FRI0061

THE CONTRIBUTION OF TENOSYNOVITIS OF SMALL JOINTS TO THE SYMPTOM MORNING STIFFNESS IN PATIENTS PRESENTING WITH UNDIFFERENTIATED AND RHEUMATOID ARTHRITIS

Aleid Boer¹, Debbie Boeters¹, Ellis Niemantsverdriet¹, Annette van der Helm - van Mil^{1,2}. ¹LUMC, Rheumatology, Leiden, Netherlands; ²ErasmusMC, Rheumatology, Rotterdam, Netherlands

Background: Morning stiffness (MS) is characteristic of Rheumatoid Arthritis (RA) that is associated with functional disability. Despite the known parallel in the circadian rhythm of MS and that of several hormones and pro-inflammatory cytokines in the systemic circulation, it is insufficiently known to what extent local inflammatory processes contribute to this symptom. The correlation between MS and the number of swollen joints is relatively weak but may be underestimated by insufficient sensitivity in measuring local inflammation. MRI is more sensitive in detecting local inflammation. Furthermore, MRI-detected tenosynovitis of small joints is increasingly recognized as early feature of RA which is also associated with functional impairments. Recently it was proposed that this may contribute to MS.

Objectives: We assessed the relationship between MS and MRI-detected inflammation and tenosynovitis in particular.

Methods: 286 consecutive patients newly presenting with undifferentiated and rheumatoid arthritis underwent contrast-enhanced 1.5T-MRI of (2-5) MCP-, (1-5)MTP-, and wrist-joints. Scans were scored for tenosynovitis according to Haavardsholm and for synovitis, osteitis conform the RAM-RIS-method. MS was dichotomized as <60 minutes. Associations between MS and tenosynovitis/synovitis were tested with logistic regression and the presence of a biologic interaction was assessed categorically (solitary or simultaneous presence of synovitis/tenosynovitis).

Results: MS was present in 40% of patients. Tenosynovitis was more often present in patients with MS than without MS (80% versus 65%), OR 2.11 (95%CI 1.21;3.69). Also synovitis was more often present in patients with MS (58% versus 44%), OR 1.83 (1.12;2.96). In categorized analyses the largest association was found for concurrent synovitis and tenosynovitis OR 2.43 (1.30;4.54); whereas single presence of synovitis was not associated (OR 0.85 (0.21;3.47)). The variance explained in all analyses on morning stiffness was small, ranging 3-6%.

Conclusion: Tenosynovitis, and simultaneous presence of tenosynovitis and synovitis in particular, was associated with MS. However, effect sizes suggested that the contribution of local inflammation to this symptom is rather limited.

Acknowledgement: E.C. Newsum and W.P. Nieuwenhuis are acknowledged for scoring MRI-scans.

Disclosure of Interests: Aleid Boer: None declared, Debbie Boeters: None declared, Ellis Niemantsverdriet: None declared, Annette van der Helm - van Mil Grant/research support from: The research leading to these results has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (Starting grant, agreement No 714312) and from the Dutch Arthritis Foundation.

The funding source had no role in the design and conduct of the study.

DOI: 10.1136/annrheumdis-2019-eular.1782

FRI0062

INFECTIONS AMONG RHEUMATOID ARTHRITIS PATIENTS STARTING OR SWITCHING BIOLOGICAL AGENTS. A SYSTEMATIC LITERATURE REVIEW

Marta Novella-Navarro¹, Alejandro Gomez-Gomez², Maria Auxiliadora Martin-Martinez³, Mercedes Guerra-Rodriguez³, Enrique Raya⁴. ¹Hospital Universitario de Torrejón, Rheumatology, Madrid, Spain; ²Hospital Universitario Infanta Sofía, Rheumatology, Madrid, Spain; ³Spanish Society of Rheumatology, Research Unit, Madrid, Spain; ⁴Hospital Universitario San Cecilio, Rheumatology, Granada, Spain

Background: The increased rate of infections is one of the most relevant issues regarding biologic therapies in Rheumatoid Arthritis (RA). There is a large number of studies comparing different biologic agents and biologic vs synthetic DMARDs in order to assess their safety profile. Nevertheless, the main question is whether biologics really increase the infection risk by themselves. Up to date, different studies tried to clarify the actual role that these drugs have in this potentially serious adverse effect, searching for other predisposing conditions related to patient clinical characteristics.

Objectives: To compare the risk of infections between patients starting biologic for the first time (naïve) and patients with an inadequate response to a previous biologic agent (switchers)

Methods: A search strategy was performed by the Spanish Society of Rheumatology documentalists over Pubmed, Embase and Cochrane Library

databases (from January 2008 to February 2018). All the references retrieved were managed using Endnote X7[®]. Screening of studies, data collection and data analysis was performed by 2 reviewers. Meta-analysis, systematic reviews of Randomized Controlled Trials (RCT), Clinical Trials or Cohort studies, comparing data from adult RA patients starting biologics and switching biologics, were selected. After the first screening, a critical review was performed using electronic FLC platform for critical appraisal tools (Osteba[®]) and The Scottish Intercollegiate Guidelines Network (SIGN) was considered to classify the scientific evidence of the selected studies. Studies including patients with chronic infections, tuberculosis reactivations or surgical infections were excluded.

Results: 8 studies were included: 1RCT, 2 Open label study, 1 Open label extension from RCT, 2 subgroups analysis from RCTs and 2 prospective cohort studies.

Overall infection rate was higher in switchers than in naïve patients, with a mean variation between 0.9 and 1.8 100 PY, serious infections were also higher in switchers patients, 2.2 100PY. In both groups, (naïve and switchers), patients treated with more cumulative dose of glucocorticoids (GC) had an increased risk of infections, and it was higher in patients with an inadequate response to previous biologic agents. Mean disease duration was longer in switchers, but this fact was not related to increase of infections.

Conclusion: This systematic review show that overall rate of infections is slightly higher in switchers than in naïve patients, but the fact of having received several biologic agents does not present itself as a risk factor for infection. However, the most important risk factor in the development infections was the higher cumulative doses of GC.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.3175

FRI0063

EFFECTS OF MALALIGNMENT AND DISEASE ACTIVITY ON SECONDARY OSTEOARTHRITIS PROGRESSION IN KNEES OF RHEUMATOID ARTHRITIS PATIENTS

Noriaki Okumura, Taku Kawasaki, Kosuke Kumagai, Mitsuhiro Kubo, Takafumi Yayama, Tomohiro Mimura, Tsutomu Maeda, Shinji Imai. Shiga University of Medical Science, Orthopaedics Surgery, Otsu, Japan

Background: Recent advancements in treatment of rheumatoid arthritis (RA) with disease-modifying anti-rheumatic drugs (DMARDs) have been remarkable, with disease symptoms nearly disappearing due to their strong anti-inflammatory action and many patients achieving remission. As a result, the need for RA-related surgery has shown a yearly decreasing trend, especially knee surgery and synovectomy procedures [1]. On the other hand, cases of secondary osteoarthritis (OA) in knee joints as a symptom associated with RA following a total knee arthroplasty (TKA) are increasing.

Objectives: We investigated the morphology of osteophytes by quantitatively evaluating their size using images obtained prior to performing a TKA. Additionally, the relationships of osteophyte size with patient background, disease activity, and degree of inflammation were examined.

Methods: Radiographs of 35 consecutive knees in 30 RA patients (26 females, 4 males; mean age 63.0 years; median disease duration 15 years) who underwent TKA, including preoperative standing AP view radiographs of the knee joint, were retrospectively analyzed. Using the Image-J software package, osteophyte size in the medial femur (MF), medial tibia (MT), lateral femur (LF), and lateral tibia (LT) regions was determined. Written informed consent for data collection was obtained from all patients in accordance with the Declaration of Helsinki.

Results: Preoperative Larsen grade was 2, 3, 4, and 5 in 1, 12, 18, and 2 patients, respectively, while the mean range of motion of the knee joint was 118° for flexion and -10° for extension. The mean femorotibial angle (FTA) was 178±13.6°, with varus (FTA >180°, n=14) more frequently observed as compared to valgus (FTA <170°, n=7) cases. Mean osteophyte size in the MF, MT, LF, and LT regions was 37.2, 17.0, 27.2, and 4.57 mm², respectively, and significantly greater in the medial compartment (MF+MT) than the lateral compartment (LF+LT) (p<0.001). In the varus cases, osteophyte size in the medial compartment was significantly larger as compared to the normal and valgus cases (p=0.0016). Furthermore, osteophyte size in the medial compartment was negatively correlated with the inflammatory markers CRP (r=-0.492, p=0.0027) and ESR (r=-0.529, p=0.0016), whereas that in the lateral compartment was negatively correlated with disease activity (r=-0.589, p=0.0023).

Conclusion: Our results suggest that secondary OA is a more prominent symptom in RA patients in whom inflammation is controlled, while disease activity has effects on osteophyte size.

REFERENCE:

- [1] Momohara S, Ikari K, Mochizuki T, et al: Declining use of synovectomy surgery for patients with rheumatoid arthritis in Japan. *Ann Rheum Dis* 2009;68:291-2.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.3998

FRI0064

INCREASE OF RHEUMATOID ARTHRITIS AS A CONTRIBUTORY CAUSE OF DEATH IN THE ELDERLY. A NATIONWIDE STUDY IN ITALY, 2003–2015

Francesca Ometto¹, Ugo Fedeli², Costantino Botsios¹, Leonardo Punzi¹, Enrico Grande³. ¹University of Padova, Department of Medicine, DIMED, Padova, Italy; ²Veneto Region, Epidemiological Department, Padova, Italy; ³Italian National Institute of Statistics (ISTAT), Integrated system for health, social assistance, welfare and justice, Rome, Italy

Background: Metanalyses failed to show a decrease of the mortality risk in cohorts of patients with rheumatoid arthritis (RA) between 1950 and 1995. Mortality rates obtained with the analysis of multiple causes of death (MCD) can provide a more complete estimate of the burden of mortality related to RA compared to analysis considering only the underlying cause of death (UCD). Such analyses are available from a limited number of countries, and trends for RA mortality based on MCD were divergent.

Objectives: The objective of the study was to evaluate trends of rheumatoid arthritis (RA) mortality reported as the underlying cause of death (UCD) and as multiple cause of death (MCD) in Italy between 2003 and 2015.

Methods: Analyses were carried out on the Italian National Cause of Death Register, managed by the Italian National Institute of Statistics (ISTAT). Diseases mentioned in the death certificate are coded according to the International Classification of Diseases, 10th Edition (ICD-10, 2009 version). Deaths from January 1, 2003 to December 31, 2015 with mention of RA were included. Time trends of age-standardized rates were analyzed for RA both as UCD and MCD; and the annual percent change (APC) was estimated.

Results: Overall 26,564 deaths with mention of RA were retrieved out of 7,595,214 deaths (0.35% of all certificates). The yearly number of RA-related deaths increased through the study period, meanwhile the probability of selection as the UCD decreased: MCD/UCD ratio was 3.7 in 2003-2006 and 4.8 in 2012-2015 in males; 3.0 and 4.1 in females (Tab.). Mortality rates based on the UCD decreased (males APC -3.1%, CI -3.9, -2.3; females APC -3.3%, CI -4.1, -2.4); while MCD rates for RA-related mortality were stable. Specifically, rates were stable or declined among younger subjects, whereas an increase was registered for the elderly: RA-related deaths in subjects aged ≥ 80 years raised from 48% in 2003-2006 to 59% in 2012-2015 (Fig.).

Conclusion: RA is increasingly mentioned among diseases contributing to death in Italy. Rheumatoid arthritis declined as underlying cause of death in the last decades. We observed a shift of RA-related mortality towards the elderly, possibly because of the progress in therapeutic strategies allowing increased survival of RA patients.

Table. Rheumatoid arthritis-related number of deaths and mortality rates, based on underlying and multiple causes of death.

	2003-2006	2007-2011	2012-2015
Males			
Average annual number of RA-related deaths	441	502	535
Share of all deaths	0.16%	0.18%	0.18%
UCD, average age-standardized rate (x100,000)	0.54	0.47	0.41
MCD, average age-standardized rate (x100,000)	2.01	2.04	1.95
RA selected as the UCD	26%	23%	22%
Females			
Average annual number of RA-related deaths	1392	1557	1699
Share of all deaths	0.49%	0.52%	0.54%
UCD, average age-standardized rate (x100,000)	1.34	1.20	0.98
MCD, average age-standardized rate (x100,000)	4.00	4.04	3.98
RA selected as the UCD	33%	29%	25%

RA, rheumatoid arthritis; UCD, underlying cause of death; MCD, multiple causes of death.

Figure. Multiple causes of death: rheumatoid arthritis-related mortality rates (x100,000) by calendar period and age class.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.3121

FRI0065

PATIENT-REPORTED PALINDROMIC SYMPTOMS IN EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT

Leah Ellingwood¹, Orit Schieir², Marie-France Valois³, Susan J. Bartlett³, Louis Bessette⁴, Carol Hitchon⁵, Gilles Boire⁶, Glen Hazlewood⁷, Edward Keystone², Diane Tin⁸, Carter Thorne⁸, Vivian Bykerk⁹, Janet Pope¹⁰, Canadian Early Arthritis CoHort. ¹Western University, London, Canada; ²University of Toronto, Toronto, Canada; ³McGill University, Montreal, Canada; ⁴Laval University, Quebec, Canada; ⁵University of Manitoba, Winnipeg, Canada; ⁶Universite de Sherbrooke, Sherbrooke, Canada; ⁷University of Calgary, Calgary, Canada; ⁸Southlake Regional Health Centre, Newmarket, Canada; ⁹Hospital for Special Surgery, New York, United States of America; ¹⁰Western University, Rheumatology, London, Canada

Background: The frequency and characteristics of patients with Palindromic Rheumatism (PR) (transient acute attacks of articular inflammation) prior to early rheumatoid arthritis (ERA) are unknown.

Objectives: To compare ERA patients who did versus did not report a history of transient episodes of joint inflammation preceding RA diagnosis.

Methods: Study participants were patients with ERA or suspected RA (symptoms <1 year; 83% met 2010 ACR/EULAR criteria) enrolled in the Canadian Early Arthritis CoHort (CATCH) between April 2017 to March 2018 who completed a questionnaire on prior inflammatory joint symptoms that "come and go". Chi-square and t-tests were used to compare characteristics in patients with versus without a reported history of prior palindromic symptoms. Simple, and multivariable logistic regression with backward selection ($p < 0.2$) were used to determine crude and adjusted predictors of palindromic symptoms.

Results: 154 ERA patients were included; 66% were female and mean (sd) age was 54 (15) years. 54% had previous joint pain and swelling prior to their current episode; 42% endorsed prior episodic joint pain and swelling, approximately half of whom (20% of total, N=31) reported transient joint symptoms for over six months. Patients reporting previous palindromic symptoms were more often female, seropositive, had more comorbidities, and lower swollen joints and baseline CDAI ($p < 0.05$). In multivariable regression, female sex, higher income, seropositivity, back or spine issues, and lower CDAI were associated with history of palindromic symptoms (Table 1).

Conclusion: Half of ERA patients self-reported transient episodes of inflammatory arthritis prior to being diagnosed with RA. They are more likely female, seropositive, with higher income and lower disease activity.

Acknowledgement: The CATCH study was designed and implemented by the investigators and financially supported through unrestricted research grants from: Amgen and Pfizer Canada - Founding sponsors since January 2007; AbbVie Corporation since 2011; Medexus Inc. since 2013; Eli Lilly Canada since 2016 and Merck Canada since 2017. Previously funded by Hoffmann-LaRoche and Janssen Biotech from 2011-2016, UCB Canada and Bristol-Myers Squibb Canada from 2011-2018, and Sanofi Genzyme from 2016-2017.