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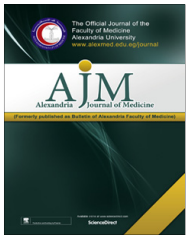

Evaluation of early changes of cartilage biomarkers following arthroscopic meniscectomy in young Egyptian adults

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Abstract *Background:* The metabolic imbalance in the articular cartilage following meniscectomy includes an increase in cartilage degradation with an insufficient reparative or anabolic response resulting in structural, biochemical and mechanical changes that can progress from pre-clinical, to pre-radiographic, to radiographic damage of the joint.
Purpose: To evaluate combinations of imaging and biochemical biomarkers for cartilage breakdown, synthesis and quantity in the early period of post-arthroscopic meniscectomy.
Subjects and methods: Twenty young adults (three of them were females) who underwent unilateral arthroscopic partial meniscectomy were evaluated. The patients had a mean age of 32.5 years (range, 24–39), mean BMI of 28.5 kg/m^2 (range, 24–34). Preoperative and six months postoperative US and MRI-based markers (cartilage thickness and volume, respectively) were quantified for medial and lateral tibio-femoral compartments for both knees. Preoperative, three and six months postoperative biochemical markers serum assays were measured; COMP and Col II (cartilage matrix breakdown) and PIICP (cartilage synthesis). These three markers were measured in an age, sex and BMI matched twenty healthy subjects for comparison.

Abbreviations: AUC, area under the receiver-operator characteristics curve; BMI, body mass index; CI, confidence interval; Col II, collagen type II-specific neoepitope; COMP, cartilage oligomeric matrix protein; MRI, magnetic resonance imaging; OA, osteoarthritis; PIICP, procollagen molecule of type II collagen C-propeptides; US, ultrasonography

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Results: The meniscectomized knees had significantly lower total knee cartilage volume, $P < 0.05$ but non-significant mean thickness than the intact contralateral knees. Among the individual biochemical markers, PIICP had the highest significant diagnostic accuracy quantified as the area under the receiver-operator characteristics curve (AUC) of 0.75 (95% confidence interval: 0.509–0.912) higher than all others, $P < 0.05$ to distinguish subjects with progressive cartilage loss from non-progressors. Diagnostically, ratio of COMP and Col II to PIICP scored AUC of 0.90 (0.69–0.98, higher than PIICP: $P = 0.0001$). For prediction of cartilage loss, none of the individual markers could be used.

Conclusion: Cartilage volume loss by MRI combined with changes in cartilage matrix turnover detected by molecular biomarkers may reflect the initial changes associated with cartilage degeneration that account for early OA.

1. Introduction

Knee trauma, such as cruciate ligament or meniscus injury, is a strong predictor of subsequent knee osteoarthritis (OA). Considering the young age at which many of these injuries occur, knee joint replacement at a relatively young age is a distinct possibility.[1] So, secondary prevention of OA is important. The hallmark of OA is loss of articular cartilage which is characterized by high wear resistance, and poor regenerative qualities.[2] Osteoarthritis is a disease with a long silent period. Early identification of OA is crucial to improve clinical decision making and advancing treatment options. Thus preventing further cartilage destruction and joint failure, especially in athletes, in whom unnecessary treatment or intervention may be detrimental to a competitive future. Hence, diagnostic tests that can detect and monitor molecular events early in the pathogenesis of OA would be potentially very useful.[3]

A variety of risk factors work together to incite a cascade of pathophysiologic events within joint tissues leading to OA including advancing age, gender, genetics, obesity and trauma. The repetitive nature of stress on a previously healthy, yet traumatized, articular surface, has also been related with early cartilage changes and degeneration that may stay invisible for a long period of time before evolving into irreversible cartilage lesion.[4]

The menisci are two semilunar-shaped fibrocartilaginous structures, containing water, collagen (mainly type I), and proteoglycans. Their unique anatomy is comprised of circumferentially oriented collagen fibers which provide resistance to hoop stresses and radially oriented fibers which resist shear forces.[5] Long-term follow-up studies showed that virtually all meniscectomized knees develop arthritic changes with time.[1] The severity of these changes seems to be proportional to the amount of meniscus removed.[6] The frequent bone and cartilage changes found after partial meniscectomy are thought to be due to the decrease in contact area up to 50–70% with a resulting increase in contact stresses,[6] and loss of the load distributing function which prevents the menisci from extruding out the joint during axial loading and decreased stability of the knee.[7] Moreover, as 74% of the total weight of the meniscus is water which could be squeezed out into the joint space during compression forces adding to the joint lubrication, thus increased coefficient of friction between the gliding joint surfaces is one of the consequences of meniscectomy.[7]

The increased intra-articular contact stresses within the knee are thought to 'overload' the articular cartilage, with associated structural, biochemical and mechanical changes. The macroscopic and microscopic signs of failure of articular cartilage after meniscectomy have also been demonstrated by animal models, ranging from fibrillation of the surface to necrosis and loss of the cartilage layer.[8]

Cartilage is a connective tissue made of cells (chondroblasts/chondrocytes) that produce an extracellular matrix of proteoglycans and collagen fibers with high water content. The tensile strength of cartilage is due to the collagen component. Its resistance to compression is due to the ability of proteoglycan to attract and hold water.[9]

Biomarker is a detectable biologic parameter, whether biochemical, genetic, histologic, anatomic, physical, functional, or metabolic.[10] Biomarkers are used in diagnosis of disease, in addition they allow classification of disease severity, risk of onset and progression, as well as assessment of the efficacy of a treatment.[10]

Cartilage imaging biomarkers have gained a significant role in various aspects of OA. Magnetic resonance imaging (MRI) is the most promising imaging modality to detect structural changes in cartilage tissue, as it is direct and noninvasive.[11] MR-based morphological cartilage biomarkers are superior to radiographs in characterizing disease burden. Their role in characterizing prognosis and risk of OA is showing great promise. Many techniques enable imaging of fissuring and focal or diffuse cartilage loss. The 3D-spoiled gradient recalled echo imaging with fat suppression either using selective fat suppression or selective water excitation provide higher spatial and contrast resolution, and are the current standard for morphological imaging of cartilage.[12] The articular cartilage has a very high signal intensity, joint fluid has an intermediate to low signal intensity, and subchondral bone and bone marrow are dark. Reported sensitivity and specificity for directly assessing knee structural alterations, such as cartilage volume, cartilage defects, subchondral bone changes and meniscal lesions are 75–85% and 95–97%, respectively, which has increased our understanding of early joint changes.[13]

Morphologic changes in the cartilage matrix and chondrocytes could be detected on the molecular level. The molecules released could be measured by biochemical markers. Measurement of biochemical markers in blood, urine or synovial fluid samples could reflect dynamic and quantitative changes in joint remodeling and therefore disease progression. Because