



Early clinical findings may predict long-term development of radiographic knee osteoarthritis in patients with anterior cruciate ligament reconstruction

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The ideal consultation for a patient with anterior cruciate ligament (ACL) injury is when he or she receives evidence-based advice and information regarding future knee function and knee health—both short and long term—for different treatment options. Several guidelines for adequate rehabilitation programs and procedures after ACL injury and reconstruction leading to good knee function in the short term have been published (1,2). Although development of knee osteoarthritis (OA) at a relatively young age is unfortunately the reality for about half of the patients with an ACL injury regardless of treatment (3), very little clinical evidence exists for long-term outcomes.

The lack of evidence for long-term outcomes exists despite that there are more than 50 cohort studies with over 10 years of follow-up of individuals with ACL injury, the majority treated with ACL reconstruction (4-7). These studies are summarized in reviews on the consequences of ACL injury. For instance, Ajuied *et al.* published a systematic review and meta-analysis of radiographic knee OA, and found a 5 times risk of radiographic knee OA after ACL tear (5). Riccardo *et al.* reported mild signs of joint degeneration summarizing 12 studies that had investigated isolated ACL tear (6).

Shelbourne and colleagues (8) followed 423 ACL reconstructed knees over a period of 20 to 33 years after ACL reconstruction with prospective data sampling. They found the prevalence of radiographic knee OA to be 28.6% on average 22.5 years after ACL reconstruction. They aimed to evaluate

the association between radiographic knee OA and the following factors at the time of discharge from postoperative physical therapy: meniscal injuries, cartilage damage, age at surgery, chronicity of injury, and reduced knee range of motion (ROM)—particularly loss of full knee extension. They hypothesized that the risk of radiographic knee OA at 20 years after surgery would be statistically significantly higher when the severity of these factors was present.

The ACL injured patient is nearly always most worried about short-term symptoms and function and return to their preinjury activity level. However, both the health care provider and the patient should plan and conduct the treatment and rehabilitation sessions with the goals of regaining and sustaining good long-term function as well as to prevent development of knee OA by focusing on factors that are modifiable. The factors Shelbourne and colleagues examined are of great clinical interest, especially the loss of full extension. ROM exercises are often emphasized in the early phases after ACL injury, and achieving full ROM should be aimed at in phase one of the rehabilitation programme along with normalization of walking pattern and reduction of effusion. According to the IKDC ROM ratings, Shelbourne and colleagues found that, at the time of discharge, 97% of the sample had normal (83.5%) or nearly normal (13.5%) knee extension. At long-term follow-up, the corresponding numbers were 78.3% (normal) and 16.3% (nearly normal). The odds of patients lacking knee extension at follow-up if they lacked it at discharge was 19.3

(95% CI, 10.59–36.65), indicating that those who do not regain full extension in the early phase will probably not regain full extension later. Furthermore, in the multivariate analysis model, the authors found that knee extension less than normal at the time of discharge (on average 6 months postsurgery) from physical therapy predicted the presence of radiographic knee OA at long-term follow-up.

Shelbourne and colleagues also found that meniscectomy was the strongest predictor for later development of radiographic knee OA. Additional meniscus injury treated with meniscectomy has shown to be the most important risk factor for development of radiographic knee OA in ACL injured patients across many studies (4,9), and the only risk factor consistently reported across substantial literature. Meniscal injury has also showed to be an important risk factor for progression rate of OA (10), and secondary prevention strategies should be emphasised (11). There seems to be a strong correlation between meniscal lesions and development of knee OA also in patients without ACL injury (12). The meniscus provides femorotibial joint stability by distributing load and shock absorption (13), and as such, the menisci have an essential role in load distribution in the knee joint. A meniscal tear treated with meniscectomy would highly influence the biomechanics of the knee joint. In combination with reduced ROM and muscle weakness, the loading condition in the joint may overload some areas and initiate the degenerative changes. However, we still do not know how the degenerative process starts. Importantly, as stated by Shelbourne and colleagues, the early phase treatment seems to be essential for long-term knee function and probably also for development of radiographic knee OA. Prevention of meniscal injuries additionally to prevention of ACL injuries should be a priority in pivoting sports with high frequency of such injuries. Prevention interventions have been shown to be effective in the short term (14), and may also prevent future degenerative knee joints.

In addition, Shelbourne and colleagues found that older age was a significant factor associated to radiographic OA. However, neither sex, lateral meniscus removal, cartilage damage, chronicity of injury, or flexion deficit were associated with later development of radiographic knee OA. From a clinical point of view, this data suggests that more functional testing and clear goal setting with a focus on regaining full ROM are most important in the early phase after ACL reconstruction. Other clinically important aspects not assessed in the study include quadriceps strengthening and achieving dynamic stability. Quadriceps strengthening

exercises and exercises for improving dynamic stability are extremely important in the early phase after ACL injury (11). Although consistent clinical evidence is lacking, studies suggest that quadriceps weakness may be a risk factor for development of knee OA (15). Quadriceps strengthening exercises are easy to do and convenient for each individual patient regardless of physical status. Adequate and frequent measurements of ROM, quadriceps strength and dynamic stability should be included in all ACL treatment algorithms regardless of whether the aim is to return to pivoting sports or to enjoy recreational hiking. The need for adequate recovery of quadriceps strength highlights the importance of consistent clinical follow-up for one year and beyond after ACLR because patients have not been shown to reach their full functional potential until 1 to 2 years post-surgery (16).

A large number of patients with ACL injury do not develop knee OA, and they seem to have better short-term knee function. We found in a cohort of 164 ACL reconstructed patients that poor self-reported knee function after 2 years predicted symptomatic knee OA 10 years later (17). Again, examination of knee function should be conducted repeatedly in the early rehabilitation phase—at least up to 12 months post-operatively, ideally maybe up to 2 years postinjury. The evaluation results should be in line with the return to sport criteria given in other papers, both to regain optimal self-reported and objective knee function, but also to decrease the risk of reinjury for those patients who return to sport (18).

Shelbourne and colleagues conducted one of very few (10) prospective studies with more than 20 years follow-up after ACLR. Of 1,428 ACL reconstructed knees eligible for inclusion in this study, 423 knees in 398 patients were successfully followed prospectively. This constitutes a follow-up rate of only 30%. The authors argue that the sample is representative because those who returned for follow-up did not deviate from those lost to follow-up in terms of age, sex, injury type, and meniscus injury. Selection bias is always a threat to the validity in cohort studies, and in this study selection may have occurred on factors such as clinical outcomes, activity levels, body mass index and genetic components leading to the radiographic changes. Nevertheless, a sample size of over 400 patients followed for more than 20 years should be recognized. While substantial loss to follow-up is expected in studies lasting over 20 years, it should still be taken into consideration when interpreting study results.

Of note, the prevalence of radiographic OA reported by Shelbourne at 20 years is lower than that of many studies

with shorter follow-up. While this could be due to selection bias as noted above, factors related to radiographic grading systems, surgical technique and surgeon commitment to patient rehabilitation and long-term outcomes may have contributed to the more positive long-term outcomes reported in this study. Herein, all patients received ACL surgery performed using a two-incision technique by the senior author. In addition, a large proportion of patients regained full extension, a rehabilitation outcome associated with improved clinical outcomes after ACL reconstruction. These factors both highlight potential areas for renewed clinical emphasis and reduce generalizability of the findings.

Another general limitation to the study by Shelbourne and colleagues and other long-term follow-up studies is the emphasis on radiographic knee OA. Early stages of OA are rarely symptomatic and the weak correlations between knee symptoms and radiological findings are well known. Patients seek health care because they have symptoms and knee pain, not due to abnormal radiographs. Thus, future research teams should also investigate factors important to development of symptomatic knee OA over the long term—as defined by an universal definition, e.g., the ACR criteria (19).

Importantly, a recent systematic review (20) reported alarmingly high prevalence of MRI features of knee OA signs in asymptomatic uninjured individuals. The authors found summary prevalence of knee OA features among asymptomatic uninjured knees to be 4–14% in adults aged <40 years with the corresponding prevalence of 19–43% in adults ≥ 40 years. These numbers indicate that degenerative findings in the knee joint are pre-existing in around 1 of 4 asymptomatic, uninjured individuals. Ultimately, we do not know who, among those with radiographic findings after ACL reconstruction, will develop symptomatic knee OA. This research question needs attention. The same dilemma is true for the back pain literature (21) with high prevalence of spine degeneration findings in asymptomatic individuals, increasing with age (22). State-of-the-art of longitudinal outcomes after ACL injury and reconstruction involve nevertheless mostly radiographic knee OA, with the exception of a few studies (10), although many of the studies include knee function outcomes (23,24). A credit to the study by Shelbourne and colleagues is that the included patients had no existing radiographic findings or other ligamentous laxity, and no known graft tear at the time of inclusion.

With decades of research, we are still not able to give evidence-based advice and information to patients regarding which treatment methods are best for preventing development of symptomatic knee OA. While new imaging

and biomarker assessment protocols now support evaluation of early intervention strategies for knee OA prevention in ACL injured patients (25,26), the importance of additional well-designed longitudinal studies examining this aspect of knee health cannot be overstated. Nevertheless, as highlighted in the results from Shelbourne and colleagues, rehabilitation programs with the aim of restoring ROM early with an emphasis on achieving full knee extension, normalized quadriceps strength and dynamic stability should be main treatment targets in these patients regardless of surgical or nonsurgical treatment. Optimizing neuromuscular training and recovery may also help prevent ACL reinjuries and meniscal injuries, and is therefore of great importance in developing protocols to assist in preventing future development of symptomatic knee OA.

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