and visual analogue score (VAS) ( $P = 0.0092$ ).

**Conclusions:** RA patients without clinical evidence of CV diseases showed an early impairment of coronary microcirculation and endothelial dysfunction before structural changes of large vessels occur. This suggests that reduced CFR is an early marker of enhanced atherosclerosis in a preclinical stage and it is associated with endothelial dysfunction. Moreover, indexes of disease activity resulted negatively associated with coronary microcirculation function

**Disclosure statement:** The authors have declared no conflicts of interest.

**161. RARE AND OPPORTUNISTIC INFECTIONS IN PATIENTS EXPOSED TO ANTI-TNF THERAPY: RESULTS FROM THE BSR BIOLOGICS REGISTER (BSRBR)**

James Galloway<sup>1</sup>, Audrey Low<sup>1</sup>, Louise K. Mercer<sup>1</sup>, Will Dixon<sup>1</sup>, Andrew Ustianowski<sup>2</sup>, Kath Watson<sup>1</sup>, Mark Lunt<sup>1</sup> and the BSRBR Control Centre Consortium<sup>1</sup>, Kimme Hyrich<sup>1</sup> and Deborah Symmons<sup>1</sup> on behalf of the BSRBR

<sup>1</sup>Arthritis Research UK Epidemiology Unit, University of Manchester, Manchester, United Kingdom; <sup>2</sup>Department of Infectious Diseases, North Manchester General Hospital, Manchester, United Kingdom

**Background:** Anti TNF therapy is associated with a small increased risk of infection. There are biological reasons to expect that certain infections might be disproportionately increased, especially those caused by intracellular pathogens.

**Methods:** The BSRBR was established in 2001 to evaluate the safety of anti-TNF therapies etanercept (ETN), infliximab (INF) and adalimumab (ADA) in patients with RA. The anti-TNF treated cohort was recruited alongside a comparator group with active disease (DAS28 >4.2) treated with DMARDs. Patients were recruited between 01/10/2001 and 30/06/2008 and followed up by consultant and patient questionnaires until 31/12/2009 or death, whichever came first. The BSRBR defined a list of opportunistic infections at its outset. In addition to these, we included infective endocarditis. Tuberculosis was excluded from this analysis as we have reported on this previously.

**Results:** 11 864 anti-TNF and 3666 DMARD patients were included (Table 1). 58 rare or opportunistic infections were identified during the follow up (Anti-TNF 53; DMARD 5). The absolute rates of these infections were low in both cohorts (anti-TNF 10/10000 patient years follow up (pyrs); DMARD 4/10000 pyrs). Within the anti-TNF cohort, endocarditis was the most frequent event (13/53). The other reported opportunistic infections in the anti-TNF cohort were: invasive fungal infection (2 aspergillus, 2 candida), legionellosis (6), listeriosis (8), multidermatomal shingles (8), pneumocystis pneumonia (7), and invasive salmonellosis (7). These events were distributed amongst patients on each of the 3 anti-TNF agents.

**Conclusions:** The crude rate of rare or opportunistic infections and in particular endocarditis, was higher in anti-TNF exposed patients. We cannot conclude whether this is directly attributable to the anti-TNF therapy itself or other confounders, such as concurrent corticosteroid exposure. The clinician managing a sick patient on anti-TNF therapy should be aware of this spectrum of infection.

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**Disclosure statement:** The authors have declared no conflicts of interest.

#### 162. FINE SPECIFICITY OF ANTI-CITRULLINATED PEPTIDE ANTIBODIES IS ASSOCIATED WITH RESPONSE TO ANTI-TNF AGENTS IN RHEUMATOID ARTHRITIS: RESULTS FROM THE BRITISH SOCIETY OF RHEUMATOLOGY BIOLOGICS REGISTER

Benjamin Fisher<sup>1</sup>, Darren Plant<sup>2</sup>, Karin Lundberg<sup>3</sup>, Peter J. Charles<sup>1</sup>, Anne Barton<sup>2</sup> and Patrick Venables<sup>1</sup>

<sup>1</sup>Kennedy Institute of Rheumatology, Imperial College London, London, United Kingdom; <sup>2</sup>Arthritis Research UK Epidemiology Unit, University of Manchester, London, United Kingdom; <sup>3</sup>Rheumatology Unit, Karolinska Institutet, Stockholm, Sweden

**Background:** Anti-CCP antibodies have been associated with a poorer response to anti-TNF agents in RA. However, CCP is not an autoantigen but a group of synthetic peptides designed to maximise diagnostic sensitivity and which may fail to differentiate important disease subsets. We examined whether antibodies to immunodominant epitopes from three candidate citrullinated autoantigens could further define a subset of RA patients with a poor response to anti-TNF.

**Methods:** Samples from 450 patients enrolled in the British Society of Rheumatology Biologics Register were analysed for antibodies to CCP2 and to peptides from citrullinated  $\alpha$ -enolase (CEP-1), vimentin (cVim) and fibrinogen (cFib). Associations with change in DAS28 scores at 6 months were analysed by linear regression, and with EULAR response criteria by ordinal logistic regression.

**Results:** Anti-CEP-1, anti-cVim, anti-cFib and anti-CCP antibodies were present in 39%, 42%, 75% and 84% respectively. Anti-cFib antibodies were associated with a poorer response to anti-TNF therapy at 6 months using linear regression adjusted for baseline characteristics, and with a trend towards lower EULAR response. The subset with antibodies to both anti-CCP and anti-cFib antibodies had a worse outcome (linear regression coefficient for DAS28 score at 6 months 0.55; 95% CI 0.13, 0.97;  $p=0.01$ ) than the anti-cFib/CCP+ subset (coefficient 0.31; 95% CI -0.24, 0.87;  $p=0.27$ ) when compared to those negative for both antibodies. The presence of anti-CEP-1 and anti-cVim antibodies was not associated with a poorer response.

**Conclusions:** The association of anti-cFib antibodies with a poorer response to anti-TNF therapy justifies further investigation of antibodies to specific citrullinated antigens as predictors of clinical outcomes in RA.

**Disclosure statement:** K.L. and P.V. own a patent on the use of CEP-1 peptide. All other authors have declared no conflicts of interest.

#### 163. DOES ROUTINE MUSCULOSKELETAL ULTRASOUND USE ADD VALUE TO THE DIAGNOSIS OF RA AMONG EARLY UNDIFFERENTIATED ARTHRITIS PATIENTS?

Arthur G. Pratt<sup>1,2</sup>, Alice R. Lorenzi<sup>2</sup>, Gill Wilson<sup>2</sup>, Philip N. Platt<sup>2</sup> and John Isaacs<sup>1,2</sup>

<sup>1</sup>Institute of Cellular Medicine (Musculoskeletal Research Group), Newcastle University, Newcastle upon Tyne, United Kingdom;

<sup>2</sup>Musculoskeletal Unit, The Freeman Hospital, Newcastle upon Tyne, United Kingdom

**Background:** It remains to be demonstrated whether, in an early arthritis clinic, a system of routine MSUS evaluation may be implemented that adds value to more readily available clinical and laboratory predictors for diagnosing RA amongst UA patients.

**Methods:** A small joint MSUS screening protocol was devised, which focussed on 16 small joints of the upper and lower limbs, but had flexibility to incorporate additional joints as directed by clinical symptoms and signs. A validated, semi-quantitative score adapted from published systems was used to record findings for 3 MSUS “domains” at each joint site: effusion / grey-scale synovitis, power Doppler and erosions. Consenting UA patients attending an early arthritis clinic were followed up for >1 year (median 28 months); those for whom a definitive outcome diagnosis was not reached within the study period (1987 ACR classification criteria required for RA) were excluded. Optimum baseline MSUS parameters (and cut-offs) for independently predicting RA were identified. An “RA prediction score” was developed using baseline clinical and laboratory predictors (but not MSUS), according to an approach described previously by others [1]. The discriminatory utility of this score for RA versus non-RA outcomes was compared to that of a similarly derived score that did incorporate the optimum MSUS parameters.

**Results:** Data for 90 UA patients were analysed, of whom 33 (37%) developed RA. Out of 25 non-MSUS clinical and laboratory variables at baseline, 11 were found to differ significantly between RA and non-RA outcomes; 7 of these (SJC, joint pattern score, ESR, ACPA, RF, IgA and Ferritin) contributed to a final prediction score, which had an excellent ability to discriminate RA from non-RA outcome (area under ROC curve = 0.95; SEM = 0.029;  $p < 0.001$ ). The best independent MSUS predictors of RA outcome were grey-scale synovitis score  $\geq 1$  for 16 joints and power Doppler synovitis score  $\geq 3$  for all examined joints. These 2 variables were incorporated into the development of a modified prediction score comprising 6 variables (SJC, joint pattern score, ESR, ACPA, Ferritin and power Doppler synovitis). The ability of the modified score to discriminate RA from non-RA outcomes in the current cohort was virtually identical to that of the score derived without the benefit of MSUS (area under ROC curve = 0.95; SEM 0.029;  $p < 0.001$ ).

**Conclusions:** Our data imply that the incorporation of routine MSUS into early arthritis clinics as a diagnostic adjunct may not be essential for optimally diagnosing RA amongst patients who present with UA. Refinement of MSUS screening protocols and stratification of the UA population may yet delineate a clearer clinical role for MSUS in this setting.

**Disclosure statement:** The authors have declared no conflicts of interest.

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## Sjögren's syndrome and other connective tissue disorders

#### 164. POTENTIALLY TREATABLE SYMPTOMS IN PRIMARY SJÖGREN'S SYNDROME-ASSOCIATED FATIGUE

Julia Newton<sup>1</sup>, Danielle Powell<sup>1,2</sup>, Sheryl Mitchell<sup>2,3</sup>, Bridget Griffiths<sup>3</sup>, Simon Bowman<sup>4</sup>, Wan-Fai Ng<sup>2,3</sup> and UK primary Sjogren's syndrome Registry<sup>2</sup>

<sup>1</sup>Institute of Ageing and Health, Newcastle University, Newcastle upon Tyne, United Kingdom; <sup>2</sup>Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom;