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INVOLVEMENT OF PATELLA DAMAGE IN PAIN SENSITISATION AND TREATMENT OUTCOME IN KNEE OSTEOARTHRITIS

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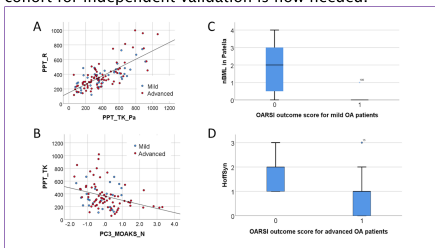
Abstract:

Purpose: Chronic pain is a major clinical symptom of knee osteoarthritis (OA) and the target of treatment with analgesics in early stage mild OA prior to later stage treatment by total knee replacement (TKR) in advanced OA. However, not all patients show a good treatment response in terms of pain management. By using detailed analysis of knee MRI we aimed to better understand what pathological factors of knee damage relate to patient reported pain, pain sensitisation and treatment outcome.

Methods: A retrospective analysis was performed on a dataset of 120 knee OA patients. MRI of the most affected (target) knee included sagittal T1w and T2w images in 3 planes. These were assessed using the MRI Osteoarthritis Knee Score (MOAKS) over 12 individual anatomical regions for number of bone marrow lesions (nBML), number of regions with cartilage damage (nCD), number of osteophytes (nOst), and also for overall effusion and Hoffa synovitis (EffSyn, HoffSyn). The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire was used to obtain scores for pain, stiffness and function (WOMAC_P, WOMAC_S and WOMAC_F) at study entry for mild OA (N=42) and advanced OA (N=78), and at 12 months post-treatment with analgesics (N=31) or TKR (N=66) for mild and advanced OA groups. Pain-pressure thresholds (PPT) were evaluated with an algometer at study entry for the patella and averaged over the whole knee for the target knee (PPT_TK, PPT_Pa), the contralateral knee (PPT_CK, PPT_CK), and at the malleolus (PPT_M) and radius of the wrist (PPT_R). Clinical parameters included Age, BMI and Anxiety and Depression score (HADS). Patient outcomes were defined as good or poor according to OARSI criteria assessed from changes in the three WOMAC scores from study entry to 12 months post-treatment. The maximum number of patients was used in each analysis.

Results: All pain scores at study entry showed significant correlation to HADS and BMI (typically $R > 0.5$, $p < 0.005$) and were used as covariates. All WOMAC scores were strongly correlated with each other ($R > 0.7$, $p < 0.001$), as were the PPT measures at different anatomical sites, (typically $R > 0.7$, $p < 0.001$ as in Fig 1A). Principle Component Analysis (PCA) of the 12 MOAKS scores yielded 3 PCs, with PC1 being dominated by nOst and nCD measures, PC2 by nBML measures and PC3 comprised of nBML and nCD at the patella and nBML in the trochlear region. WOMAC_P was not significantly correlated to the MOAKS PCs or to PPT measures, but WOMAC_S and WOMAC_F were significantly correlated with PC1 ($R > 0.25$, $p < 0.005$). PPT measures were strongly correlated to PC3, see Fig 1B for PPT_TK ($R = -0.316$, $p = 0.003$). Assessing correlations for MOAK scores for individual anatomical regions indicated that WOMAC_P was most strongly correlated to nBML in the sub-spinous region ($R = 0.293$, $p = 0.006$) and nCD in the tibia ($R = 0.272$, $p = 0.01$). PPTs of both target and contralateral knees showed significant correlations to nBML ($R = -0.219$, $p = 0.04$) and nCD ($R = -0.282$, $p = 0.008$) in the patella of the target knee in keeping with the PCA results. Patients were divided into good and poor outcome groups for mild (N=17) and advanced OA (N=60) separately and a Mann-Whitney comparison made of the 14 MOAK scores. Significant differences were for nCD in the patella ($p = 0.037$) for mild OA (Fig 1C) and HoffSyn ($p = 0.001$) for advanced OA (Fig 1D). ROC analysis using these parameters to predict good/poor outcome gave AUC=0.83 for mild OA and AUC=0.80 for advanced OA.

Conclusions: Pathological changes within and around the patella appear key in determining whole body pain pressure thresholds and in predicting patient outcome. The strong correlation of PPTs between target knee and at non-OA regions of the malleolus and radius, suggest most patients are sensitised. Average PPTs of both knees and patellas also correlate to measures of CD and BMLs in the target knee patella, and may indicate either greater pain sensitivity to damage at the patella, or that damage in this region is a good reflection of the overall stage of the disease and degree of sensitisation. In mild OA BML numbers in the patella provided a good predictor of 12 month outcome, so may represent the onset of the more progressive phase of OA. Increasing levels of Hoffa synovitis were associated with greater likelihood of poor outcome after TKR, hence may reflect more extensive damage that is not addressed by surgical replacement. Detailed quantification of regional damage by MRI in the patella region may aid patient stratification and understanding treatment response but further studies with a larger cohort for independent validation is now needed.



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