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Role of medial abrasion phenomenon in the pathogenesis of knee osteoarthritis

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ABSTRACT

Osteoarthritis of the knee affects a large population worldwide and is associated with an extremely high economic burden largely attributable to the effects of disability, comorbid disease, and the expense of treatment. Since the initiating events that result in the cartilage degradation are poorly understood, there has been very limited success in demonstrating disease modification in clinical trials of potential therapies. Medial plica related medial abrasion phenomenon has recently been identified to have close relationship with medial compartment osteoarthritis. We hypothesized that this abrasion phenomenon will elicit lifelong interplay between pathologic medial plica and the facing medial femoral condyle and might play a role in the pathogenesis of knee osteoarthritis by both physical and chemical effects. After evaluating current evidence, we designed a study to prove that the concentrations of total protein, cartilage degrading related cytokines (tumor necrosis factor-α and interleukin-1β) and enzyme (matrix metalloproteinase-3) are higher in the medial compartment of the knee having the phenomenon of medial abrasion. The accumulating data and findings about medial abrasion phenomenon might be important for the understanding of the pathogenesis or progression of this common disease. We hope that our hypothesis will stimulate further studies verifying if medial abrasion phenomenon plays more roles in the pathogenesis of knee osteoarthritis. Further clinical observations for its appropriate treatment based on this hypothesis are also mandatory for the benefits of patients.

Introduction

Osteoarthritis (OA) of the knee is the major cause of chronic musculoskeletal pain and is ranked as a main reason of mobility disability in elderly population. It is a disease process of uncertain multifactorial etiology, which eventually affects the entire joint. Various etiologic risk factors have been proposed, but the exact pathogenesis for OA knee is unknown so far.

Many literatures mentioned medial compartment is more commonly involved than the lateral one and the pathogenesis may be different [1–7]. In 2006, it was reported that in patients with medial compartment osteoarthritic knees, the prevalence of medial plica was significantly higher than that of others and that two distinct foci of cartilaginous lesion were found on the facing medial femoral condyle in almost all of the patients who had the structure of medial plica [8]. A further study disclosed the kinematic relationship of the medial plica with the medial femoral condyle during knee motion in vivo [9]. In that study, it was revealed that all medial plicae, regardless of their size, would move reciprocally and would keep in touch with the medial femoral condyle and therefore might cause some degree of abrasion on the facing medial femoral condyle during knee motion. Another histomorphological study of the medial plica also implied the close interplay between this structure and the medial femoral condyle in patients with knee OA [10].

The hypothesis

We postulated that in the knee having the structure of medial plica demonstrating medial abrasion phenomenon, the repeated abrasion and impingement between medial plica and medial femoral condyle would elicit both physical and chemical effects

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on the adjacent cartilage and the medial plica itself which might play a role in the pathogenesis of knee OA.

Evaluation of the hypothesis

Construction of three-dimensional dynamic finite element model

An experimental study on the tensile strength of the medial plica from 50 knees was conducted using high precision micro-force tensile tests [11]. The force–deflection curves resulting from these tests were transferred to stress–strain curves to obtain Young's moduli of these specimens. In another selected 30 knees with different sizes of medial plica [9], the inner margins of the plicae were located by inserting needles percutaneously under direct vision during arthroscopic examination. The topographic changes of the margins of these plicae during knee motion were recorded by fluoroscopy and analyzed. Based on the findings of these pilot studies, a three-dimensional dynamic finite element model was constructed and used to investigate the magnitudes of the cyclic pressures acting on the cartilage of the medial femoral condyles by different types of medial plicae with various Young's moduli [12]. Young's modulus of the plica was found to be ranging from 10 to 110 MPa and has positive correlation with patient's age [11]. All types of plicae remained in contact with the medial femoral condyles and shifted medially when the knees moved from extension to flexion [9]. The contact pressures were positively correlated with Young's moduli of the medial plicae. The maximum contact pressures of all simulation scenarios occurred when the knees moved beyond 50° of flexion. When the Young's moduli of medial plicae were set greater than 60 MPa, all types of plicae would elicit contact pressures greater than 10 MPa on the medial femoral condyles which are damaging to the cartilage [12].

Conclusions

Young's modulus of the plica was found to be ranging from 10 to 110 MPa and has positive correlation with patient's age. During knee motion, all types of medial plicae would remain in contact with the facing medial femoral condyle and present repeated abrasion on it. The contact pressures on the cartilage of the medial femoral condyles were positively correlated with Young's moduli of the medial plicae. When the knees were bent beyond 50°, all types of medial plicae would elicit high contact pressures enough to cause apoptosis of the chondrocytes on the cartilage of the medial femoral condyles when Young's moduli of medial plicae were set greater than 60 MPa.

Biochemical analysis

Interleukin-1β (IL-1β), matrix metalloprotease-3 (MMP-3) and MMP-3 mRNA expressions in the plica isolated from 24 knees were investigated by immunohistochemistry, Western blotting, reverse transcriptase polymerase chain reaction (PCR) and real-time PCR to clarify the impact of medial plica on cartilage destruction [13]. Immunohistochemistry showed that MMP-3 was highly expressed in the plica. Western blotting of cultured supernatants showed that IL-1β treatment induced MMP-3 release by cells isolated from the plica. Reverse transcriptase PCR and real-time PCR analysis showed that MMP-3 mRNA levels were increased after IL-1β treatment of the cultured cells from the plica. MMP-3 and IL-1β mRNAs were also found highly expressed in the plica. Another study [14] examined the expression of MMPs, tissue inhibitors of metalloproteinases (TIMPs), IL-1β, and tumor necrosis factor (TNF)-α in the medial plica in the knees of patients with medial compartment OA who underwent either arthroscopic medial release (stage II; 15 knee joints from 15 patients) or total knee replacement (stage IV; 18 knee joints from 18 patients). MMP-2, MMP-3, MMP-9, IL-1β, and TNF-α mRNA and protein levels measured, respectively, by quantitative real-time PCR and Quantibody human MMP arrays, were highly expressed in extracts of medial plica from stage IV knee joints. Immunohistochemical staining also demonstrated high expression of MMP-2, MMP-3, and MMP-9 in the plica of stage IV OA knees. Some TIMP/MMP ratios decreased significantly in medial plica as disease progressed from stage II to stage IV. Furthermore, the migration of cells from the plica cell was enhanced by TNF-α. The results suggest that medial plica may be involved in the process of cartilage degradation in medial compartment OA of the knee.

Conclusions

These biochemical analyses demonstrated that medial plica may play roles in the process of cartilage degradation in osteoarthritic knee by producing extracellular matrix degradation enzymes during inflammation and that the imbalance between TIMP and MMP levels in this tissue increases protease activity in the medial compartment and this may also contribute to cartilage breakdown and progression of osteoarthritis.

Clinical applications

Based on these constitutional studies about medial plica related medial abrasion phenomenon, an arthroscopic procedure called arthroscopic medial release (AMR) was developed. The outcome of AMR of 255 knees in 173 patients for varying grades of OA involving the medial compartment was reported [15]. It can reduce the pain in the majority of these patients over a period of at least 4 years. Evidence of disease modification was also found in some cases. Furthermore, the concept of AMR has been extended and evolved into a conceptualized arthroscopic procedure called arthroscopic cartilage regeneration facilitating procedure (ACRFP) to treat knee OA [16]. In this report, 571 knees of 367 patients with knee OA received this procedure. After a mean follow-up period of 38 months, 85.5% of patients satisfied with the outcomes and the degeneration process of the medial compartment was found being reversed in 82.1% of these knees.

Conclusions

In comparison with the uncertain beneficial mechanism and the diversity of outcomes of current widely used therapeutic arthroscopic techniques for knee OA including lavage, debridement, abrasional chondroplasty and microfracture, the concept of AMR and ACRFP based on our hypothesis has more precise target and rationale of treatment and the outcomes were encouraging.

New evidence: total protein, TNF-α, IL-1β and MMP-3 concentrations are higher in the medial compartment of the knee with medial abrasion phenomenon

There are a variety of proteins or debris in the synovial fluid of osteoarthritic knee. These proteins include glycoprotein debris and collagen fragments derived from destructed cartilaginous tissue and enzymes such as metalloproteinase, collagenase and proinflammatory cytokines (ILs, TNF-α, etc) [17–19]. All of these proteins in synovial fluid might reflect the pathological status of the knees. It has been reported that cartilage debris in the traumatized and osteoarthritic joint may increase the concentration of TNF-α in the joint, contributing to joint symptoms and cartilage destruction [20]. Interleukin-1β, like TNF-α, is a documented proinflammatory cytokine that may play an important role in the pathogenesis and progression of knee OA [21–28]. On the other hand, MMPs are enzymes involved in the degradation of cartilage matrix