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Impact of Non-steroidal Anti-inflammatory Drugs (NSAIDs) on Synovitis and the Progression of Osteoarthritis: Data from the Osteoarthritis Initiative (OAI)

#### **PURPOSE**

Synovitis and associated inflammation have been shown to play a major role in promoting progression of osteoarthritis (OA). Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used to treat pain in OA patients and could also influence the progression of the disease through their anti-inflammatory effect. To investigate these mechanisms, the goals of this study were (1) to analyze the association between the use of NSAIDs and synovitis and (2) to assess how treatment with NSAIDs impacts structural outcomes over four years.

#### METHODS AND MATERIALS

Participants from the Osteoarthritis Initiative (OAI) cohort with moderate to severe OA (Kellgren-Lawrence (K/L) grades 2-4) and sustained NSAID treatment for =1 year between baseline and 4-year follow-up were included and compared with non-NSAID treated participants (controls). All participants underwent a 3T MRI of the knee at baseline and after 4 years. Images were semi-quantitatively scored for MR biomarkers of synovial inflammation (effusion-synovitis, size and signal intensity of infrapatellar fat pad (IFP), synovial proliferation score (SPS)). Cartilage thickness and T2-relaxation time measurements served as non-invasive biomarkers for evaluating OA progression. The associations between baseline and findings after 4 years were investigated with linear regression models (including adjustment for sex, BMI, age, pain, K/L grade).

# **RESULTS**

A total of 721 participants matched the inclusion criteria (129 with and 592 participants without regular usage of NSAID). At baseline, significantly higher signal intensity in the IFP was observed in NSAID users as compared to controls (adjusted difference in score, 95% CI, p) (0.26; [-0.5, -0.129], 0.039). Additionally in the longitudinal analysis, there was a significantly higher increase in signal intensity of IFP (0.46; [0.2, 0.72], < 0.001) and higher increase in effusion synovitis (0.27, [0.06, 0.47], 0.01) in NSAIDs users compared to controls. The size of IFP and SPS did not show a significant difference between groups at baseline and no significant change over time. NSAID users showed more degenerative changes regarding T2-relaxation time and cartilage thickness over time, but this did not reach statistical significance.

### **CONCLUSIONS**

NSAID users demonstrated higher signal intensity in IFP and more effusion/ synovitis than controls, suggesting that longtime NSAID usage is associated with more synovitis.

# CLINICAL RELEVANCE/APPLICATIONS

In this study, no structural long-term benefit of NSAID use in patients with OA could be found. Furthermore, users showed more synovitis at baseline and change over 4 years, which may lead to an increase in pain and a decrease in joint function.