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Can imaging improve outcome in OA?

OP0197

EVALUATING THE RELATION OF STRUCTURAL DAMAGE BY MRI TO CLINICAL PAIN SCORES, PAIN SENSITISATION AND TYPE II COLLAGEN DEGRADATION IN KNEE OSTEOARTHRITIS

Nidhi Sofat¹, Vivian Ejindu², Christine Heron², Lena Assi³, Anasuya Kuttapitiya⁴, Guy Whitley⁵, Soraya Koushesh³, Abiola Harrison¹, Franklyn Howe⁶. ¹Infection and Immunity, Musculoskeletal Research Group, London, United Kingdom; ²St George's Hospital, Department of Radiology, London, United Kingdom; ³Institute for Infection and Immunity, Musculoskeletal Research Group, St George's, University of London, London, United Kingdom; ⁴Institute for Infection and Immunity, Musculoskeletal Research Group, St George's, University of London, London, United Kingdom; ⁵Molecular and Clinical Sciences Research Group, St George's, University of London, London, United Kingdom; ⁶Molecular and Clinical Sciences Institute, St George's, University of London, London, United Kingdom

Background: The evolution of pain in relation to damage in the synovium, bone and cartilage in osteoarthritis (OA), coupled with their relation to wet biochemical markers are not well understood.

Objectives: In this study we evaluated the relation between structural damage by MRI, clinical and pain sensitisation measures and wet biochemical biomarkers in knee OA.

Methods: We recruited 130 participants fulfilling ACR criteria with advanced OA requiring total knee replacement (TKR) (n=80), mild OA having standard care (n=42) and non-OA controls (n=8). Knee MRI in 90 subjects (72 F, 18 M) was acquired and assessed by two radiologists with the MRI Knee Osteoarthritis Score (MOAKS). Overall MOAKS scores were created for Bone Marrow Lesions (BML), Cartilage Degradation (CD) and effusion/Hoffa synovitis (tSyn). Type II collagen cleavage products (CTX-II) were determined by ELISA. Clinical scoring was performed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for pain levels (WOMAC_P), Hospital Anxiety and Depression Scale (HADS), Body mass index (BMI) and pain sensitisation with pain pressure thresholds (PPT) of the patella by Quantitative Sensory Testing (QST).

Results: The mild OA group had a mean age of 63 +/-9 yr and the advanced OA group 69 +/-9 yr. The advanced OA group had higher levels of pain, with a mean WOMAC_P of 58 +/- 22 compared with the mild OA group who had a mean WOMAC_P of 40 +/-22. WOMAC_P correlated with the total number of regions with cartilage damage (nCD) (R=0.225, p=0.033) and total number of BMLs (nBML) (R=0.195, p=0.065) using BMI, age and HADS as covariates. Levels of CTX-II correlated with tSyn (R=0.313, p=0.03), nBML (R=0.252, p=0.019), number of osteophytes (R=0.33, p=0.002) and nCD (R=0.218, p=0.042), using BMI and age as covariates. The correlation for urinary CTX-II with tSyn (p=0.006) is shown in Figure 1 using a partial linear regression analysis of MOAKS, BMI and age. We also found CTX-II correlated with lesion load scores (total number of lesions multiplied by MOAKS size by% damage scores) for CD (R=0.277, p=0.009) and BML (r=0.308, p=0.004). PPT correlated with patella MOAKS scores for nBML (R=-0.221, p=0.038) and nCD (R=-0.279, p=0.009), with HADS, BMI and age as covariates.

Conclusion: There is a direct correlation between the degree of cartilage damage and BMLs with pain in OA. Type II collagen degradation products were higher when there was more severe MRI-detected synovitis, BMLs and cartilage damage in the knee joint, suggesting that the source of enzymes degrading type II collagen in OA, including matrix metalloproteinases, are also likely to be produced by synovium and bone (1) and not just cartilage, as previously hypothesised in other studies. There was also a correlation between pain sensitisation and frequency of BMLs and cartilage degradation, suggesting that molecular mediators of pain sensitisation, which we have shown are produced by BMLs (1), are a cause of patient-reported OA pain.

REFERENCES:

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Figure 1

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MRI-DETECTED STRUCTURAL ABNORMALITIES AND DEVELOPMENT OF INCIDENT RADIOGRAPHIC KNEE OSTEOARTHRITIS OVER 10 YEARS OF FOLLOW-UP

C. Kent Kwok¹, Frank Roemer², Leena Sharma³, Erin Ashbeck⁴, Chengcheng Hu⁴, Ali Guermazi⁵, For the Biomarkers of Early Arthritis of the Knee (BEAK) Investigators. ¹University of Arizona, Tucson, United States of America; ²University of Erlangen-Nuremberg, Erlangen, Germany; ³Northwestern University, Chicago, United States of America; ⁴University of Arizona, Tucson, United States of America; ⁵Boston University, Boston, United States of America

Background: Structural joint pathology on MRI has been found in knees without radiographic evidence of osteoarthritis (OA). We have previously shown that structural abnormalities on MRI may be precursors of disease and associated with the detection of incident radiographic knee OA (ROA) up to 2 years later, and in some circumstances up to seven years later. The prognostic value of structural abnormalities on MRI for knee OA, however, is unknown.

Objectives: Estimate the probability of incident ROA over 10 years of follow-up, according to structural abnormalities detected on baseline MRIs.

Methods: A subcohort of participants (862 knees, one knee/person) from the Osteoarthritis Initiative (OAI) with at least one knee at risk of developing ROA (i.e., Kellgren-Lawrence (KL) 0,1 at baseline) was randomly selected. MRI-detected structural features of the knee were assessed by expert readers using the MRI Osteoarthritis Knee Score (MOAKS). Participants underwent bilateral posteroanterior fixed-flexion weight-bearing knee radiography at baseline and annually through year 4, and then every two years until year 10. Radiographs were centrally read for KL grade, with ROA defined as KL₂ or greater. Survival was estimated with the Turnbull non-parametric maximum likelihood estimator, a generalization of Kaplan Meier curves for interval censored data. Survival curves were compared using a log rank permutation test available in the R package interval. Hazard ratios were estimated using Cox models fit using the R package icenReg, designed for interval censored data. Features were considered one at a time, with no adjustments.

Results: Knees with any of the following structural abnormalities had higher estimated probabilities for the development of radiographic OA within two, four and 10 years of follow-up: effusion-synovitis, Hoffa-synovitis, bone marrow lesions in the medial compartment and whole knee, surface area and full thickness cartilage damage in the medial compartment and whole knee, and medial meniscal extrusion (Table 1). Differences in the probability for the development of ROA within two, four, and 10 years of follow-up were significant (pointwise 95% confidence intervals did not include 0), between knees without the abnormality and knees in the most severe category for all features, with one exception at the two-year follow-up. All of these abnormalities were significantly associated with time to ROA over 10 years of follow-up.

Table 1. Baseline MRI-Detected Structural Abnormalities and Incident Radiographic Osteoarthritis

MRI-detected abnormalities at baseline	Knees	Estimated Probability of Radiographic OA			P value*	Hazard Ratio	(95% CI)
		Within 2 years	Within 4 years	Within 10 years			
Effusion-Synovitis							
Physiologic amount	692	0.06	0.10	0.27	<.0001	1.00	ref
Small	146	0.15	0.31	0.46		2.11	(1.81, 2.40)
Medium/Large	24	0.48	0.62	0.67		5.10	(3.55, 7.34)
Hoffa-Synovitis							
Normal	593	0.05	0.11	0.25	<.0001	1.00	ref
Mild	248	0.16	0.24	0.44		1.97	(1.72, 2.26)
Moderate/Severe	21	0.43	0.43	0.54		4.09	(2.75, 6.07)
BML, Medial knee Max Score							
0: none	733	0.08	0.13	0.27	<.0001	1.00	ref
1: <33%	110	0.12	0.19	0.49		1.82	(1.54, 2.15)
2/3: >=33%	19	0.39	0.57	0.59		3.82	(2.49, 5.86)
BML, Whole knee Max Score							
0: none	339	0.06	0.10	0.21	<.0001	1.00	ref
1: <33%	333	0.08	0.13	0.33		1.43	(1.22, 1.67)
2: 33-66%	143	0.14	0.25	0.43		2.14	(1.76, 2.57)
3: >66%	47	0.24	0.41	0.56		3.25	(2.49, 4.24)
Cartilage Damage, Surface Area, Medial Max Score							
0: none	558	0.08	0.12	0.21	<.0001	1.00	ref
1: <10%	146	0.05	0.12	0.36		1.63	(1.38, 1.94)
2: 10-75%	158	0.19	0.28	0.56		2.85	(2.45, 3.32)
Cartilage Damage, Full Thickness, Medial Max Score							
0: none	824	0.09	0.15	0.30	<.0001	1.00	ref
1/2: Any	48	0.18	0.35	0.57		2.70	(2.17, 3.36)
Cartilage Damage, Surface Area, Whole Knee Max Score							
0: none	146	0.04	0.06	0.13	<.0001	1.00	ref
1: <10%	235	0.03	0.06	0.18		1.41	(1.05, 1.90)
2: 10-75%	454	0.13	0.21	0.43		3.67	(2.81, 4.80)
3: >75%	27	0.43	0.43	0.66		8.66	(3.40, 13.86)
Cartilage Damage, Full Thickness, Whole Knee Max Score							
0: none	574	0.07	0.11	0.25	<.0001	1.00	ref
1: <10%	167	0.11	0.20	0.39		1.73	(1.47, 2.02)
2/3: >10%	121	0.18	0.28	0.52		2.41	(2.04, 2.90)
Meniscus Extrusion, Medial							
<2 mm	677	0.06	0.12	0.24	<.0001	1.00	ref
2: 2-3 mm	141	0.19	0.32	0.55		2.51	(2.15, 2.97)
2/3: >3 mm	44	0.20	0.25	0.55		2.88	(2.27, 3.66)

*Asymptotic Logrank k-sample test (permutation form), Sun's scores

Conclusion: Our results demonstrate the prognostic value of effusion-synovitis, Hoffa-synovitis, bone marrow lesions, cartilage damage, and meniscal extrusion