Association between hypoxia-inducible factor-1a levels in serum and synovial fluid with the radiographic severity of knee osteoarthritis

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ABSTRACT. Osteoarthritis (OA) is primarily characterized by articular cartilage degradation. Hypoxia-inducible factor-1a (HIF-1a), a subunit of the basic helix-loop-helix-containing PER-ARNT-SIM (PAS) domain transcription factors, plays a vital role in the survival of articular chondrocytes to the hostile hypoxic microenvironment and complicates the progression of OA. In this study, we examined whether HIF-1a levels in the serum and synovial fluid (SF) of patients with knee OA were increased and whether the increase was correlated with the radiographic severity of the disease. A total of 278 knee OA patients and 203 healthy controls were enrolled in this study. Knee OA radiographic grading was performed according to Kellgren-Lawrence (KL) grading system by evaluating X-ray changes observed on anteroposterior knee radiography. HIF-1a levels in the serum and SF were determined using an enzyme-linked immunosorbent assay. Serum HIF-1a levels in patients with knee OA were higher than those in healthy controls. Knee
OA patients with KL grade 4 showed significantly elevated HIF-1α levels in the serum and SF compared with those with KL grades 2 and 3. Knee OA patients with KL grade 3 showed significantly higher SF levels of HIF-1α than those with KL grade 2. HIF-1α levels in the serum and SF of knee OA patients were significantly correlated with disease severity according to KL grading criteria. HIF-1α levels in the serum and SF were closely related to the radiographic severity of OA and may serve as an alternative biomarker for the progression and prognosis of knee OA.

**Key words:** HIF-1α; Osteoarthritis; Radiographic severity; Synovial fluid