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**Defining the characteristics of pain in osteoarthritis to guide treatments**   
  
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**Background:** Osteoarthritis (OA) is a debilitating condition involving multiple joint changes, including cartilage degradation, bone marrow lesions (BMLs) and synovitis. OA pain afflicts millions of citizens worldwide and whilst its origins remain obscure, recent studies link pain to the presence, size and frequency of BMLs, cartilage degradation and synovitis. The aim of this study was to evaluate the relationship between clinical features of pain and structural damage in participants with knee OA.  
**Methods:** We conducted a longitudinal study in participants with full informed consent. Participants were recruited with differing stages of OA, including mild, moderate and severe changes based on Kellgren-Lawrence grading. Data for pain characteristics, including pain scores by WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) and the Visual Analogue Scale (VAS), pain pressure algometry (PPT) and structural damage by MRI using the MRI Knee Osteoarthritis Score (MOAKS) were used to assess the level of pain and structural damage respectively. Dataset analyses were then performed to evaluate the level of structural damage in relation to pain by clinical outcome scores and PPT. Data was corrected for confounding by age and body mass index (BMI). We measured response to treatment after 12 months using the OARSI (Osteoarthritis Research Society International) response criteria, based on detailed WOMAC and VAS scores obtained in the study.  
**Results:** We evaluated a total of 124 participants with knee OA. Of the whole group, 74% had advanced OA requiring a total knee replacement (TKR) and 26% had mild OA requiring medical management. We found that participants undergoing total knee replacement for OA had significantly higher MRI measures of structural damage that included BMLs, synovitis and cartilage damage, than patients undergoing standard medical management (p=0.009 correcting for age and BMI). Whilst 83% of participants undergoing TKR showed a positive treatment outcome, only 24% who were undergoing medical management showed an improvement with standard treatment, with 36% of participants showing relative stability and 29% showing progression in disease symptoms. Participants undergoing standard medical care had a range of structural damage with total MOAKS scores overlapping with those going for TKR, and the progression in disease symptoms was not related to MOAKS, but was related to sensitisation by PPT (p=0.025 between responders and non-responders to conventional medical treatment).  
**Conclusion:** Our data suggest that it is possible to stratify people into distinct subgroups with knee OA. We found that the majority of participants undergoing knee replacement have a good improvement after surgery. However, subjects undergoing medical management have a poorer outcome when they displayed features of pain sensitisation. Our data suggest that subgrouping of participants by pain sensitisation measures may improve stratification and guide improved therapeutic pathways for osteoarthritis.