

Synovitis in knee osteoarthritis: a precursor or a concomitant feature?

We read with deep interest the article by Atukorala *et al*¹ aimed at determining if synovitis precedes the development of radiographic knee osteoarthritis (ROA). This nested case-control study suggested that effusion-synovitis and Hoffa-synovitis strongly predicted the development of incident ROA. We really appreciate the work which was done by the authors. The findings supported the potential role of targeted therapies for synovitis in the prevention of knee osteoarthritis (OA). However, there are some worthwhile issues that need to be explored.

Effusion-synovitis and Hoffa-synovitis were assessed by MRI, while ROA was evaluated by a posterior-anterior radiograph. We agree with the authors' point of view that the best imaging method to identify synovial inflammation is by MRI, and MRI is useful to investigate early 'preclinical' disease before radiographic changes occur. However, we have no idea why the authors did not use MRI to evaluate the ROA. A new study conducted by Culvenor *et al*² reported that of all the knee osteophytes (OSPs) presented on MRI (67%), just over one-third (26%) were visible on radiographs following anterior cruciate ligament reconstruction (ACLR). Of the 21 ACLR knees with MRI-defined tibiofemoral OA, 18 (86%) did not have radiographic tibiofemoral OA, which means that MRI is also useful in diagnosing early OA before radiographic changes occur. So it is hard to say that the sequence of synovitis and ROA was not because of unequal diagnostic method. We very much look forward to the causal relationship between synovitis and development of ROA, which were both evaluated by MRI. In addition, ROA was defined as Kellgren-Lawrence (K-L) grade ≤ 2 . However, there were some other studies that regarded patients with a K-L grade of 1 or 2 as having early ROA.³⁻⁶ We are also very curious about whether the causal relationship between synovitis and development of early ROA (K-L grade 1 or 2) still remained. The result of this sensitivity analysis is worthy of expectation.

In addition to all the above, there are some other issues that need to be mentioned. First, the authors indicated that pro-inflammatory cytokines contribute to OA pathogenesis by increasing cartilage degradation. Since K-L grade is largely driven by the presence of OSP, particularly between grades 0 and 2, OSP and joint space narrowing assessed individually according to the Osteoarthritis Research Society International atlas⁷ would be better. The result of this subgroup analysis is also worthy of expectation. Second, the authors indicated that their study suggested that synovial membrane inflammation plays a role early in ROA. Is it possible that synovitis and ROA were caused by some common pathogenesis? Third, there should be some other confounders that need to be addressed,

such as serum C-reactive protein level. Finally, the OR for occurrence of ROA associated with the presence of effusion-synovitis in P0 was 4.7 (2.35–9.34), while it was 4.7 (1.10–2.95) in the Abstract. This needs to be corrected.

We respect the great contributions of the authors and we would also be very much interested in the authors' response to these issues.

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