Disc Displacement Induced Condylar Bone Resorption in the Early- Stage of Temporomandibular Joint Osteoarthritis via the RANTES- CCRs-Akt2 Pathway

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Objectives: Condylar bone resorption in temporomandibular joint osteoarthritis (TMJ OA) is closely associated with disc displacement without reduction. However, the molecular mechanisms underlying this phenomenon remain unclear. The goal of this study was to establish a rat TMJ OA model with disc displacement and to investigate early molecular events that mediates condylar bone resorption in TMJ OA.

Methods: In this study, a new rat TMJ OA model with disc displacement in vivo and a pressure loading system for condyles in vitro were developed. A sterile flexible pressure sensor was placed in the rat model to measure biomechanical stress. Micro-CT was used to analyze subchondral bone mass of condyles and TRAP staining was harnessed to measure osteoclastogenesis of macrophages. Immunohistochemistry and Western blot analysis were applied to clarify the expression, location and interaction of RANTES, CCRs, and phospho-Akt2/total-Akt2.

Results: Condylar bone resorption occurred 3-7 days after disc displacement in the rat model. The pressure on the anterior surface of the condyle caused by displaced disc was about 5 times that of the control group. The increased pressure produced chemokine RANTES and triggered subchondral bone resorption. Furthermore, we found RANTES exhibited a direct promoting effect on osteoclast formation via the RANTES-CCRs- Akt2 pathway. Inhibiting the RANTES-CCRs-Akt2 pathway activation prevented osteoclastogenesis and subchondral bone loss.

Conclusions: Biomechanical stress-associated RANTES-CCRs-Akt2 pathway modulation plays a critical initiating role for condylar bone resorption, possibly shedding light on the mechanisms of TMJ OA.

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