

(JKOM) score (J Rheum 2005). The measure was proven to have sufficient reliability and validity by means of a statistical evaluation and comparison with other health-related scales such as the WOMAC and the SF-36. The Zung self-rating depression scale (SDS) was used to evaluate depression. When a patient showed SDS greater than 40, he/she was defined as a state of depression. Logistic regression analysis was conducted with statistics software SPSS (Ver. 21) using SDS scores as a dependent variable and clinical data (age, BMI, JKOM-pain and stiffness in knee, JKOM-condition in daily life, JKOM-general activities, JKOM-health conditions, radiographic knee OA severity [K/L grade 2 group and K/L grade 3 or 4 group]) as covariates. Each covariate was divided into two groups according to the median value.

Results: The ninety-three of 250 patients showed the K/L grade 2 group, while the remaining 157 patients showed the K/L grades 3 or 4. The mean SDS score of the patients in the present study was 39.6 points, and 50.8% (127 patients) of the patients were identified to be in a depressive state. No significant differences of the SDS scores of the patients with K/L grade 2 were observed in comparison to those of the patients with K/L grade 3 or 4. In logistic regression analyses using SDS as a dependent variable, the independent variables those had achieved a statistically significant regression coefficient were the following two factors: JKOM-condition in daily life scores [$\beta=1.264$, $p=0.002$, odds ratio (OR); 3.54 (95% CI; 1.57 to 7.99)] and JKOM-health condition scores [$\beta=0.917$, $p=0.005$, OR; 2.50 (95% CI; 1.32 to 4.76)].

Conclusions: Among the patients with knee OA, approximately half of the patients were defined as a depressive state. The radiographic OA severities of the patients were not associated with the depressive state, but the daily life conditions and the health conditions evaluated by the patient-oriented outcome measure were the independent significant influential factors for the severity of depressive state in patients with knee OA.

496 HISTOPATHOLOGICAL CLASSIFICATION AND SCORING OF OSTEOARTHRITIS AS A MULTI-TISSUE DISEASE

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Purpose: Osteoarthritis (OA) might be the end result of a variety of pathological processes in several joint tissues. Changes in articular cartilage, subchondral bone and synovium may each contribute to OA symptoms. Histopathological scoring systems for OA focus on articular cartilage. Although logically derived, they have been subjected to only limited validation and have reportedly poor ability to distinguish OA cases from healthy controls. Rasch analysis is a psychometric tool used to validate or improve outcome scales. We aimed to optimise the fit of the 4-item Mankin score to the Rasch model and extend this to develop a validated histopathological score that reflects OA as a multi-tissue disease.

Methods: Medial tibial plateaus and synovium were collected from 345 post-mortem (PM) and 143 total knee replacement (TKR) donations, and histological changes were graded. Osteophytes, a hallmark of OA, were visualised on the dissected knee for PM cases, or using radiographs in end-stage OA (TKR) cases. The presence of osteophytes or cases with end-stage OA (TKR) was used as reference standard for OA classification, and histopathological features were selected that displayed statistically significant associations with OA classification. The Mankin histological grading score was subjected to Rasch analysis and items were rescaled where appropriate, and supplemented with histological scores for subchondral bone marrow replacement by fibrovascular tissue and synovitis. Weightings for the 6 items were derived by principle components analysis (PCA). The resulting weighted 6-item score was compared with the original 4-item Mankin score using area under receiver operating characteristic curves (AUC). Multiple partitioning of the data was used to test reliability of the results.

Results: Cartilage integrity, chondrocyte appearance, proteoglycan loss, tidemark breaching, subchondral bone marrow replacement and synovitis were each significantly associated with TKR ($P \leq 0.006$) and with osteophytes ($P \leq 0.002$). Rasch analysis indicated misfit of the Mankin

score to the Rasch model. Chondrocyte morphology scoring showed evidence of disordered thresholds, which was resolved by collapsing scores for chondrocyte hypercellularity and cloning. Person separation index was low (< 0.7). PCA indicated raw weightings which were transformed to produce a scale with a range of 0 to 10. The final score comprised of contributions of cartilage surface integrity (46%), proteoglycan depletion (20%), synovitis (16%), chondrocyte morphology (10%), subchondral bone marrow replacement (5%) and tidemark integrity (3%). The revised 6-item weighted score was better than the 4-item Mankin score for determining cases with end-stage OA (AUC; 0.85 and 0.75, respectively, $P < 0.0001$) or with osteophytes (AUC; 0.79 and 0.73, $P = 0.0001$).

Conclusions: Synovitis and subchondral marrow replacement by fibrovascular tissue are characteristics of knee OA, and incorporating histological scores for these features alongside chondropathy improved ability to distinguish OA from non-OA cases. Chondrocyte hypercellularity and cloning may not represent incremental OA severity, but rather be parallel processes in cartilage samples with similar chondropathy. Tidemark integrity is a feature of OA, but might contribute less to diagnostic classification than do chondropathy and synovitis. All histological scores tested displayed limitations as measurement tools, and better understanding of pathological processes in early disease is needed to inform further modifications that might improve targeting across the range of OA, including non-TKR populations.

497 BASELINE MAGNETIC RESONANCE IMAGING CARTILAGE T2 RELAXATION TIME MEASUREMENTS AS PREDICTORS OF TOTAL KNEE ARTHROPLASTY IN AFRICAN-AMERICANS – DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: Total knee arthroplasty (TKA) represents a prevalent outcome for end-stage knee osteoarthritis (OA), but the procedure is costly and postoperative complications are common. We currently lack reliable prognostic markers that can be used at early stages of OA to predict the eventual need for TKA later on. A predictive biomarker of this nature could also be helpful to physicians and patients in their treatment planning. Thus, the aim of this study was to determine whether baseline cartilage T2 relaxation time obtained with 3 Tesla magnetic resonance imaging (MRI) can be used as a predictive biomarker for TKA 4 to 7 years later.

Methods: An observational nested case-control study was performed using data from the Osteoarthritis Initiative (OAI), a longitudinal multicenter study including 4796 subjects with or at risk of knee OA, with the exception of a small control group of subjects without OA risk factors. Subjects who sustained a right knee TKA 4 to 7 years following enrollment in the OAI study were identified as cases ($n=81$). Subjects without total knee arthroplasty but with radiographic knee OA were identified as controls ($n=228$). Subjects were frequency-matched using a 1:3 ratio of cases to controls according to the following parameters: baseline Kellgren-Lawrence grade (0-3), age (45-79 years), gender, BMI, and race (Caucasian-Americans: $n=70$ cases, 204 controls; African-Americans: $n=8$ cases, 22 controls). 3 Tesla magnetic resonance images were obtained in the right knee of each patient at the enrollment visit. Knee cartilage was segmented semi-automatically in a sagittal T2 map 2-D Multi-Slice Multi-Echo (MSME) spin-echo sequence. Mean cartilage T2 relaxation time values were quantified in 5 cartilage compartments: lateral femur (LF), lateral tibia (LT), medial femur (MF), medial tibia (MT), and patella (PAT). A global T2 value (GLO) per whole joint was obtained by calculating the mean of the T2 values per compartment. A conditional logistics regression model was run using STATA version 12 software (StataCorp LP, College Station, TX). Odds ratios were calculated per standard deviation (SD) change in T2.

Results: Although no associations were found between baseline T2 values and the occurrence of TKA in the entire cohort, stratification by race yielded significant associations. In the African-American cohort, a one SD rise in global baseline mean T2 value was significantly associated with an approximate 70% increase in the risk of undergoing TKA 4 to 7 years later (GLO: OR=1.74, $p=0.04$). Specifically, a one SD rise in lateral