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Concepts Important to Secondary Prevention of Posttraumatic Osteoarthritis

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Joint injuries occur when primary prevention fails or the joint is subjected to overwhelming forces. Although the incidence of noncontact anterior cruciate ligament (ACL) injuries can likely be reduced, ACL tears will continue to occur due to accidents, contact sports, falls, and any number of unpredictable situations resulting in knee trauma. Thus, a substantial role remains for improving patients' surgical and rehabilitative outcomes in the aftermath of ACL tears. To achieve these goals, validated and appropriate outcome measures are key to evaluating and optimizing current treatment protocols and developing new strategies to prevent poor outcomes, including posttraumatic osteoarthritis (PTOA).

Understanding the concept of pre-osteoarthritis (pre-OA) is important for optimizing protocols for rehabilitating patients with ACL injury.[1,2] In the early years after joint injury, most patients do not have signs or symptoms of clinical osteoarthritis (OA). However, measurable changes to the joint that persist and progress in a large proportion of patients are observable after injury and reconstructive surgery.[3–14] Developing and validating new techniques to measure potentially reversible and clinically occult joint changes reflective of OA risk are critical to identifying pre-OA.

Pre-osteoarthritis has been defined as "conditions where clinical OA has not yet developed; rather, joint homeostasis has been compromised and there are potentially reversible markers for heightened OA risk."[1] The existence of pre-OA after ACL injury can be demonstrated using a systems-based approach to assess the OA risk by evaluating the interactions among structural, biological, and mechanical factors in patients during the first 2 years after ACL reconstruction (ACLR).

Evidence for subclinical cartilage damage after ACL injury has been shown using compositional magnetic resonance imaging (MRI) techniques, such as T2 mapping,[5] T1rho,[6] dGEMRIC,[7] and the newer MRI ultrashort echo time (UTE) enhanced T2* mapping.[8] The *UTE* designation refers to the incorporation of image data using research software (instead of conventional MRI) to acquire echo times of less than 1 millisecond. Acutely, after ACL injury, novel compositional MRI UTE enhanced T2* mapping[9–11] showed elevated values for menisci and cartilage that appeared normal on conventional MRI.[9,11] Two years after anatomic ACLR, these values were no longer different from those of uninjured control participants,[9] which demonstrates the potential reversibility of the observed changes and is suggestive of healing. The detection of possibly reversible cartilage matrix changes in this longitudinal study of patients with ACL injuries supports the potential demonstration of pre-OA using UTE-T2* mapping.

The next steps to identifying pre-OA include linking to OA risk. Prior authors[12] found that the knee-adduction moment (KAM) predicted the progression of medial knee OA. Higher KAM values 2 years after ACLR also predicted worse patient-reported outcomes at 8 years.[3] Thus, KAM can be considered an established mechanical marker of OA risk. Significantly, the finding that medial knee MRI UTE-T2* correlated with KAM in patients 2 years after ACLR supports the potential use of MRI UTE-T2* mapping for the clinical diagnosis of pre-OA.[13] Of concern, after ACLR, nearly half of patients demonstrated higher UTE-T2* values than uninjured control patients, and 37% had UTE-T2* values more than 2 standard deviations greater than those of control patients.[14]

Finally, serum biochemical biomarkers may play a role in the clinical assessment of OA disease states and OA risk. Previous researchers[15,16] showed that the change in serum biomarkers in response to a mechanical challenge provided insight into OA disease states. Specifically, changes to serum cartilage oligomeric matrix protein after a 30-minute walk predicted cartilage-thickness changes 5 years later in patients with knee OA.[15] A follow-up study of patients with medial knee OA indicated that changes to CS846, a marker of cartilage matrix synthetic activity, predicted cartilage thickening in the less involved lateral compartment.[16] Similar elevations of CS846 were present in a subset of patients 2 years after ACLR. These data support the need to evaluate OA risk and rehabilitation outcomes by assessing the interplay among structure, biology, and mechanics after ACL injury.[1]

When primary prevention has failed and ACL injury has occurred, the optimal treatment strategies for enhancing timely recovery and maintaining joint health remain ill defined.[17] Although ACLR can provide a stable knee to many patients, return to work and sports is not guaranteed and the risks of PTOA and early disability remain unabated. Linking measurable joint changes to the risks of reinjury, reduced work and sport participation, and later development of poor clinical outcomes and PTOA constitutes substantial knowledge gaps that must be bridged for us to understand the effectiveness of current and new treatment strategies for optimizing clinical outcomes after ACL injury.

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