CURRENT CONCEPTS REVIEW

Knee Osteoarthritis Following Anterior Cruciate Ligament Reconstruction: Frequency, Contributory Elements, and Recent Interventions to Modify the Route of Degeneration

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Abstract

Half of the individuals who experience an anterior cruciate ligament reconstruction (ACLR) suffer from knee osteoarthritis (OA) 12–14 years later. Elements that make a contribution to the appearance of OA following ACLR are anomalous anterior tibial displacement and anomalous tibial rotation in the course of the stance phase of walking (exhibited in 85% of operated knees). Individuals who undergo an early ACLR (5 days on average following anterior cruciate ligament [ACL] breakage) have an inferior frequency of radiographically apparent tibiofemoral OA at 32–37 years of follow-up than individuals with ACL who did not experience the procedure. Nevertheless, the percentage of symptomatic OA, radiographically apparent patellofemoral OA and knee symptoms are alike in both groups. At 15 years of follow-up, 23% of knees that experienced an anatomic ACLR suffer from OA, while this percentage augments to 44% if the ACLR was non-anatomic. Knees of individuals who experience ACLR need total knee arthroplasty at an earlier age than healthy knees. Intra-articular injections of interleukin-1 receptor antagonist and corticosteroids may reduce the peril of OA after ACLR.

Level of evidence: III

Keywords: Anterior cruciate ligament reconstruction, Osteoarthritis, Risk factors

Introduction

A torn anterior cruciate ligament (ACL) is common in athletes who engage in sports that need quick pivoting and cutting (football, soccer, skiing). [1,2] The published frequency of ACL ruptures in the general community is 0.8 per 1000 inhabitants, although this figure is probable to increase in younger, more athletic individuals. [2,3] Although patients who suffer an ACL rupture and are treated with the technique that is currently considered the gold standard [ACL reconstruction (ACLR)] generally return to sport, 50% of ACLR patients experience osteoarthritis (OA) within 12-14 years. [4-19] Given the elevated frequency of ACL ruptures, especially in young patients, determining the elements that can make a contribution to the appearance of OA following ACL rupture is essential.

The objective of this paper is to review the prevalence of OA after ACLR, the circumstances that favor the occurrence of osteoarthritis after an ACL rupture, and factors that can alter the knee's natural progression after an ACLR.

Frequency of OA following ACL reconstruction (ACLR)

Although the causes of OA are diverse, 12% of symptomatic OA cases are attributed to post-traumatic OA.[20] One of the most frequent sources of post-traumatic knee OA is ACL tears ,which occur primarily in young, active individuals who do not usually have additional risk

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factors for suffering from knee OA. [5,21,22] ACL tears can seriously affect the normal function of the damaged knee. The published frequency of knee OA following an isolated ACL tear is 13%. [23] When meniscal injury is present with an ACL tear, this percentage increases to 21–48%.[23] Diagnostic imaging studies and long-run research have demonstrated that articular cartilage involvement occurs first in the medial compartment. [24] In addition, the medial compartment is usually more damaged in the long term than the lateral compartment. [25]

Although ACL tears are known to cause radiographically evident OA, the association between radiographically evident OA and knee pain and function is not entirely clear.[26-28] Øiestad et al analyzed 210 patients who underwent ACLR. After a follow-up of 10 to 15 years, the aforementioned authors compared the knee radiographs with the Knee Injury and Osteoarthritis Outcome Scores (KOOS) and found that individuals with radiographically evident knee OA had significantly more symptoms than those without radiographically evident OA.[29] Although radiographically evident OA can be a casual finding, a published study found that individuals with a history of ACLR undergo total knee arthroplasty (TKA) at a significantly younger age than individuals with no history of surgery. The mean age of individuals that underwent previous ACLR surgery and required TKA was 50.2 years, while the mean age of those who had no previous surgery was 59.9 years.[30]

Circumstances favoring the appearance of OA after an ACL rupture

Considering that ACL rupture is one of the main causes of osteoarthritis in young patients, it is essential to understand the circumstances that can favor or disfavor the appearance of OA following ACL rupture.

Kinematic and neuromuscular changes

Although ACLR theoretically restores knee stability, a report found that an abnormal anterior tibial translation could be related to early degenerative cartilage changes within a year of surgery, suggesting that abnormal kinematics can make a contribution to the appearance of post-traumatic OA.[31] Biomechanical investigations have demonstrated that 85% of knees that underwent ACLR had anomalous tibial rotation in the course of the stance phase of walking, which the contralateral knees did not experience.[32] Given that ACL plays a paramount function in knee proprioception as well, knee rupture can cause the dynamic joint stabilizers (quadriceps and hamstrings) to inadequately detect knee position, which can contribute to joint instability.[33] It follows that a combination of the above kinematic changes could make a contribution to the appearance of radiographically evident OA early following ACLR.

Following an ACL tear, quadriceps atrophy takes place. Within 2–5 years of ACLR, only 50% of patients achieve normal levels of strength.[34] Quadriceps weakness after ACLR has been directly associated with narrowing of the radiographic articular line in individuals with post-traumatic OA.[34] Psychological factors (pain and fear of re-injury) have also been reported to impact muscle activation patterns and thus knee stability.[35] Therefore, a combination of the above factors could produce an anomalous allocation of forces and torques throughout the articulation, which would alter the contact forces of the cartilage, leading to variations in chondrocyte gene expression and therefore variations in the configuration and mechanical attributes of the cartilaginous tissue of the knee.[36,37]

Inflammatory reaction

Immediately after an ACL tear, the levels of several cytokines (tumor necrosis factor-alpha, interleukin [IL]-1beta, and matrix metalloproteinase [MMP]-1 and MMP-13) increase within the joint.[38,39] Tumor necrosis factor-alpha has been associated with an increased apoptotic caspase pathway in chondrocytes.[37] In the days following ACL rupture, there is an increase in chondrocyte apoptosis.[40] While cytokine levels in healthy knees slowly decrease over time, knees with ACL rupture continue to have high levels of these cytokines for at least 1 year after injury.[41,42]

Mechanical activation of chondrocytes in the course of ACL rupture has been reported to change their gene expression, resulting in the activation of degrading enzymes such as MMPs, which make a contribution to the degeneration of extracellular matrix proteins such as glycosaminoglycans and collagen.[37] Studies have shown that elevated MMP levels within the knee last long following the ACL rupture, consequently producing a non-stop degradation of glycosaminoglycans and collagen up to 1 year later.[43,44] Although chondrocytes have a certain capacity to react to ACL tears, the threshold at which the catabolic cascade of MMPs exceeds the chondrocytes' regenerative capacity might be exceeded. This mechanism could therefore makes a contribution to the appearance of post-traumatic OA following ACL rupture.

There have been a number studies that investigated whether the inflammatory and catabolic cascade produced after an ACL rupture could be counteracted pharmacologically during the acute period of the injury. IL-1 levels increase after ACL rupture, and there is a relationship between IL-1 beta levels and the severity of chondral damage.[45] Therefore, one of the goals of future treatments would be to decrease IL-1 beta levels. Kraus et al compared the clinical impact of early knee arthrocentesis and injection of an IL-1 beta receptor antagonist (IL-1Ra) with a placebo injection.[46] Patients treated with an early injection of IL-1Ra following ACL rupture were found to have better patient-reported outcomes than those treated with placebo injections. In another study, Lattermann et al assessed the effects of arthrocentesis and corticosteroid injection versus a saline solution.[47] Although the authors found no change in the patient-reported outcomes, they observed substantially fewer collagen breakdown products after the corticosteroid injection than after the placebo injection. These preliminary studies seem to indicate that modulation of the early inflammatory reaction following ACL rupture could decrease early joint cartilage degeneration.

Meniscal and/or cartilaginous damage at the time of ACL rupture

During any joint injury, shear and compressive forces on the cartilaginous tissue can produce stress fractures in the cartilage matrix and the underlying osseous tissue.[48] Contrary to osseous tissue, cartilaginous tissue has no regenerative ability, which probably makes a contribution to the appearance of post-traumatic OA following an ACL rupture.[49, 50]

Although the majority of ACL ruptures do not have connected intra-articular bone fractures, joint trauma is sometimes severe enough to cause enduring cartilaginous damage. When an ACL rupture occurs, impaction damage with subchondral bone marrow edema usually happens, denoting load transmission across the cartilaginous tissue. Bone marrow contusions are usually present in the posterolateral part of the tibial plateau and in the central area of the lateral femoral condyle from the early blow. The frequency of cartilage damage after ACL tear has been declared to be 16%–46%.[51] However, the true prevalence of joint cartilaginous injury might be greater. Utilizing magnetic resonance imaging (MRI), up to 100% of knees were found to have some type of cartilage damage following ACL ruptures.[52] However, the aforementioned immediate cartilage damage is insufficient to explain the appearance of post-traumatic OA after ACL tears. The majority ACL ruptures also involve injury to the lateral part of the tibial plateau and the lateral femoral condyle, although post-traumatic OA usually affects the medial compartment more.

In addition to the previously mentioned cartilage damage after an ACL tear, there is often meniscal damage. Published studies have shown that the prevalence of meniscal ruptures in individuals with ACL tears is 47%–61%.[53,54] Lateral meniscus tears are more frequent in the acute phase. Of the individuals who experienced arthroscopic surgery for ACL rupture and other connected damages within 2 months of ACL rupture, 69.4% experienced lesions in the lateral meniscus, 19.9% in the two menisci, and 10.8% in the medial meniscus.[55] In the same study, the patients who underwent surgery 2 months after the ACL rupture showed a higher frequency of injuries to the medial meniscus and both menisci, which could be explained by the fact that the medial meniscus functions as a tributary stabilizer to anterior migration and experiences greater stress in ACL-impaired knees and is consequently more inclined to damage.[55] The types of meniscal tears are varying, with each category having distinct clinical consequences. Detecting meniscal root tears (defined as those that are radial and occur within 1 cm of the posterior insertion areas of the meniscus) is essential, given they can produce an incapacity of the meniscus to withstand hoop forces, resulting in a significant increase in tibial-femoral contact pressure, which can predispose the knee to osteoarthritic changes.[56] Repairing medial and lateral meniscal root breaks could be critical to the knee's long-term function. One publication mentioned that 35% of individuals with partial medial meniscectomy due to root damage underwent TKA within 5 years of the ACL tear, while no patient with medial meniscus root repair underwent TKA.[57] A study reported that the lateral meniscal root was damaged in 7%–12% of individuals with ACL tears and that lateral meniscal root restoration can reestablish tibial-femoral contact forces.[58,59] In short, meniscal injuries are known to be associated with ACL rupture, and the various treatments for these lesions impact the natural progression of post-traumatic OA. Therefore, every effort should be made to reestablish the soundness of the meniscal structure by repairing and preserving the menisci, which will ameliorate knee kinematics and minimize the occurrence of post-traumatic OA.

Factors that alter the natural history of the knee after ACL reconstruction (ACLR)

Given that ACL tears are a principal source of post-traumatic OA in young patients, determining the factors that can alter the knee's natural progression after an ACLR is critical. ACL tears alone can lead to knee osteoarthritis, whether the patient has undergone ACLR surgery or conservative treatment. Fifty-seven percent of cases reported knee osteoarthritis at 14 years after ACLR, compared with 18% in the contralateral knee.[60]

There is a common misconception that ACLR prevents OA. Although ACLR does not prevent the eventual occurrence of knee OA, a number of authors have stated that ACLR might delay it.[60] In contrast, other studies have reported greater evidence of knee osteoarthritis after ACLR in chronic fractures than in conservatively treated fractures.[61] Although ACLR might not prevent knee OA, ACLR might reduce secondary meniscal and cartilage injuries.[62]

Ultimately, patients without ACL tears have a lower risk of suffering from knee OA than those with solitary ACL tears. On the other hand, those individuals with assembled ACL and meniscal or cartilaginous injuries have a greater risk of developing OA.

A highly controversial issue is whether the timing of the ACLR after the injury could have an effect on the appearance of knee OA. Jomha et al analyzed 72 individuals over 7 years following patellar bone-tendon-bone ACLR. In the radiographic follow-up, the authors observed that early reconstruction with meniscus preservation resulted in a lower incidence of degenerative changes than late ACLR or reconstruction with meniscus debridement.[63] However, Harris et al indicated that early ACLR resulted in a higher proportion of radiographically evident tibiofemoral OA than late ACLR (16% vs. 7%).[64] In contrast, another study showed that the peril of suffering a a meniscal tear or experiencing a TKA was similar between individuals who underwent early ACLR and patients without ACLR tears.[65] A study by de Campos et al indicated that early ACLR (within the first 6 months of injury) had an inferior peril of conjoint meniscal surgery and, within 1 yearof ACL rupture, had an inferior peril of conjoint cartilaginous damage.[66]

The impact of combined lesion and connections with osteoarthritic characteristics established by MRI

Pertinacious symptoms and bad quality of life (QoL) are freqnent after an ACLR. Patterson et al investigated the impact of a combined ACL lesion (i.e., connected meniscectomy and/or arthroscopic chondral defect at the time of the ACLR and/or secondary ACLR knee lesion/surgery) and the influence of cartilaginous defects in MRI, bone marrow damage, and meniscal injuries on patient-reported outcomes (PROMS) after 1–5 years of follow-up.[67] The authors analyzed 80 patients (50 men; mean age, 32 years) who completed the KOOS and the International Knee Documentation Committee (IKDC) questionnaire. The authors also evaluated 3T MRIs at 1 year and 5 years of follow-up. They then compared the mean scores of PROMS between single and combined ACL lesions with standard data published in the literature. Utilizing multivariate regression, the authors assessed the relationship between compartment-specific MRI cartilage, bone marrow lesions, meniscal injuries, and PROMS at 1 year and 5 years of follow-up. Patients with a combined lesion had significantly inferior scores on the KOOS subscale of function in sport and recreation (KOOS sport/recreation), the IKDC questionnaire at 12 months, the KOOS subscales of pain (KOOS pain), symptoms (KOOS symptoms), and quality of life (QoL) (KOOS QoL) and on the IKDC questionnaire at 5 years than those with a solitary injury. Even though no characteristic of the MRI was related to PROMS at 1 year, patellofemoral (PF) cartilage defects at 1 year were significantly related to worse KOOS symptoms at 5 years and poorer KOOS sport/recreation, KOOS QoL and IKDC scores. PF cartilage defects at 5 years were also significantly related to worse KOOS symptoms and poorer KOOS QoL scores. In short, combined lesions and PF cartilage defects observable on MRI were related to inferior long-run results.

Early ACL surgery versus no ACL surgery

In a phase 2 evidence-based cohort study (registry: NCT03182647 - ClinicalTrials.gov identifier), Kvist et al. analyzed the long-run frequency of knee OA following ACL rupture, particularly in non-ACL individuals (68). The first objective was to report the frequency of radiographically evident OA, symptomatic OA, and the need for TKA in acute ACL injuries after 32–37 years of follow-up. As a second objective, the authors compared the prevalence of radiographically evident OA, symptomatic OA, and knee symptoms between individuals assigned to prompt ACL surgical procedure or no ACL surgical proedure and those who crossed over to ACL surgical procedure. The patients (who were 15–40 years old when the ACL rupture occurre) were assigned to either surgical management (augmented or no ACL repair in the first 2 weeks after the injury) or non-surgical management. After a follow-up of 32 to 37 years from the initial lesion, 153 patients were analyzed using plain weightbearing radiographs and 4 subscales of the KOOS score. Radiographically evident OA was considered when the Kellgren and Lawrence classification was grade 2 or superior. Symptomatic OA was determined by KOOS (radiographically evident OA along with knee symptoms). Patients in the surgery group (n = 64) underwent surgery 5 days after the injury on average. Of the 89 individuals who did not undergo surgery, 53 remained without surgical treatment, while 27 underwent surgery for the ACL within the first 2 years after the lesion, and 9 underwent surgery 3–21 years after the injury. Of the series, 95 patients (62%) experienced radiographically evident tibiofemoral OA, including 11 (7%) who underwent TKA. The prevalence of radiographic tibiofemoral OA was lower in the surgical group than in the non-surgical group (50% vs. 75%; $P = .005$). The frequency of symptomatic OA (50% in the whole series) and radiographically evident PF OA (35% in the whole series) was similar in the 2 groups. Ultimately, individuals who underwent prompt surgery (5 days on average) following ACL tear had an inferior freqnency of radiographically apparent tibiofemoral OA at 32–37 years of follow-up than the ACL individuals who did not experience surgery. However, the prevalence of symptomatic OA, PF radiographically apparent OA and knee symptoms was alike in the 2 groups.

Anatomic versus non-anatomic ACL reconstruction

In a systematic literature review (level of evidence: IV), Rothrauff et al studied the radiographic frequency of OA following autograft ACLR by comparing studies employing anatomic and non-anatomic techniques, with a minimum follow-up of 10 years.[69] The study hypothesis was that the long-term incidence of osteoarthritis would be lower after an anatomic ACLR than after a non-anatomic ACLR. The technique was considered anatomic when the Anatomic ACL Reconstruction Scoring Checklist (AARSC) score was 8 or higher. The technique was considered non-anatomic when the score was less than 8. Other parameters analyzed were graft failure, knee stability (measured with a KT-1000 arthrometer and the pivot shift test) and functional results (Lysholm, Tegner, subjective and objective IKDC scores). The prevalence of OA was also assessed on all radiographic scales, adapting them to a standardized scale. Using this scale, 87 out of 375 patients (23.2%) with anatomic ACLR showed OA after 15.3 years on average, while 744 out of 1696 patients (43.9%) with non-anatomic ACLR showed OA after 15.9 years on average. AARSC scores were 9.2 for anatomic ACLR and 5.1 for non-anatomic ACLR. The remaining parameters were somewhat alike in the two groups. The study demonstrated that, over the long term, anatomic ACLR (defined as an AARSC score ≥ 8) was related to an inferior frequency of OA. After an ACL injury, anatomic ACLR appears to diminish the peril of OA in the long run more than non-anatomic ACLR.

Intact ACL graft versus ruptured ACL graft

In a retrospective cohort study (level of evidence III), Soderman et al assessed the long-run outcomes of ACLR using the following parameters: graft failure, knee laxity, and the presence of OA.[70] The authors' hypothesis was that an intact ACL graft would reduce the peril of OA. With a mean follow-up of 31 years, the authors analyzed 60 patients using MRI images, X-rays, KT-1000 arthrometer and the pivot shift test. Of the 60 individuals,

30 (50%) had an undamaged ACL graft and 30 (50%) had a ruptured or absent graft. Individuals with ruptured grafts had more OA in the medial tibial-femoral compartment than individuals with undamaged grafts (*P= 0.0003*). In the individuals with ruptured ACL grafts, the OA was asymmetric, with more OA in the medial tibiofemoral compartment than in the lateral tibiofemoral compartment and PF compartment. In the patients with undamaged ACL grafts, the distribution of OA between compartments was similar. The KT-1000 values for anterior knee laxity were greater in the individuals with ruptured ACL grafts than in those with undamaged grafts. In side-by-side comparisons, the KT-1000 values were greater in the individuals with ruptured ACL grafts, although the outcomes were similar for those with undamaged grafts. The pivot shift grade was greater in the group with ruptured ACL grafts. Overall, 50% of the individuals had undamaged ACL grafts and no side-to-side differences in anterior knee laxity after a mean follow-up of 31 years. Individuals with a ruptured ACL graft had more OA in the medial tibial-femoral compartment than those with undamaged ACL grafts.

Other risk factors for OA

In a phase 3 evidence-based study, Bodkin et al investigated the incidence of osteoarthritis in patients who underwent ACLR surgery and the risk factors that might be associated with the occurrence of osteoarthritis.[71] The authors analyzed a database and calculated the cumulative prevalence of knee OA in ACLR patients, stratifying the incidence by the time elapsed since the operation. To analyze the factors related to the diagnosis of OA (age, sex, body mass index [BMI], meniscus involvement, use of osteochondral grafts, and tobacco consumption), the authors calculated the odds ratios using logistic regression. They identified 10,565 ACLR patients without OA, 517 of whom were diagnosed with knee osteoarthritis at 5 years after the surgical procedure. When classified by follow-up time points, the prevalence of newly diagnosed OA was 2.3% at 6 months, 4.1% at 1 year, 6.2% at 2 years, 8.4% at 3 years, 10.4% at 4 years, and 12.3% at 5 years. The risk factors for OA were age, gender, fatness, tobacco use, and meniscal implication. In short, 5 years after the ACLR, 12% of the patients were diagnosed with OA The factors related to an augmented peril of OA at 5 years were age, gender, BMI, tobacco use, and coincidental meniscal surgery.

Curado et al assessed the incidence and risk factors of knee OA following ACLR after a minimum follow-up of 20 years.[72] The aforementioned authors hypothesized that the elements related to the appearance of knee OA were meniscal injury, physical activity level, time from injury to surgery, BMI, remaining laxity, tunnel position, and cartilaginous damage. A multicenter retrospective study (level of evidence IV) analyzed 182 patients, two-thirds of whom were women. ACLR was carried out arthroscopically in 82% of the patients. A bone-patellar tendon-bone transplant was employed in 92.8% of the patients. The individuals´ mean age at the time of surgery was 26 years. The clinical results were evaluated using the IKDC questionnaire (objective and subjective) and KOOS, and the radiographic evidence of OA was assessed using the IKDC questionnaire. The elements assessed as possible predictors of the occurrence of OA were age, gender, BMI, physical activity level, time from lesion to surgical procedure, meniscectomy, cartilaginous lesion, tunnel position, and remaining laxity. At the last follow-up, the IKDC score was A (normal) in 48% of the knees, B in 35%, and C or D in 17%. The mean subjective IKDC score was 82.7, with moderate to severe OA present in 29% of the cases. The following risk factors for OA were found: medial or lateral meniscectomy, remaining laxity, age >30 years at the time of the surgical procedure and engaging in a pivoting sport. Meniscectomy was one of the main factors making a contribution to the appearance of OA (17% of knees without meniscectomy versus 46% with meniscectomy). Lastly, the ACL re-rupture percentage was 13%. Overall, ACLR provided satisfactory knee stability. The peril of further OA depended mainly on the condition of the menisci, and remaining laxity was also related to the appearance of OA.

Possible future investigations

Quantitative MRI helps in the early detection of joint cartilage changes, enabling orthopedic surgeons to act promptly and assess the impact of their interventions over time. Thanks to the greater understanding of knee kinematics at present, the surgical technique of ACLR will be improved (to better recreate normal knee kinematics). Lastly, it remains to be seen whether injectable biological and pharmaceutical products can affect the inflammatory cascade.

Severe knee OA usually requires a TKA eventually. Given that many ACL ruptures happen in young individuals, reducing the frequency of knee OA and the eventual need for a TKA is critical. ACL tears alone increase inflammatory markers in the knee, which can have influence over the appearance of OA. The biomechanical changes that occur in knees with ACL tears can predispose individuals to secondary chondral and meniscal lesions. Given that biomechanical research and ACLR surgical techniques have greatly improved, we will be better able to restore normal knee kinematics through ACLR in the future. The keys to preserving good long-term knee function are preventing ACL tears, reducing post-breakage catabolic cytokine levels, restoring normal joint kinematics through ACLR, and preserving menisci and cartilage.

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