Synovial Fluid Biomarkers in Knee Osteoarthritis Change with Progression of Radiographic Severity

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The purpose of the current study was to analyze the synovial fluid concentrations of known inflammatory biomarkers in the setting of symptomatic osteoarthritis (OA) of the knee and assess for any differences in biomarker concentrations based on the extent of radiographic disease.
This IRB-approved study was a retrospective review of a prospectively collected database of patients enrolled between December 2016 and April 2018.

Patients presenting with knee complaints were invited to provide synovial fluid samples from the symptomatic knee during their initial office visit.

For this study, a subset of patients with OA was analyzed.
The concentration of 16 synovial fluid biomarkers was measured:
- TIMP-1
- TIMP-2
- TIMP-3
- MMP-13
- IL-6
- MCP-1
- MIP-1β
- VEGF
- bFGF
- Eotaxin
- IL-1Ra
- MMP-1
- MMP-3
- MMP-9
- RANTES
- TSG-6

Samples were analyzed using a multiplex magnetic bead immunoassay
Knee radiographs for each patient were evaluated, and both Kellgren-Lawrence (K-L) score and the joint space narrowing component of the Osteoarthritis Research Society International (OARSI) scores were recorded to determine the extent of cartilage damage and severity of disease.

For purposes of analysis, patients were then divided into a low-grade cartilage damage group (K-L ≤ 2 or OARSI ≤ 1) or a high-grade cartilage damage group (K-L > 2 or OARSI > 1).
Results

• 101 patients were included in this analysis (63% female)

• The mean age for all patients was 59.85 +/- 12.88 years, and the mean BMI for all patients was 30.73 +/- 5.92

• Based on K-L score, 39.51% of patients were determined to have low grade cartilage damage (K-L score 1 or 2) and 60.49% were determined to have high grade cartilage damage (K-L score 3 or 4)

• Based on OARSI criteria, 37.04% of patients had low grade joint space narrowing (OARSI score 0 or 1) and 62.96% had high grade joint space narrowing (OARSI score 2 or 3)
Results

• There was a significant difference in log-transformed MIP-1β (p = 0.025) and bFGF (p = 0.015) concentrations between OARSI grade groups.

• Post hoc analysis revealed that OARSI grade 1 knees had significantly lower concentrations of bFGF compared to OARSI grade 2 knees (p = 0.018) and OARSI grade 3 knees (p = 0.003).

• When divided into low-grade and high-grade joint space narrowing, the high-grade group had significantly greater concentrations of MIP-1β (p = 0.022) and bFGF (p = 0.003).
Results

• There was a significant difference in log-transformed MIP-1β concentration between K-L grade groups (p = 0.013)

• Post hoc analysis revealed that K-L grade 2 knees had a significantly lower level of MIP-1β compared to K-L grade 1 knees (p = 0.036), K-L grade 3 knees (p = 0.008), and K-L grade 4 knees (p = 0.004)

• When divided into low-grade and high-grade cartilage damage based on K-L score, the high-grade group had a significantly greater concentration of MIP-1β (p = 0.020)
Boxplots demonstrating synovial fluid concentration of log-transformed bFGF across OARSI joint space narrowing grades (A) and log-transformed MIP-1β across K-L grades (B).
Discussion

• The synovial fluid concentrations of two synovial fluid biomarkers were found to differ significantly based on the extent of radiographic OA present

• MIP-1β is a pro-inflammatory growth factor known to induce the synthesis of other inflammatory factors including interleukins and TNF-α

• bFGF is a growth factor that is known to promote chondrogenesis, angiogenesis, wound healing, and granulation tissue formation
Significance

Continued study of synovial fluid biomarkers in the setting of symptomatic OA may improve our understanding of the pathogenesis of disease and identify treatment targets in an attempt to halt disease progression.
THANK YOU