# Expression of Inflammatory and Fibrotic Markers of the Hoffa's Fat Pad in Knee Osteoarthritis

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INTRODUCTION: While knee osteoarthritis (OA) research traditionally focuses on cartilage degeneration, emerging evidence suggests that Hoffa's fat pad (HFP), an extrasynovial adipose tissue, may mediate harmful cross-talk between tissues.[1] Studies have demonstrated that fibrotic changes in HFP are related to cartilage degeneration, yet the fundamental role of HFP in OA pathogenesis remains incompletely understood.[2–4] This study investigated the relationship between inflammatory, anti-inflammatory, and fibrotic markers in HFP and the severity of knee OA to identify potential biomarkers.

METHODS: HFP specimens were collected from patients undergoing knee surgery and stratified into three groups based on the surgical procedure: 1) Severe OA: patients undergoing patellofemoral arthroplasty; 2) Early OA: patients receiving cartilage restoration procedure such as osteochondral allograft (OCA) or matrix-induced autologous chondrocyte implantation (MACI) procedures; 3) No OA: young patients undergoing meniscectomy or meniscal repair without cartilage lesions. Gene expression analysis of inflammatory markers IL1β, IL6, and monocyte chemoattractant protein-1 (MCP1), along with the degradation marker like MMP13, anti-inflammatory markers PPARγ, adiponectin, along with the fibrotic marker TGFβ, was performed using real-time PCR. Statistical analysis was performed using the Fisher's exact test, one-way ANOVA, and the Kruskal-Wallis test, as appropriate. Data are presented as a mean and standard deviation. The study was approved by the institutional review board and all patients provided informed consent.

RESULTS: HFP was analyzed in 11 patients. The Severe OA group (1 male, 3 females) was 50.3 ± 8.2 years old with a BMI of 31.9 ± 1.5 kg/m². The Early OA group (1 male, 3 females) was 34.3 ± 8.6 years with a BMI of 30.3 ± 2.8 kg/m². The No OA group (3 females) was 32.0 ± 10.4 years with a BMI of 30.6 ± 10.0 kg/m². Age showed a significant difference between groups (p=0.04), whereas sex and BMI did not. The cytokines IL1β and TGFβ demonstrated significantly elevated expression in the Severe OA group compared to both Early OA and No OA groups (IL1β: p=0.03; TGFβ: p=0.04). Moreover, MCP1 and adiponectin exhibited increased expression trends in Severe OA, though not reaching statistical significance (MCP1: p=0.18; Adiponectin: p=0.18). No statistical significance was detected for IL6, TNFα, MMP13, or PPARγ across groups.

DISCUSSION: The significantly elevated IL1β and TGFβ expression in the Severe OA group indicates these markers play a role in HFP during disease progression. IL1β drives pro-inflammatory responses that progressively contribute to cartilage degeneration, while TGFβ contributes to tissue fibrosis and osteophyte formation. The elevated MCP1 trend aligns with established synergistic interactions between TGFβ and IL1β, which upregulate MCP1 expression, promote cellular recruitment, and sustain inflammation.[5] Additionally, the elevated adiponectin trend contradicts its traditional anti-inflammatory characterization, suggesting a context-dependent pro-inflammatory role in osteoarthritic tissues where it is associated with metalloproteinases and inflammatory mediators.[6] Study limitations include the relatively small sample size, which may limit statistical power to detect differences in markers showing trends of significance, such as MCP1 and adiponectin. Patient heterogeneity may introduce confounding variables. The results of this study highlight the potential of HFP as an active tissue in knee OA rather than a passive bystander, suggesting the need for further investigation with larger cohorts.

CLINICAL RELEVANCE: This study demonstrates that HFP from patients with severe knee OA exhibits a unique inflammatory and fibrotic molecular signature, characterized by elevated IL1β and TGFβ expression. The identification of these molecular markers positions HFP as both a potential therapeutic target for anti-inflammatory interventions and a source of biomarkers for early detection of OA, potentially enabling the development of targeted therapies to prevent disease progression.

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