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We aimed to gain a deeper understanding of OA pathophysiology by assessing how structural changes including bone marrow lesions (BMLs), cartilage loss, synovitis or effusion relate to clinical pain measures in people with knee OA. We were particularly interested to assess how specific structural abnormalities related to pain measured by validated questionnaires that are used as clinical endpoints in knee OA clinical studies. **Methods:** We conducted a prospective, observational study in people with advanced and mild OA who were attending rheumatology and orthopaedic clinics at a London teaching hospital. Participants were assessed for their level of pain using the Western Ontario and MacMaster Universities Osteoarthritis Index (WOMAC) pain, stiffness and function scores, the Visual Analogue Scale (VAS) for pain, sensitisation scores using painDETECT and the Hospital Anxiety and Depression Scale (HADS). In addition, each subject underwent magnetic resonance imaging (MRI) of their target painful knee using standard T1-weighted and fat-suppressed T2-weighted images with a 3T scanner. Two Consultant Radiologists independently scored the level of cartilage degradation, BMLs, synovitis and effusion severity using the semi-quantitative MRI knee osteoarthritis score (MOAKS). We compared radiographic severity for structural changes in the two groups: mild OA (receiving standard medical management for knee OA) and advanced OA (undergoing joint replacement surgery). We also conducted correlation analyses of radiographic changes with individual pain scores using the analysis of covariance (ANCOVA). **Results:** We evaluated n=88 participants who had completed pain and function questionnaires and undergone MRI evaluation of their target painful knee. Our group comprised of participants with mild OA (n=22) and advanced OA (n=66). The mean age in the mild OA group was 61.8 (8.2) and the advanced OA group was 68.8 (7.8). The mean BMI in the mild OA group was 28.6 (4.1) and the advanced group was 32.3 (5.7). A summary of the MOAKS grading, WOMAC pain and VAS pain are summarized (see Table). We observed a significant correlation between MOAKS identified cartilage loss and WOMAC pain (p=0.009), WOMAC stiffness (p=0.004), WOMAC function (p=0.004) and VAS for pain (p=0.047) when adjusting for BMI and age as confounders. A correlation was also observed between MOAKS-identified BMLs and VAS pain (p=0.029) - however, this correlation was not significant after adjusting for BMI and age as confounders (p=0.057). We also observed a significant correlation between VAS pain and WOMAC pain and HADS scores (p<0.05). No significant correlations were observed between synovitis/effusion and pain scores (data not shown). **Conclusions:** Our study found that the strongest correlation was between the outcome scores for WOMAC pain, stiffness, function and VAS pain with cartilage degradation. We did not observe a significant correlation between painDETECT and MOAKS-assessed structural damage, suggesting that painDETECT is a marker of pain sensitization rather than nociceptive pain reflected by structural damage. Our data also demonstrate that participants with knee OA who report the highest pain levels are also more likely to experience significant anxiety and/or depression. Our data show that in a cohort of knee OA subjects with a range of structural damage from mild OA to advanced OA, the strongest structural correlates with clinical pain are cartilage degradation. It would be useful for future studies to include clinical and structural damage measures to ensure optimal patient stratification of OA phenotypes.   |  |  |  |  | | --- | --- | --- | --- | | Summary of MOAKS damage and clinical pain scores | | | | | MOAKS parameter | Frequency N(%) | WOMAC Pain Mean (SD) | VAS Pain Mean (SD) | | Bone Marrow Lesion Severity Score |  |  |  | | MOAKS=0 | 24 (27.3) | 46.1 (25.9) | 4.1 (2.8) | | MOAKS=1 | 61 (69.3) | 58.3 (22.2) | 5.7 (2.2) | | MOAKS=2 | 3 (3.4) | 40.1 (21.6) | 4.7 (3.3) | | MOAKS=3 | - | - | - | | Cartilage Damage Severity Score |  |  |  | | MOAKS=0 | 8 (9.0) | 28.6 (24.7) | 2.6 (2.6) | | MOAKS=1 | 27 (30.7) | 46.6 (19.7) | 4.5 (2.1) | | MOAKS=2 | 46 (52.3) | 63.2 (22.2) | 6.1 (2.2) | | MOAKS=3 | 7 (8.0) | 55.8 (18.6) | 5.6 (3.3) | | |

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