Aggrecan Degradation Is Not Just Aggrecan Degradation – A Study of Neo-Epitopes (NITEGE and ARGS) of Aggrecanase Degradation

Siebuhr, Anne Sofie; He, Yi; Hoielt, Sabine; Luo, Yunyun; Karsdal, M.A.; Bay-Jensen, A-C

Publication date:
2016

Document version
Publisher's PDF, also known as Version of record

Citation for published version (APA):
Siebuhr, A. S., He, Y., Hoielt, S., Luo, Y., Karsdal, M. A., & Bay-Jensen, A-C. (2016). *Aggrecan Degradation Is Not Just Aggrecan Degradation – A Study of Neo-Epitopes (NITEGE and ARGS) of Aggrecanase Degradation*. 955.1-955.

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/310779197>

AB0171 Aggrecan Degradation Is Not Just Aggrecan Degradation – A Study of Neo-Epitopes (NITEGE and ARGS) of Ag....

Conference Paper in *Annals of the Rheumatic Diseases* · June 2016

DOI: 10.1136/annrheumdis-2016-eular.3832

CITATIONS

0

READS

5

6 authors, including:

Anne Sofie Siebuhr

Nordic Bioscience

75 PUBLICATIONS 277 CITATIONS

[SEE PROFILE](#)

Yi He

Nordic Bioscience

40 PUBLICATIONS 265 CITATIONS

[SEE PROFILE](#)

Sabine Hoielt

Nordic Bioscience

7 PUBLICATIONS 6 CITATIONS

[SEE PROFILE](#)

Yunyun Luo

Nordic Bioscience

11 PUBLICATIONS 90 CITATIONS

[SEE PROFILE](#)

observation period only 52.4% of patients were vitamin D sufficient. New erosions in ultrasound examination were found in 14 (21.5%) patients. We have found no significant difference between vitamin D sufficient and insufficient patients according to the average indices of disease activity, disease activity improvement, time to achieve remission, duration of the remission and disease progression during the first year of therapy.

Conclusions: Higher disease activity at RA onset is associated with lower serum vitamin D concentration. Vitamin D supplementation does not improve disease outcome during the first year of therapy.

References:

- [1] M. Salehi, Z. Farajzadegan. Efficacy of vitamin D in patients with active rheumatoid arthritis receiving methotrexate therapy. *Rheumatol Int* 2012; 32: 2129–2133
- [2] K. Gopinath, D. Donda. Supplementation of 1,25 dihydroxy vitamin D3 in patients with treatment naïve early rheumatoid arthritis: a randomized controlled trial. *International Journal of Rheumatic Diseases* 2011;4: 332–339

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2016-eular.2634

AB0171 AGGREGAN DEGRADATION IS NOT JUST AGGREGAN DEGRADATION – A STUDY OF NEO-EPITOPES (NITEGE AND ARGS) OF AGGREGANASE DEGRADATION

A.S. Siebuhr, Y. He, S. Hoielt, Y.R. Luo, M.A. Karsdal, A.-C. Bay-Jensen. *Biomarkers and Research, Nordic Bioscience, Herlev, Denmark*

Background: Cartilage degradation is a hallmark of arthritic disease. The main constituents of cartilage is aggrecan and type II collagen. Previous studies have shown that aggrecan degradation is prior to type II collagen degradation and that only aggrecanase degradation but not matrix metalloproteinases (MMP) degradation of aggrecan was reversible¹. It is therefore essential to have biomarkers that can detect reversible and irreversible aggrecan degradation to identify the condition of the cartilage. Of the well-known aggrecanase degradation site at NITEGE^{373,374} ARGS, ARGS is released by only aggrecanase, but NITEGE is retained in the aggrecan molecule and in theory needs additional aggrecan degradation to be released. The numbers indicate the aggrecanase cleavage site.

Objectives: Investigate the profile of two neo-epitope biomarkers of aggrecanase degraded aggrecan at NITEGE373–374ARGS in a bovine cartilage explants model.

Methods: Catabolic stimulated (oncostatin M and TNF- α ; O+T) bovine cartilage explants were treated with or without the generic MMP inhibitor, GM6001. Explants without catabolic stimulation was used as negative control. In the culture supernatant two biomarkers investigating aggrecanase degraded aggrecan was measured. The AGNxl competitive ELISA detects the NITEGE³⁷³ neo-epitope and the ARGS sandwich ELISA detects the ³⁷⁴ARGSVI neo-epitope. Statistical differences between groups were tested by two-way ANOVA.

Results: The AGNxl level was significantly increased compared to w/o from day 5 to day 17. GM6001 significantly lowered the release of AGNxl compared to O+T alone at day 7 ($p < 0.0001$), day 10 ($p = 0.0007$) and 12 ($p = 0.01$). In addition, GM6001 shifted the release to 2 days later in the culture period, as the AGNxl level was first significantly increased compared to w/o at day 7 to day 17, where the level was higher than O+T, but non-significant. The ARGS level was significantly increased at day 5, 10 and 12 for both O+T and O+T + GM6001 compared to w/o. At day 10 the ARGS level was higher in O+T + GM6001 than O+T ($p < 0.0001$).

Conclusions: The prolonged release of AGNxl and the significantly lowered level of AGNxl with the MMP-inhibitor, suggest that the AGNxl release is somewhat dependent of MMP activity. In contrast, the ARGS release seems not to be MMP-dependent as there was a significant increase in O+T with the MMP-inhibitor compared to w/o and the peak was pronounced. In summary, aggrecan degradation is not just aggrecan degradation and different neo-epitopes have different importance in cartilage degradation.

References:

- [1] *Arthritis Res Ther.* 2008;10(3):R63

Disclosure of Interest: A. S. Siebuhr Employee of: NORDIC BIOSCIENCE A/S, Y. He Employee of: NORDIC BIOSCIENCE A/S, S. Hoielt: None declared, Y. Luo: None declared, M. Karsdal Shareholder of: NORDIC BIOSCIENCE A/S, Employee of: NORDIC BIOSCIENCE A/S, A.-C. Bay-Jensen Employee of: NORDIC BIOSCIENCE A/S

DOI: 10.1136/annrheumdis-2016-eular.3832

AB0172 USEFULNESS OF THE JAPANESE VERSION OF THE PATIENT-RATED ELBOW EVALUATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. Takeshita¹, D. Kaneda¹, M. Horita¹, T. Machida¹, R. Nakahara¹, Y. Nasu², K. Hashizume³, K. Nishida⁴, T. Ozaki¹. ¹Orthopaedic Surgery; ²Medical Materials for Musculoskeletal Reconstruction, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences; ³Rehabilitation, Japan Labour Health and Welfare Organization Okayama Rosai Hospital; ⁴Human Morphology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama City, Japan

Background: Patient self-administered questionnaires remove the possibility of observer bias, and are important instruments for the assessment of clinical outcome. The patient-rated elbow evaluation (PREE) is a joint-specific, self-administered questionnaires.

Objectives: We aimed to investigate the correlation between the Japanese version of PREE (PREE-J) and other clinical parameters in rheumatoid arthritis (RA) patients before and after total elbow arthroplasty (TEA).

Methods: Thirty-five elbows in 32 RA patients (M/F: 3/29) were replaced by TEA. The mean age was 62.1 (range 41–79) years at the time of surgery, the mean follow-up period was 21.5 (range 12–36) months. All patients were assessed pre- and post-operatively by PREE-J, elbow and forearm range of motion (ROM), Disease Activity Score with 28 joint using CRP (DAS28-CRP), Mayo Elbow Performance Score (MEPS), Japanese version of the Disabilities of the Arm, Shoulder and HAND (DASH-JSSH) and Health Assessment Questionnaire Disability Index (HAQ-DI). The changes of parameters after surgery were examined by Wilcoxon signed-rank test, and the correlation between PREE-J and other parameters was examined using Spearman's correlation coefficients.

Results: Both pre- and post-operative PREE-J significantly correlated with DAS28-CRP, DASH-JSSH, and HAQ-DI. Significant improvement was observed after surgery in all parameters except for HAQ-DI. The mean postoperative MEPS improved from 50.3±16.4 points to 98.1±3.2 points, the average postoperative PREE-J improved from 54.7±19.3 points to 27.1±24.4 points. The correlation between PREE-J and MEPS was significant preoperatively ($p < 0.01$), but the correlation disappeared postoperatively. The correlation between PREE-J and ROM was not significant pre- and post-operatively.

Conclusions: The current study indicated that elbow evaluation by patients who underwent TEA showed significant correlation with disease activity, upper limb function and disability in daily life. It was revealed preoperative PREE-J also well correlated with MEPS, which is widely accepted evaluation system by elbow surgeons. Interestingly, PREE-J did not correlate with MEPS and ROM postoperatively. As PREE-J contains many questions about complex motions required the multiple joint function of upper extremity, it is possible PREE-J might be influenced by other joints affected by RA. MEPS (up to 100 points) evaluates pain (45), ROM (20), function (25) and instability (10) of the elbow, and reached almost perfect score by TEA. PREE-J evaluates pain and function with more detailed questionnaires than MEPS, some of them cannot be solved by a single joint surgery. Our results suggested PREE-J might be useful and wide range evaluation instrument for functional improvement of upper extremity after TEA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2016-eular.2637

AB0173 ROLE OF ANTI CITRULLINATED PROTEIN ANTIBODIES IN FOLLOW-UP AND RADIOGRAPHIC DAMAGE IN A GROUP OF PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

C. Carrasco Cubero¹, E. Vergara Prieto², I. Alcalá Peña², J.L. Álvarez Vega¹, J.M. Salazar Vallinas¹, M. Mota Medina³, C. Rodríguez Godoy⁴, D. Sánchez Paré⁴, M.L. Vargas Pérez². ¹Rheumatology; ²Immunology, Hospital Infanta Cristina; ³Mathematics, University of Extremadura; ⁴Radiology, Hospital Infanta Cristina, Badajoz, Spain

Background: Autoantibodies in early rheumatoid arthritis (RA) have important diagnostic value. Anti citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) are believed to be associated with more severe clinical outcomes, but the utility of both autoantibodies in the clinical follow-up of disease is controversial. It has recently been described that bone damage in early and even recent-onset RA is attributed to ACPAs, which form years before clinical symptoms start to emerge¹.

Objectives: To investigate the longitudinal course of immunological markers, ACPA and RF, during the first year after diagnosis of RA, to see their utility for the clinical follow-up. In addition, to assess if the baseline values of ACPA are associated with the severity of initial radiographic involvement.

Methods: The study population was 52 patients diagnosed with early RA according to ACR-EULAR 2010 classification criteria, with ACPA positive. Serum samples at baseline, 3, 6 and 12 months were analyzed, and levels of ACPA, RF, C reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were determined. Values of DAS 28, SDAI and HAQ were employed as clinical activity markers. To analyse the variations of the measured parameters, we expressed the values of each analytic and clinical parameter as "Variation Index" on the baseline value for each patient (VI (x month)=Value (x month)/Value (baseline)). The statistical study was made through canonical correlation analysis and linear regression. Radiographic damage was evaluated using Sharp scores modified