HHS Public Access

Author manuscript

Clin Sports Med. Author manuscript; available in PMC 2019 June 04.

Published in final edited form as:

Clin Sports Med. 2013 January ; 32(1): 1–12. doi:10.1016/j.csm.2012.08.017.

The Role of ACL Injury in the Development of Posttraumatic Knee Osteoarthritis

Nicole A. Friel, MD and **Constance R. Chu, MD***

Department of Orthopaedic Surgery, University of Pittsburgh Medical Center, University of Pittsburgh, 200 Lothrop Street, Pittsburgh, PA 15213, USA

Keywords

ACL; ACL reconstruction; Cartilage; Posttraumatic osteoarthritis

The anterior cruciate ligament (ACL) a relatively common injury in young, physically active individuals. ACL injuries are seen at high incidence in adolescents playing sports that involve pivoting, such as football, soccer, basketball, and team handball. Young women have a 35 times higher risk of ACL injury than do men when participating in these sports.[1–3] Most patients with acute ACL tears are younger than 30 at the time of their injury. As such, ACL injuries result in early onset osteoarthritis (OA) were associated with pain, functional limitations, and decreased quality of life.[4] The reported incidence of posttraumatic osteoarthritis (PTOA) following ACL injury as high as 87%.[5,6] By comparison, the prevalence of OA in all adults older than 45 years of age was 19.2%, as reported by the Framingham Osteoarthritis Study, and 27.8%, as reported by the Johnston County Osteoarthritis Project.[7] It has also been estimated that an ACL rupture ages the knee by 30 years.[1] Variations in the incidence of PTOA may be due to different methods used to evaluate patients, various surgical techniques, the time interval between surgery and reconstruction, and the duration of follow-up after ACL injury. In addition, clinical symptoms do not always correlate with imaging or physical assessments, resulting in many areas of ongoing debate in the management of ACL injuries. Management of a torn ACL ranges from nonoperative treatment to reconstructive surgery. The primary goals of ACL reconstruction are to restore knee stability, allowing the patient to resume his or her preinjury activities. ACL reconstruction has not been shown to delay later development of PTOA. Study results vary, with reports showing decreased, equal, or even increased levels of PTOA in patients who have had ACL reconstruction. As such, there is high need for improved understanding of OA development after ACL injury to inform development of strategies to reduce OA risk in this population.

BIOMECHANICS AND BASIC SCIENCE OF PTOA

The mechanism responsible for cartilage breakdown and progression to OA following ACL injury is multifactorial and not completely understood. The development of OA after ACL

*Corresponding author: chucr@upmc.edu.

injury may be the result of the initial injury to the subchondral bone and hyaline cartilage. At the time of injury, the high force of the trauma disrupts the intra-articular structures.[8] Occult osteochondral lesions, or bone bruises, as measured on magnetic resonance imaging (MRI), occur in 80%–90%[9] of patients with an acute ACL injury, most commonly on the posterolateral tibial plateau and the anterolateral femoral condyle. These lesions suggest that articular cartilage sustains a considerable mechanical impact at the time of injury.[10]

In addition to initial trauma, the lack of a functionally normal ACL leads to chronic changes in the static and dynamic loading of the knee and increased forces on the cartilage and other joint structures.[11] Therefore, subsequent intra-articular injuries occur over time, especially to the cartilage and the meniscus. These lesions play a role in the development of OA, as seen in many studies that show higher rates of OA in patients with concomitant intra-articular injuries.

ACL reconstruction, or even the historically performed ACL repair, has been postulated to prevent OA by restoring the biomechanical stability of the knee joint. Although ACL reconstruction does improve knee stability in ACL deficient knees, it does not restore *normal* knee kinematics.[12] While ACL reconstruction has not been shown to prevent PTOA, there is substantial interest in whether more anatomical reconstruction techniques will restore knee kinematics and reduce OA risk.

Despite the ability of ACL reconstruction to reduce knee instability, the incidence of posttraumatic OA remains high. ACL disruption initiates a cascade of pathogenic processes. Lohmander and colleagues[13] have shown repeatedly an increased turnover of the cartilage proteoglycan aggrecan and type II collagen within days and weeks following joint injuries. In a histologic study of cartilage biopsies at the time of ACL reconstruction, there is histologic evidence of degeneration and a persistent increase in collagenase cleavage and denaturation of type II collagen, occur within a year of ACL injury that is associated with an early transient increase in the total content of proteoglycan, similar to that seen in idiopathic OA.[14]

Any injury to the knee joint, including ACL rupture, alters in levels of synovial fluid of compounds that may contribute to joint degeneration. Multiple inflammatory cytokines, or biomarkers, such as tumor necrosis factor-alpha, interleukin-1 (IL-1β), and IL-6, are upregulated after joint injury.[15–20] Although these studies show a wide variation in the time periods in which these inflammatory cytokines remain elevated, it is consistent that cytokines are elevated immediately following injury and likely persist for a prolonged period of time. Furthermore, if ACL surgery is pursued, the joint is again traumatized, resulting in prolonged joint inflammation with a postoperative hemarthrosis. The cytokines involved in this inflammation have been associated with cartilage destruction and have been identified as inhibitors to chondrogenesis.

RISK FACTORS FOR PTOA

In an effort to reduce the incidence or progression of PTOA, the identification of risk factors associated with the development of this disabling process would be beneficial. Candidate risk factors for PTOA include the following:

- Neuromuscular factors
- Meniscus status
- Body mass index (BMI)
- Chondral damage
- Age
- Graft choice
- Time interval between injury and surgical intervention.

Nonsurgical Versus Surgical Management

ACL injury dramatically increases OA risk, the surgical objectives of ACL reconstruction are to reestablish function and to prevent instability that can result in added repetitive damage to the articular cartilage and other soft tissues.[21,22] However, no studies show that ACL reconstruction can prevent PTOA.

Before the advent of ACL reconstruction, when ACL injuries were more often treated nonoperatively, 1 study[23] showed that at 14 years after injury, one-third of ACL ruptures treated without repair or reconstruction demonstrated joint space narrowing or unequivocal OA. In this study, 86% of these patients had removal of 1 or both menisci at the time of surgery, and 75% of patients returned to the previous sport. In a retrospective cohort clinical study with longer follow-up, Nebelung and Wuschech[24] evaluated 19 Olympic athletes who sustained an ACL injury and were treated without reconstruction. All athletes returned to high-level activity, but at the 20-year follow-up, 95% of the knees showed severe symptoms of OA and instability, and more than 50% had undergone total joint replacement after 35 years.

Van der Hart and colleagues[25] concluded that bone-patellar tendon-bone ACL reconstruction does not prevent the occurrence of radiological OA after 10 years, as 45% of patients had radiographic OA per the Kellgren-Lawrence grading scale versus 3% on the contralateral knee. In a study of radiological outcome of patients who had undergone ACL reconstruction in comparison to a group of nonoperatively treated patients, at 17 to 20 years after injury, both groups showed degenerative changes on radiographs.[26] Half of the patients treated with ACL reconstruction had mild degenerative changes and 16.5% had severe OA. However, in nonoperatively treated patients there were no normal knees and 56% of the patients had severe OA. The authors concluded that reconstruction of ACL cannot prevent OA but may lead to a lower prevalence of its onset. Potter and colleagues,[10] following both nonoperative and reconstructive treatments by MRI, found an increased risk of cartilage degeneration of the medial tibial plateau and patella in nonsurgical patients compared to the surgically treated patients. Kessler and colleagues[27] also compared nonoperative versus reconstructive

treatment of arthroscopically confirmed ACL ruptures, observing that ACL reconstructed patients had significantly better knee stability but more OA. However, the authors excluded 2 important groups of patients: patients with concomitant injuries (to the meniscus, cartilage, or other ligaments) and patients who required revision operation within the study period. Nonoperative management of ACL injury results in a significantly higher rate of meniscal lesions requiring later surgery than surgically treated ACL injury. However, this study did not incorporate the degree of OA in the knees with secondary meniscal tears, which may have changed their conclusions regarding the rate of OA.

This highlights the heterogeneity of people, treatments and assessments in ACL injury. It is possible that some patients with characteristic injury patterns are better candidates for surgery than others. For example, it is unclear what secondary damage occurs when ACL injuries are treated nonoperatively. Removing the variable of meniscal injury provides a more homogeneous population of patients with isolated ACL injuries. Hoffelner and colleagues[28] found that athletes with an isolated ACL rupture had no increased risk for the development of PTOA after ACL reconstruction in the long term when compared to the uninjured contralateral knee. This offers several interpretations. It lends support to ACL reconstruction in this population, because surgery may prevent secondary meniscal and chondral injuries that advance OA. Further, there is an increased rate of reconstruction after a period of nonoperative treatment, which may be considered an argument in favor of primary ACL reconstruction. Conversely, if a patient is willing to modify activities to avoid instability primary nonoperative treatment, may be preferable. Neuman and colleagues[29] reported low rates of OA after ACL injured patients who agree to moderate their level of activity to avoid reinjury.

Daniel and colleagues[30] concluded that patients who had undergone reconstruction had a higher level of arthrosis by radiograph and bone scan evaluation. Although this study does show significant results, it is not without limitations, because the more severely injured knees (ie, concomitant injuries) were more often reconstructed. The authors state that an increased incidence of degenerative joint disease in patients with reconstructed knees can in part be explained by a higher incidence of meniscal surgery in the patients who have undergone knee reconstruction. However, a comparison of bone scan scores for patients who did not have meniscal surgery revealed a greater incidence of arthrosis in patients who had reconstructed knees.

Meniscus Status

The status of the meniscus is a critically important factor in the development of OA after injury to the ACL. Multiple studies have reported that meniscal injury, meniscus surgery, or meniscectomy at the time of ACL repair or reconstruction increases OA risk.[1,6,21,23–25,29–46]

A recent systematic review,[47] including 31 different studies, reported meniscal injury and meniscectomy as the most frequently reported risk factors. The status of the meniscus has been identified as the most important factor for developing posttraumatic OA after an ACL injury regardless of whether the patient undergoes ACL surgery or nonoperative treatment.[21] Wu and colleagues[45] compared radiographic findings of patients at 10 years postoperatively, dividing the patients into 2 different groups: those with an intact meniscus at the time of

ACL reconstruction and those who underwent concomitant meniscectomy at the time of ACL reconstruction. Two of 25 patients with intact menisci had radiographic OA, whereas 9 of 9 patients undergoing meniscectomy had radiographic OA. Thus, the authors noted that the meniscus should be repaired, not removed, whenever possible. Lohmander and colleagues[1] found a very high prevalence of radiographic knee OA, pain, and functional limitations in young women who sustained an ACL tear during soccer play 12 years earlier. The authors note that ACL-injured players who also underwent meniscus surgery had a higher prevalence (69%) of radiographic knee OA than those without such surgery (39%). Similarly, von Porat and colleagues[44] evaluated male soccer players, with a higher percentage (59%) of radiographic OA in patients who had meniscal injury compared to those with an isolated ACL injury (31%). Li and colleagues[48] found that 24 of 37 (65%) patients who underwent concurrent meniscectomy developed radiographic OA, differing from the 72 of 212 (34%) patients who did not undergo concurrent meniscectomy but developed radiographic OA. The authors further evaluated patients who had undergone prior meniscectomy, noting that 16 of 19 (84%) patients who had undergone prior meniscectomy developed evidence of radiographic OA. In perhaps the most striking example, Nakata and colleagues[6] found that degenerative joint disease changes were present in 13 of 15 (87%) meniscectomized knees, whereas those changes were seen in only 12 of 46 knees (26%) with intact or repaired meniscus.

In an interesting study,[49] a population of men and women with OA underwent MRI, in which 49 of the 265 participants were found to have loss of ACL integrity. Remarkably, ACL deficiency increased the risk for cartilage loss of the medial tibiofemoral compartment; however, following adjustment for the presence of medial meniscal tears, there was no increased risk for cartilage loss. Based on this study, it seems that increased risk for cartilage loss is mediated by concomitant meniscus pathology in those with OA.

Findings of increased OA associated with meniscus injury may be explained by decreased stability and altered contact mechanics of the knee after partial or total meniscectomy.[48] Further, it is possible that the decreased tibiofemoral joint space associated with a meniscectomy can change the relationship of the patellar to the femoral trochlea, causing patellofemoral cartilage degeneration.[38]

The injured meniscus is addressed with meniscal repair or partial meniscectomy rather than complete meniscectomy. In recent years, even though partial rather than total meniscectomies have been performed, the incidence of OA associated with ACL surgery remains high, especially in comparison to ACL surgery with no meniscal damage. Meniscus repair in the presence of ACL injury is also common, as results have shown a lower incidence of OA in ACL-reconstructed patients with repaired menisci compared to those with partial meniscectomies.[50]

Body Mass Index

BMI is well known to be associated with onset and progression of knee OA in patients without ACL rupture.[51] Not surprisingly, multiple studies have found that patient BMI is correlated with joint space narrowing or OA following injury to the ACL.[22,23,27,48]

Bowers and colleagues[52] aimed to identify demographic and anthropometric risk factors for intra-articular injuries observed during ACL reconstruction and found that height, weight, and BMI are significant risk factors for injuries to articular surfaces and menisci as observed during ACL reconstruction. Although the authors did not correlate any of their findings to the development of OA, other studies have supported that intra-articular injuries (ie, meniscus and cartilage) are risk factors for the development of OA. The authors, therefore, hypothesize that athletes could possibly reduce risk of certain intra-articular pathologies with maintenance of lower body weight and BMI and thus potentially improve long-term functional outcomes after ACL reconstruction.

Chondral Damage

Damage to the cartilage at the time of injury has been suggested as another risk factor for PTOA. Through evaluation of the articular cartilage during arthroscopy, Ichiba and Kishimoto[36] found that the "cartilage-damaged" group had an increase in OA scores compared to the "no cartilage-damage" group. In another study, when the tibiofemoral and patellofemoral joints are analyzed separately, chondral lesions were shown as risk factors for the development of OA in both joint compartments.[38] Conversely, Li and colleagues[48] found that chondrosis in the lateral compartment was not significantly associated with knee OA, whereas patellofemoral chondrosis was significantly associated with knee OA.

Multiple different theories exist regarding the relationship between chondral damage and OA. Damage to the articular cartilage at the time of trauma may lead directly to OA. Similarly, instability after ACL injury with recurrent episodes of pivot shifting may increase cartilage damage and result in the development of OA.[53] Chondral injuries also produce a biochemical cascade, with increased concentrations of chondrodestructive cytokines and decreased concentration of chondroprotective cytokines compared to the contralateral knee.[54]

The relationship between occult osteochondral lesions, or bone bruises, and articular cartilage damage is unclear. Bone bruises occur in 80%–90%[9] of patients with an acute ACL injury, most commonly on the posterolateral tibial plateau and the anterolateral femoral condyle. Potter and colleagues[10] showed that the size of the bone marrow edema pattern was associated with cartilage degeneration from baseline through the third year. However, other studies show no correlation between bone bruise and cartilage degeneration or OA. Hanypsiak and colleagues[33] concluded that the presence of a bone bruise at the time of initial injury did not significantly alter the patient-oriented outcome or predict OA.

Age

Not surprisingly, age has been identified as a risk factor for the development of PTOA.[22,27,43,55–57] In 1 study,[38] age at the time of surgery proved to be a predictor for patellofemoral OA, but not for tibiofemoral OA.

Factors including chondrocyte senescence and preexisting joint degeneration increase the possibility of developing OA. In other words, because OA is a process not only of degeneration but also of mechanical wear and remodeling, the balance between anabolic and

catabolic processes decrease with age. Age is often overlooked in ACL studies, however, because most patients who undergo ACL reconstruction are young.

Graft Choice

With improvements in surgical technique, there have been several graft choices, from allograft to autograft, and from bone-patellar tendon-bone to hamstring. Differences in opinion regarding graft choice indicate the lack of research identifying the optimal graft choice. Although most studies report outcomes of ACL reconstruction based on their preferential graft choice, a few studies have identified a superior graft choice for the prevention of PTOA.

Pinczewski and colleagues[58] found a trend toward increasing osteoarthritic changes in both the bone-patellar tendon-bone and the hamstring tendon graft cohorts between 2 and 10 years. However, the percentage of patients with normal (**International Knee Documentation Committee** grade A) radiographs decreased by 19% in the hamstring tendon group and 34% in the bone-patellar tendon-bone group. Three other studies also reported similar results,[38,48,59] in which the use of a bone-patellar tendon-bone graft was associated with an increased prevalence of OA compared to a hamstring tendon graft.

Time Interval between Injury and Surgical Intervention

Controversy exists regarding the timing of ACL reconstruction in patients who have chosen operative intervention. Because one of the goals of ACL reconstruction is to prevent secondary meniscal or chondral injuries, many argue that ACL surgery should not be delayed unnecessarily. Studies have shown that early reconstruction of the ACL reduces the development of OA when compared with late reconstruction.[37,38,43,60]

Keays and colleagues[38] concluded that a time delay between injury and surgery may be a predictor for tibiofemoral OA. Seon and colleagues[43] established that OA developed in 52% of those who underwent reconstruction more than 6 months after the initial injury. Additionally, 4 of 5 cases of advanced degenerative OA had developed in patients who had their reconstruction more than 2 years after the initial injury, suggesting that not only does a longer interval between injury and surgery increase the risk of OA but it also increases its severity. Especially in individuals intent on continuing activities that involve sidestepping or pivoting, early ACL reconstruction is advocated before episodes of giving way occur.[37] In a review of knee radiographs of 77 patients, Kullmer and colleagues[60] found that patients with acute ACL tears had a lower degree of OA on the day of surgery compared to the patients with chronic insufficiency, but the postoperative increase was identical in both groups.

WHERE DO WE GO FROM HERE?

Surgical techniques have improved, including the advent of arthroscopic surgery and the abandonment of repair for the improved reconstructive procedures. Preservation of meniscal tissues is of the utmost importance, in which total meniscectomies are nearly nonexistent, and partial meniscectomies or meniscal repair have been the treatment of choice for concomitant meniscal injury. Early rehabilitation, both preoperatively and postoperatively, has improved outcomes. Despite these changes in operative management, PTOA continues

to be present after ACL and other joint injuries. New strategies are needed to delay or prevent the onset (of premature osteoarthritis) after ACL injury.

ADDRESSING THE BIOCHEMISTRY

From a biochemical standpoint, the ultimate method of preventing PTOA after ACL injury may be prevention of the inflammation that occurs acutely after injury. The majority of research in disease-modifying OA drugs focuses on the later stages of joint degeneration. However, in the case of PTOA, in which there is a clear precipitating event, a unique opportunity arises to intervene early in the acute posttraumatic period.[61] Prevention of the cascade of destructive processes within the joint may one day play a greater role. The use of antagonists to inflammatory cytokines such as tumor necrosis factor-alpha and IL-1 may be able to promote cartilage repair and/or restore joint homeostasis in the acute injury phase.

REHABILITATION

Whether a patient is treated nonoperatively or with ACL reconstruction, rehabilitation is an integral part of the treatment program. Rehabilitation techniques have evolved substantially over the past several decades, and the use of rehabilitation programs has become widely accepted. The goals of both nonoperative and postoperative rehabilitation include return of neuromuscular control, strength, power, and lower extremity functional symmetry.[62] Depending on the patient (high-level athlete vs a more sedentary individual), the rehabilitation protocol can be modified based on the individual patient's goals, resources, and response to treatment.

PREVENTION

Prevention of ACL injury is the number 1 approach to prevent PTOA. To reduce the risk of this injury, a large number of research studies are currently being conducted to identify ways to reduce the rate of ACL injuries and to improve rehabilitation after the injury.[63] Currently, neuromuscular training is the most effective tool to reduce the incidence of ACL injuries.[64] In a nonrandomized prospective study, female athletes enrolled in a neuromuscular and proprioceptive performance program saw in subsequent years, an 88% and 75% decrease, respectively, in ACL injury compared to the age-matched and skill-matched controls. A systemic review of the effectiveness of all ACL injury prevention training programs[65] found that a significant reduction in the risk of ACL rupture in the prevention group, with the number needed to treat as low as 5 in 1 study.

SUMMARY

Anterior cruciate ligament tear accelerates joint degeneration and leads to osteoarthritis in a high proportion of patients. While successful in stabilizing ACL deficient knees, ACL reconstruction has not been shown to conclusively reduce OA risk. Altered biomechanics, age, meniscal status, cartilage and other joint tissue injury, as well as patient factors contribute to accelerated development of OA after ACL injury. The injury typically occurs in teenagers and young adults resulting in early onset disability. Post-traumatic OA after ACL injury illustrates the concept that modifiable extrinsic factors play a substantial role in OA

development.[61] As such, improved understanding of the factors leading to early onset OA after ACL injury will be important to development of new disease modifying strategies to delay or prevent development of not just PTOA but potentially also other forms of OA.

References

1. Lohmander LS, Ostenberg A, Englund M, et al. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. Arthritis Rheum. 2004; 50:3145–52. [PubMed: 15476248]
2. Griffin LY, Albohm MJ, Arendt EA, et al. Understanding and preventing noncontact anterior cruciate ligament injuries: a review of the Hunt Valley II meeting, January 2005. Am J Sports Med. 2006; 34:1512–32. [PubMed: 16905673]
3. Piasecki DP, Spindler KP, Warren TA, et al. Intraarticular injuries associated with anterior cruciate ligament tear: findings at ligament reconstruction in high school and recreational athletes. An analysis of sex-based differences. Am J Sports Med. 2003; 31:601–5. [PubMed: 12860552]
4. Lohmander LS, Englund PM, Dahl LL, et al. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. Am J Sports Med. 2007; 35:1756–69. [PubMed: 17761605]
5. Shelbourne KD, Stube KC. Anterior cruciate ligament (ACL)-deficient knee with degenerative arthrosis: treatment with an isolated autogenous patellar tendon ACL reconstruction. Knee Surg Sports Traumatol Arthrosc. 1997; 5:150–6. [PubMed: 9335026]
6. Nakata K, Shino K, Horibe S, et al. Arthroscopic anterior cruciate ligament reconstruction using fresh-frozen bone plug-free allogeneic tendons: 10-year follow-up. Arthroscopy. 2008; 24:285–91. [PubMed: 18308179]
7. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II Arthritis Rheum. 2008; 58:26–35. [PubMed: 18163497]
8. Roos H, Lindberg H, Gardsell P, et al. The prevalence of gonarthrosis and its relation to meniscectomy in former soccer players. Am J Sports Med. 1994; 22:219–22. [PubMed: 8198190]
9. Nishimori M, Deie M, Adachi N, et al. Articular cartilage injury of the posterior lateral tibial plateau associated with acute anterior cruciate ligament injury. Knee Surg Sports Traumatol Arthrosc. 2008; 16:270–4. [PubMed: 18074118]
10. Potter HG, Jain SK, Ma Y, et al. Cartilage injury after acute, isolated anterior cruciate ligament tear: immediate and longitudinal effect with clinical/MRI follow-up. Am J Sports Med. 2012; 40:276–85. [PubMed: 21952715]
11. Andriacchi TP, Mundermann A, Smith RL, et al. A framework for the in vivo pathomechanics of osteoarthritis at the knee. Ann Biomed Eng. 2004; 32:447–57. [PubMed: 15095819]
12. Papannagari R, Gill TJ, Defrate LE, et al. In vivo kinematics of the knee after anterior cruciate ligament reconstruction: a clinical and functional evaluation. Am J Sports Med. 2006; 34:2006–12. [PubMed: 16885514]
13. Lohmander LS, Ionescu M, Jugessur H, et al. Changes in joint cartilage aggrecan after knee injury and in osteoarthritis. Arthritis Rheum. 1999; 42:534–44. [PubMed: 10088777]
14. Nelson F, Billinghurst RC, Pidoux I, et al. Early post-traumatic osteoarthritis-like changes in human articular cartilage following rupture of the anterior cruciate ligament. Osteoarthritis Cartilage. 2006; 14:114–9. [PubMed: 16242972]
15. Cuellar VG, Cuellar JM, Golish SR, et al. Cytokine profiling in acute anterior cruciate ligament injury. Arthroscopy. 2010; 26:1296–301. [PubMed: 20887928]
16. Cuellar JM, Scuderi GJ, Cuellar VG, et al. Diagnostic utility of cytokine bio-markers in the evaluation of acute knee pain. J Bone Joint Surg Am. 2009; 91:2313–20. [PubMed: 19797564]
17. Cameron ML, Fu FH, Paessler HH, et al. Synovial fluid cytokine concentrations as possible prognostic indicators in the ACL-deficient knee. Knee Surg Sports Traumatol Arthrosc. 1994; 2:38–44. [PubMed: 7584175]

18. Elsaid KA, Fleming BC, Oksendahl HL, et al. Decreased lubricin concentrations and markers of joint inflammation in the synovial fluid of patients with anterior cruciate ligament injury. Arthritis Rheum. 2008; 58:1707–15. [PubMed: 18512776]
19. Irie K, Uchiyama E, Iwaso H. Intraarticular inflammatory cytokines in acute anterior cruciate ligament injured knee. Knee. 2003; 10:93–6. [PubMed: 12649034]
20. Higuchi H, Shirakura K, Kimura M, et al. Changes in biochemical parameters after anterior cruciate ligament injury. Int Orthop. 2006; 30:43–7. [PubMed: 16333657]
21. Meunier A, Odensten M, Good L. Long-term results after primary repair or non-surgical treatment of anterior cruciate ligament rupture: a randomized study with a 15-year follow-up. Scand J Med Sci Sports. 2007; 17:230–7. [PubMed: 17501866]
22. Lebel B, Hulet C, Galaud B, et al. Arthroscopic reconstruction of the anterior cruciate ligament using bone-patellar tendon-bone autograft: a minimum 10-year follow-up. Am J Sports Med. 2008; 36:1275–82. [PubMed: 18354147]
23. McDaniel WJ Jr, Dameron TB Jr. The untreated anterior cruciate ligament rupture. Clin Orthop Relat Res. 1983; (172):158–63.
24. Nebelung W, Wuschech H. Thirty-five years of follow-up of anterior cruciate ligament-deficient knees in high-level athletes. Arthroscopy. 2005; 21:696–702. [PubMed: 15944625]
25. van der Hart CP, van den Bekerom MP, Patt TW. The occurrence of osteoarthritis at a minimum of ten years after reconstruction of the anterior cruciate ligament. J Orthop Surg Res. 2008; 3:24. [PubMed: 18544170]
26. Mihelic R, Jurdana H, Jotanovic Z, et al. Long-term results of anterior cruciate ligament reconstruction: a comparison with non-operative treatment with a follow-up of 17–20 years. Int Orthop. 2011; 35:1093–7. [PubMed: 21287172]
27. Kessler MA, Behrend H, Henz S, et al. Function, osteoarthritis and activity after ACL-rupture: 11 years follow-up results of conservative versus reconstructive treatment. Knee Surg Sports Traumatol Arthrosc. 2008; 16:442–8. [PubMed: 18292988]
28. Hoffelner T, Resch H, Moroder P, et al. No increased occurrence of osteoarthritis after anterior cruciate ligament reconstruction after isolated anterior cruciate ligament injury in athletes. Arthroscopy. 2012; 28:517–25. [PubMed: 22265043]
29. Neuman P, Englund M, Kostogiannis I, et al. Prevalence of tibiofemoral osteoarthritis 15 years after nonoperative treatment of anterior cruciate ligament injury: a prospective cohort study. Am J Sports Med. 2008; 36:1717–25. [PubMed: 18483197]
30. Daniel DM, Stone ML, Dobson BE, et al. Fate of the ACL-injured patient. A prospective outcome study. Am J Sports Med. 1994; 22:632–44. [PubMed: 7810787]
31. Cohen M, Amaro JT, Ejnisman B, et al. Anterior cruciate ligament reconstruction after 10 to 15 years: association between meniscectomy and osteoarthrosis. Arthroscopy. 2007; 23:629–34. [PubMed: 17560477]
32. Fink C, Hoser C, Hackl W, et al. Long-term outcome of operative or nonoperative treatment of anterior cruciate ligament rupture–is sports activity a determining variable? Int J Sports Med. 2001; 22:304–9. [PubMed: 11414676]
33. Hanypsiak BT, Spindler KP, Rothrock CR, et al. Twelve-year follow-up on anterior cruciate ligament reconstruction: long-term outcomes of prospectively studied osseous and articular injuries. Am J Sports Med. 2008; 36:671–7. [PubMed: 18326830]
34. Hart AJ, Buscombe J, Malone A, et al. Assessment of osteoarthritis after reconstruction of the anterior cruciate ligament: a study using single-photon emission computed tomography at ten years. J Bone Joint Surg Br. 2005; 87:1483–7. [PubMed: 16260663]
35. Hertel P, Behrend H, Cierpinski T, et al. ACL reconstruction using bone-patellar tendon-bone press-fit fixation: 10-year clinical results. Knee Surg Sports Traumatol Arthrosc. 2005; 13:248–55. [PubMed: 15690197]
36. Ichiba A, Kishimoto I. Effects of articular cartilage and meniscus injuries at the time of surgery on osteoarthritic changes after anterior cruciate ligament reconstruction in patients under 40 years old. Arch Orthop Trauma Surg. 2009; 129:409–15. [PubMed: 19050905]
37. Jomha NM, Borton DC, Clingeleffer AJ, et al. Long-term osteoarthritic changes in anterior cruciate ligament reconstructed knees. Clin Orthop Relat Res. 1999; 358:188–93.

38. Keays SL, Newcombe PA, Bullock-Saxton JE, et al. Factors involved in the development of osteoarthritis after anterior cruciate ligament surgery. Am J Sports Med. 2010; 38:455–63. [PubMed: 20051501]

39. Maletius W, Messner K. Eighteen- to twenty-four-year follow-up after complete rupture of the anterior cruciate ligament. Am J Sports Med. 1999; 27:711–7. [PubMed: 10569355]

40. Pritchard JC, Drez D Jr, Moss M, et al. Long-term followup of anterior cruciate ligament reconstruction using freeze-dried fascia lata allografts. Am J Sports Med. 1995; 23:593–6. [PubMed: 8526276]

41. Reid JS, Hanks GA, Kalenak A, et al. The Ellison iliotibial-band transfer for a torn anterior cruciate ligament of the knee. Long-term follow-up. J Bone Joint Surg Am. 1992; 74:1392–402. [PubMed: 1429795]

42. Salmon LJ, Russell VJ, Refshauge K, et al. Long-term outcome of endoscopic anterior cruciate ligament reconstruction with patellar tendon autograft: minimum 13-year review. Am J Sports Med. 2006; 34:721–32. [PubMed: 16399931]

43. Seon JK, Song EK, Park SJ. Osteoarthritis after anterior cruciate ligament reconstruction using a patellar tendon autograft. Int Orthop. 2006; 30:94–8. [PubMed: 16435149]

44. von Porat A, Roos EM, Roos H. High prevalence of osteoarthritis 14 years after an anterior cruciate ligament tear in male soccer players: a study of radiographic and patient relevant outcomes. Ann Rheum Dis. 2004; 63:269–73. [PubMed: 14962961]

45. Wu WH, Hackett T, Richmond JC. Effects of meniscal and articular surface status on knee stability, function, and symptoms after anterior cruciate ligament reconstruction: a long-term prospective study. Am J Sports Med. 2002; 30:845–50. [PubMed: 12435651]

46. Yamaguchi S, Sasho T, Tsuchiya A, et al. Long term results of anterior cruciate ligament reconstruction with iliotibial tract: 6-, 13-, and 24-year longitudinal follow-up. Knee Surg Sports Traumatol Arthrosc. 2006; 14:1094–100. [PubMed: 16845548]

47. Oiestad BE, Engebretsen L, Storheim K, et al. Knee osteoarthritis after anterior cruciate ligament injury: a systematic review. Am J Sports Med. 2009; 37:1434–43. [PubMed: 19567666]

48. Li RT, Lorenz S, Xu Y, et al. Predictors of radiographic knee osteoarthritis after anterior cruciate ligament reconstruction. Am J Sports Med. 2011; 39:2595–603. [PubMed: 22021585]

49. Amin S, Guermazi A, Lavalley MP, et al. Complete anterior cruciate ligament tear and the risk for cartilage loss and progression of symptoms in men and women with knee osteoarthritis. Osteoarthritis Cartilage. 2008; 16:897–902. [PubMed: 18203629]

50. Aglietti P, Zaccherotti G, De Biase P, et al. A comparison between medial meniscus repair, partial meniscectomy, and normal meniscus in anterior cruciate ligament reconstructed knees. Clin Orthop Relat Res. 1994; 307:165–73.

51. Englund M, Lohmander LS. Risk factors for symptomatic knee osteoarthritis fifteen to twenty-two years after meniscectomy. Arthritis Rheum. 2004; 50:2811–9. [PubMed: 15457449]

52. Bowers AL, Spindler KP, McCarty EC, et al. Height, weight, and BMI predict intra-articular injuries observed during ACL reconstruction: evaluation of 456 cases from a prospective ACL database. Clin J Sport Med. 2005; 15:9–13. [PubMed: 15654185]

53. Droll KP, Marks P. Risk factors in developing osteoarthritis in the anterior cruciate deficient knee. Univ Toronto Med J. 1999; 76:70–9.

54. Marks PH, Donaldson ML. Inflammatory cytokine profiles associated with chondral damage in the anterior cruciate ligament-deficient knee. Arthroscopy. 2005; 21:1342–7. [PubMed: 16325085]

55. Asano H, Muneta T, Ikeda H, et al. Arthroscopic evaluation of the articular cartilage after anterior cruciate ligament reconstruction: a short-term prospective study of 105 patients. Arthroscopy. 2004; 20:474–81. [PubMed: 15122137]

56. Strand T, Molster A, Hordvik M, et al. Long-term follow-up after primary repair of the anterior cruciate ligament: clinical and radiological evaluation 15–23 years postoperatively. Arch Orthop Trauma Surg. 2005; 125:217–21. [PubMed: 15875231]

57. Segawa H, Omori G, Koga Y. Long-term results of non-operative treatment of anterior cruciate ligament injury. Knee. 2001; 8:5–11. [PubMed: 11248562]

58. Pinczewski LA, Lyman J, Salmon LJ, et al. 10-year comparison of anterior cruciate ligament reconstructions with hamstring tendon and patellar tendon autograft: a controlled, prospective trial. Am J Sports Med. 2007; 35:564–74. [PubMed: 17261567]

59. Jarvela T, Paakkala T, Kannus P, et al. The incidence of patellofemoral osteoarthritis and associated findings 7 years after anterior cruciate ligament reconstruction with a bone-patellar tendon-bone autograft. Am J Sports Med. 2001; 29:18–24. [PubMed: 11206250]

60. Kullmer K, Letsch R, Turowski B. Which factors influence the progression of degenerative osteoarthritis after ACL surgery? Knee Surg Sports Traumatol Arthrosc. 1994; 2:80–4. [PubMed: 7584189]

61. Chu CR, Williams AA, Coyle CH, et al. Early diagnosis to enable early treatment of pre-osteoarthritis. Arthritis Res Ther. 2012; 41:212–22.

62. Myer GD, Paterno MV, Ford KR, et al. Neuromuscular training techniques to target deficits before return to sport after anterior cruciate ligament reconstruction. J Strength Cond Res. 2008; 22:987–1014. [PubMed: 18438211]

63. Butler RJ, Minick KI, Ferber R, et al. Gait mechanics after ACL reconstruction: implications for the early onset of knee osteoarthritis. Br J Sports Med. 2009; 43:366–70. [PubMed: 19042923]

64. Hurd WJ, Chmielewski TL, Snyder-Mackler L. Perturbation-enhanced neuromuscular training alters muscle activity in female athletes. Knee Surg Sports Traumatol Arthrosc. 2006; 14:60–9. [PubMed: 15937713]

65. Sadoghi P, von Keudell A, Vavken P. Effectiveness of anterior cruciate ligament injury prevention training programs. J Bone Joint Surg Am. 2012; 94:769–76. [PubMed: 22456856]

KEY POINTS

- Acute ACL tears commonly occur in young, physically active individuals under age 30.
- ACL injury increases osteoarthritis risk resulting in early onset OA during prime work and life years between ages 30 and 50.
- Effective strategies to prevent ACL injury and to reduce OA risk after ACL tear are needed.